
The Changing Governance of Genetic Intervention Technologies

An Analysis of Legal Change Patterns, Drivers, Impacts, and a Proposed Reform

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Abstract

Major breakthroughs in biotechnology are leading to the emergence of novel methods to select and alter future individuals' genomes. Genetic intervention technology is evolving from the medical practice of screening for life-threatening congenital malformations to the selection against embryos that might develop mild disabilities. Scientific research suggests that heritable genome-editing technology would enable the custom alteration and the enhancement of human biological characteristics, including appearance, athletic and intellectual abilities. These novel developments and their potential long-term impacts raise the question of how effective are the laws on genetic interventions in setting limits to rapidly evolving biotechnologies.

This thesis examines genetic intervention laws in the United Kingdom and France and shows it exhibits a pattern of continuous legal changes over the past several years to permit a broadening range of genetic interventions that were previously prohibited. This pattern is characterized by the regulatory licensing of genetic interventions that specific legal restrictions have sought to disallow, such as screening against conditions that are mild, treatable and not predominantly determined by genes. Moreover, governments are currently considering replacing their bans on inheritable human genetic modification with regulations that will allow the alteration of genes linked to conditions deemed “serious” and for “therapeutic” purposes. This proposed regulatory model would enable licensing the very same type of genomic alterations intended to be prohibited – genetic enhancements of human physiological and cognitive capabilities. This legal change pattern is *prima facie* inconsistent with the key legislative objectives and relevant international instruments, which seek to restrict these particular genetic interventions. The overarching objectives underpinning the restrictions are to prevent a pattern in which the legal boundaries would become gradually laxer, attempts to improve human heredity and the associated human rights, societal and medical impacts. Furthermore, the pattern in which the legal boundaries are becoming laxer over time stems from drawing the lines between permissible and impermissible genetic interventions using language that is vague, subjective and places few limits on the rules' scope. A law reform can address the current limit-setting challenges by employing clearer conceptual and normative distinctions and by articulating them using language that gives greater attention to clarity, reduced subjectivity, and explicitly delimits the rules' scope. The thesis offers a blueprint for such a reform, which includes suggestions for specific legislative amendments, clearer conceptual distinctions and newly developed legal tests. The proposed law reform aims to offer a new avenue to advance towards the key policy goal of preventing the misuse of genetic intervention technologies by strengthening its governance.

Dedication

This thesis is dedicated to the memory of the late Dr. Ian Kerr. Dr. Kerr was the Canada Research Chair in Ethics, Law and Technology, a world-class scholar and a true visionary in the field. I had the great honour of having Dr. Kerr as a member of my doctoral committee. He had immensely contributed to this project. Dr. Kerr was an inspirational figure, intellectually, professionally and personally.

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Chapter One - Introduction

Greater Choices in Child Genetics, Fewer Limitations

Throughout the ages, the idea of human hereditary improvement took on various shapes and forms, changing preferred methods and portions of its ideology to better fit with the changing spirit of the times. From Plato's "Republic" to Nozick's "Anarchy, State and Utopia," prominent thinkers have considered ways in which political ideologies can promote the goal of improving human heredity traits. For centuries, notable figures have advocated for selectively breeding people to eliminate disabilities, mental health problems, criminal tendencies and for creating a genetic elite class gifted with the best achievable traits and faculties.¹ From the decrees issued by ancient Greek city-states to 20th-century mandatory sterilization acts, laws have directly implemented measures to foster selective reproduction methods with the stated purpose of improving human heredity.²

After the revelation of the WWII human rights violations, the proponents of eugenics called to revamp the ideology by incorporating elements of laissez-faire capitalism. A leading figure in the movement, General Frederick Osborn, argued that for eugenics to flourish in the new era, it should no longer be associated with coercive state programs. Rather than force eugenics on a population and risk inducing fear and alienation, a far more effective approach would be to make heredity improvement something the public would naturally desire.³ Consumers need not directly adopt the ideology of eugenics. Instead, a combination

¹ For example, renowned philosopher Arthur Schopenhauer states, "If you want Utopian plans, I would say: the only solution to the problem is the despotism of the wise and noble members of a genuine aristocracy, a genuine nobility, achieved by mating the most magnanimous men with the cleverest and most gifted women. This proposal constitutes my Utopia and my Platonic Republic." See Arthur Schopenhauer, *Essays and Aphorisms* (London: Middlesex, 1970) at 154.

² Daniel J. Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity* (Berkeley: University of California Press, 1985).

³ Ruth McNally, "Eugenics Here and Now" in Peter Glasner, & Henry Rothman eds. *Genetic Imaginations: Ethical, Legal, and Social Issues in Human Genome Research* (Burlington: Ashgate, 1998) 75.

of mass media, growing consumerist tendencies, economic forces, and competitive tendencies would naturally lead prospective parents to develop a “eugenic consciousness”, which would steer them in the direction of producing children with better traits and faculties. Thus, the goal of heredity improvement of populations would be best served by harnessing consumerist inclinations in an increasingly competitive world.⁴

The Genesis of the Genetic Supermarket

As early as 1974, the prominent libertarian philosopher Robert Nozick pioneered the idea of a “genetic supermarket.” In Nozick’s futuristic vision, parents could access novel genetic technologies to freely select the most desirable traits for their children.⁵ Prospective parents would use genetic technologies not only to weed out disease, disabilities or mild imperfections, but to select any athletic, behavioural characteristics, or cognitive traits they desire for their future children to have. As it is with markets for other goods and services, the genetic supermarket is an exercise of free and autonomous consumers. Parents would benefit from the genetic supermarket, which enables them to select traits for their future children as they see fit. Future children with well-chosen traits would be in a more advantageous position. Society as a whole stands to gain from the progress that comes from having people with superior physical, intellectual and leadership capabilities. Since the genetic supermarket would produce positive outcomes with nearly no expected harms, Nozick goes on to argue that the state should not regulate the genetic supermarket.⁶

⁴ Osborn also commented that “society would more likely accept eugenic goals and practices if the word eugenic was avoided or omitted.” This excerpt from a 1968 interview with Osborn is quoted in Diane B Paul, *Controlling Human Heredity, 1865 to the Present* (Amherst New-York: Humanities Press, 1998).

⁵ Robert Nozick, *Anarchy, State and Utopia* (New York: Basic Books, 1974) at 315.

⁶ *Ibid.*

Could There Be a Free and Legitimate Market of Children's Traits?

The idea of a market in child genetics has evoked criticism regarding the extent it would truly be free from undue influence and pressure. Prospective parents might not act as idealized rational agents in the genetic supermarket, as they would be subject to subtle yet strong pressures from growing social expectations, self-interested clinicians and states' biopolitical interests in creating better citizens.⁷ Prospective parents who object to or those who had 'initially objected' to genetic enhancement might nonetheless feel compelled to do so out of fear that their unenhanced children would lag behind when compared with their genetically enhanced peers.⁸ A "genetic arms race" might emerge, driving prospective parents to a new form of competition to ensure their children are biologically better endowed than their peers.⁹ Once a competitive market becomes well established and normalized, the state, which has a vested interest in a more productive citizenry, could intervene and take certain actions to organize its administration.¹⁰

Academics further critiqued the very notion of a market in children's physical and mental traits. In a genetic supermarket, the parents are not ordinary consumers, and the children's traits are not ordinary goods.¹¹ Such a market would objectify and commodify children.¹² The commodification of children and the custom selection of their traits can distort familial dynamics and relations. In particular, the commodifying

⁷ Nikolas Rose, *the Politics of Life Itself: Biomedicine, Power, and Subjectivity in the Twenty-First Century* (Princeton NJ: Princeton University Press, 2009) 62-65.

⁸ Lori P Knowles & Gregory E Kaebnick, *Reprogenetics: Law, Policy, and Ethical Issues* (Baltimore, MD: Johns Hopkins University Press, 2007) at 97.

⁹ United States, Congress House Committee on Foreign Affairs Subcommittee on Terrorism Nonproliferation, *Genetics and Other Human Modification Technologies: Sensible International Regulation or a New Kind of Arms Race? Hearing Before the Subcommittee on Terrorism, Nonproliferation, and Trade of the Committee on Foreign Affairs, House of Representatives, One Hundred Tenth Congress, Second Session, June 19, 2008* (Washington DC: U.S. Government Printing Office, 2008) at 31.

¹⁰ See Suzanne Elizabeth Evans, *Parental Eugenics: Congenitally Anomalous Newborns and the Continuing Debate over Selective Non-treatment and Neonatal Euthanasia in the United States, 1915-2008* (Berkeley: University of California, Berkeley, 2008). See also Council for Responsible Genetics, "Human Germline Manipulation Position Paper" (2005) CRG Cambridge, MA. See also Daniel Callahan et al., "Biomedical Ethics and the Shadow of Nazism" (1976) 6:4 Hastings Ctr Rep 11.

¹¹ The President's Council on Bioethics, *Beyond Therapy: Biotechnology and the Pursuit of Perfection* (Washington DC: The President's Council on Bioethics, 2003) 64-67.

¹² Margaret J Radin & Madhavi Sunder, "The Object and Subject of Commodification" in Martha M. Ertman, Joan C. Williams, eds, *Rethinking Commodification: Cases and Readings in Law and Culture* (New York: New York University Press, 2005) at 11.

process of child trait selection shifts values and can be a precursor to thinking about children instrumentally:¹³ The genetically improved child could become an instrument not only to fulfill his or her parents' wishes but those of society and the state.¹⁴ As a part of the trait pre-selection process, and contrary to libertarian ideals, the children—those most affected—would be systematically denied the ability to provide or deny assent.¹⁵

As early as the 1970s, academics began raising concerns that future reproductive genetic technologies could eventually evolve from methods to prevent disease to means of heredity improvement.¹⁶ Likewise, Neuhaus has argued that left unchecked, genetic intervention in the service of disease prevention would gradually evolve into a full-fledged genetic supermarket, leading to the selection of favourable traits and the deselection of undesirable traits associated with marginalized and vulnerable populations.¹⁷ This slippery slope would lead to the reinvigoration of certain eugenic goals: endowing a group of people with enhanced physical and intellectual abilities in the pursuit of a heredity advantageous position.¹⁸

The Literature on Genetic Intervention Technologies Has Drawn Unclear, Ambiguous Lines

Over the past five decades, the topic of genetic intervention's ethics has drawn a substantial amount of attention. Despite this significant interest in the ethics of these novel technologies, the literature has not produced a set of clear ethical guidelines about its appropriate limits. Moreover, the literature often discussed abstract, highly theoretical, and non-operational (macro-level) ethical concepts, such as dignity, autonomy or

¹³ Leon R Kass, "Triumph or Tragedy? The Moral Meaning of Genetic Technology" (2000) 45:1 Am. J. Jurisat 10.

¹⁴ Hans Jonas, *Technology, Medicine and Ethics* (Frankfurt: Suhrkamp, 1985) at 165.

¹⁵ Jacques Testart, "La Eugenesia Médica : Una Cuestión De Actualidad" (1998) 8 Revista Derecho Y Genoma Humano, 22.

¹⁶ The slippery slope to eugenics is an open question in the literature for over five decades. For some of the earlier examples of the argument see, Rollin D. Hotchkiss, "Portents for a Genetic Engineering" (1965) 56:5 J Heredity, 19; Amitai Etzioni, "Sex Control, Science, and Society" (1968) 161:3846 Science 1108-1110. See also Charles Frankel, "The Specter of Eugenics" (1974) 57:3 Commentary 25.

¹⁷ Richard John Neuhaus, "The Return of Eugenics" (1988) 85:4 Commentary 24-26.

¹⁸ French W Anderson, "Human Gene Therapy: Why Draw a Line?" (1989) 14:6 J Med & Phil 681.

the assessment of a particular condition (micro-level) such as genetic screening against breast cancer,¹⁹ intersex conditions²⁰ or Down syndrome.²¹ The literature lacks an intermediate-level perspective between broad theory and particular conditions: that of generalized rules, which would be crucial for setting clear and durable boundaries.

The closest attempt to draw lines that are generally agreed upon still produced opaque outcomes. Commentators often agree that the use of genetic diagnosis to prevent disease is permissible but that the selection of non-medical traits such as eye colour, skin colour and intelligence is ethically problematic.²² However, the line between medical and social uses of genetic intervention is blurry at best.²³ In the absence of clear ethical limits (or an emergent normative consensus), the frontiers of these transformative technologies have become even more fluid and transitory.

Have Laws Set Robust Safeguards?

Several countries attempted to address the concerns relating to the slippery slope to eugenics by enacting legislation to prevent the potential misuse of genetic intervention technologies. The parliamentary debates in many Western European countries began in the early 1980s, a time when the memory of early twentieth-century eugenic programs was relatively fresh and genetic intervention technologies were still purely experimental. Yet, Western European nations such as the United Kingdom (UK) and France anticipated that genetic intervention technologies could eventually be used to revive eugenic ideals by

¹⁹ Usha Menon et al., “Views of BRCA Gene Mutation Carriers on Preimplantation Genetic Diagnosis as a Reproductive Option for Hereditary Breast and Ovarian Cancer” (2007) 22:6 Hum Repro 1573.

²⁰ Robert Sparrow, “Gender Eugenics? The Ethics of PGD for Intersex Conditions” (2013) 13:10 Am J Bioethics 29.

²¹ Stephen Wilkinson, “Prenatal Screening, Reproductive Choice, and Public Health” (2015) 29:1 Bioethics 26-35.

²² Ruth Chadwick et al., “Genetic Screening and Ethics: European Perspectives” (1998) 23:3 J Med & Phil 255.

²³ Guido Pennings, “Personal Desires of Patients and Social Obligations of Geneticists: Applying Preimplantation Genetic Diagnosis for Non-Medical Sex Selection” (2002) 22:12 Prenatal Diagnosis 1124.

imposing on future generations societal notions of which human characteristics are “desirable” and which are not.²⁴

In the 1990s, regulators in the UK and France officially begun regulating genetic intervention technologies. Both countries originally allowed genetic diagnoses for near-certain risks of developing early-onset, serious, non-treatable conditions. Moreover, the UK and French acts banned inheritable human genetic modification.²⁵ For several years, the technological capabilities and the legal boundaries were aligned.

However, since the inception of the regulation in the 1990s, the field of reproductive biotechnology has rapidly advanced. Genetic diagnosis rapidly evolved from that of preventing fatal, early-onset, rare congenital disorders into that of selecting against embryos with other “undesirable” traits such as nonfatal, arguably mild disabilities such as dwarfism and “cross-eyes”. On the horizon, genomic discoveries are opening the door to commercial applications in the field of non-medical trait selection. Scientists have isolated genes that are linked to fair skin,²⁶ eye colour,²⁷ height,²⁸ enhanced memory,²⁹ and increased IQ scores.³⁰

²⁴United Kingdom, Department of Health and Social Security, Report of the Committee of Inquiry into Human Fertilisation and Embryology (“The Warnock Report”), July 1984, Cmnd 9314, at 4; See also CCNE, “Opinion No.3 on Ethical Problems Arising Out of Artificial Reproductive Techniques” (Paris: CCNE, 1984) online: <http://www.ccne-ethique.fr/sites/default/files/publications/avis003en.pdf>

²⁵ Schedule 2, Human Fertilisation and Embryology Act 1990. HMSO, London. See also Article 16-4 France, Code Civil (1804) re the Bioethics Law (last amended - 2015).

²⁶ Patrick Sulem et al, “Genetic Determinants of Hair, Eye and Skin Pigmentation in Europeans” (2007) 39:12 Nature Genetics 1443; Pirro G Hysi et al., “Genome-wide Association Meta-Analysis of Individuals of European Ancestry Identifies New Loci Explaining a Substantial Fraction of Hair Color Variation and Heritability” (2018) 50:5 Nature Genetics 1.

²⁷ Richard A Sturm et al, “A Single SNP in an Evolutionary Conserved Region Within Intron 86 of the HERC2 Gene Determines Human Blue-brown Eye Color” (2008) 82:2 Am J Hum Genetics 424.

²⁸ Hana Lango Allen et al., “Hundreds of Variants Clustered in Genomic Loci and Biological Pathways Affect Human Height” (2010) 467:7317 Nature 832.

²⁹Annette Milnik et al., “Association of KIBRA with Episodic and Working Memory: A Meta-Analysis” (2012) 159:8 Am J Med Genetics 958.

³⁰Aysu Okbay et al, “Genome-Wide Association Study Identifies 74 Loci Associated with Educational Attainment” (2016) 533:7604 Nature 539. See also Suzanne Snieder et al., “Genome-wide Association Meta-analysis of 78,308 Individuals Identifies New Loci and Genes Influencing Human Intelligence” (2017) 49:7 Nature Genetics 1107. And see Jeanne E. Savage et al. “Genome-Wide Association Meta-Analysis in 269,867 Individuals Identifies New Genetic and Functional Links to Intelligence” (2018) 50:7 Nature Genetics 912-919.

Moreover, breakthroughs in inheritable genetic modification suggest these technologies can produce highly transformative results. Experiments on animal models suggest that the alteration of certain genes can significantly increase muscle mass,³¹ cognitive performance³² and athletic prowess.³³

The materialization of many technological prerequisites for a genetic supermarket raises a pressing question: How robust are the legal boundaries? When the Human Fertilisation and Embryology Authority (HFEA), the UK regulatory agency, discussed licensing a previously prohibited form of inheritable genetic modification, it rejected claims that the approval of this formerly banned technology is a slide down a slippery slope.³⁴ While evaluating the French law, François Fillon, the Prime Minister at the time, asked the Conseil d'État whether recent developments in genetic technologies constitute a slide down the slope to eugenics. The Conseil d'État responded in the negative, saying that the legal boundaries were robust.³⁵

On the face of things, these allegedly robust legal boundaries should provide a definitive solution to the slippery slope problem. The legal boundaries have supposedly set firm lines between permissible and impermissible uses. However, have such firm boundaries really been established? Have the laws prevented the application of genetic interventions to an excessively broadening range of physical and mental conditions? Or are the legal boundaries themselves, which were supposed to prevent a slippery slope to an increasingly less regulated market, are becoming laxer?

³¹ Antonio Musaro et al., IGF-1 Induces Skeletal Myocyte Hypertrophy through Calcineurin in Association with GATA-2 and NF-ATc1 (1999) 400 Nature 581.

³² James A Bibb et al., "Cognition Enhancement Strategies" (2010) 30:45 J Neurosci 14987. See also Dena B. Dubal et al. "Life Extension Factor Klotho Enhances Cognition" (2014) 7:4 Cell Reports 1065-1076.

³³ Parvin Hakimi et al., "Overexpression of the Cytosolic Form of Phosphoenolpyruvate Carboxykinase (GTP) In Skeletal Muscle Repatterns Energy Metabolism in The Mouse" (2007) J Bio Chem 32844.

³⁴ HFEA, "Mitochondria Replacement Consultation: Advice to Government" (HFEA: London, 2013).

³⁵ France, Conseil D'État, "La Révision des Lois de Bioéthique Étude Adoptée par L'assemblée Générale Plénière le 9 Avril 2009" Conseil D'État online : <http://www.ladocumentationfrancaise.fr/var/storage/rapports-publics/094000288.pdf> 9.

Thesis

This thesis shows that genetic intervention laws in the United Kingdom and France exhibit a pattern of continuous legal changes over the past several years to permit a broadening range of genetic interventions that were previously prohibited. This pattern is characterized by the regulatory licensing of genetic interventions that specific legal restrictions have sought to disallow, such as screening against conditions that are mild, treatable and not predominantly determined by genes. Moreover, governments are currently considering replacing their bans on inheritable human genetic modification with regulations that will allow the alteration of genes linked to conditions deemed “serious” and for “therapeutic” purposes. This proposed regulatory model would enable licensing the very same type of genomic alterations intended to be prohibited – genetic enhancements of human physiological and cognitive capabilities.

This legal change pattern is *prima facie* inconsistent with the key legislative objectives and relevant international instruments, which seek to restrict these particular genetic interventions. The overarching objectives underpinning the restrictions are to prevent a pattern in which the legal boundaries would become gradually laxer, attempts to improve human heredity and the associated human rights, societal and medical impacts. Furthermore, the pattern in which the legal boundaries are becoming laxer over time stems from drawing the lines between permissible and impermissible genetic interventions using language that is vague, subjective and places few limits on the rules’ scope. A law reform can address the current limit-setting challenges by employing clearer conceptual and normative distinctions and by articulating them using language that gives greater attention to clarity, reduced subjectivity and explicitly delimits the rules’ scope.

The Issues and Potential Ramifications of Genetic Intervention Laws’ Shortcomings in Setting Limits

The thesis’s findings of a pattern of overextensive legal change call for a critical re-evaluation of whether genetic intervention laws achieved their intended goals. By examining the legislative and regulatory history, this thesis shows that the prevention of a slippery slope to eugenics was one of the key goals

underlying genetic intervention laws. From the beginning of the early 1980s, the British and French governments recommended prohibiting genetic modification and strictly regulating genetic diagnosis. Government reports and debates repeatedly highlighted the key risk of genetic intervention technologies evolving over time from methods to prevent lethal congenital malformations to those used for selecting physical, cosmetic and behavioural traits parents deemed desirable.³⁶ Without proper boundaries, prospective parents would increasingly seek to exploit the real and perceived benefits of genetic interventions, resulting in a gradual emergence of heredity improvement practices. Furthermore, the prevention of the slippery slope has been continuously mentioned as a key legislative objective of the 2008 HFE Act and the 2011 Bioethics Law³⁷ as well as in more recent parliamentary and governmental reports.³⁸ Yet, the legal change analysis shows a pattern that is gradually bringing about similar outcomes to those sought to be prevented by committees, lawmakers, and ethical commissions.

³⁶ See Mary Warnock, Committee of Inquiry into HFE, “Report of the Committee of Inquiry into Human Fertilisation and Embryology” Department of Health and Social Security (UK) (London: HMSO, 1984), at para 1.2; Department of Health and Social Security, Human Fertilisation and Embryology: A Framework for Legislation (cmd 259) (London: HMSO, 1987) [Hereafter: The White Paper] at S 6; CCNE, “Opinion No. 8 on Research and Use of In-Vitro Human Embryos for Scientific and Medical Purposes”. - December 15, 1986; J.-F. Mattei, “Rapport fait au nom de la Commission Spéciale, sur les Projets de Loi n° 957 et 962” Publications de l’Assemblée Nationale, 30 mars 1994, n° 1057, 140-147.

³⁷ For instance, official government reports on the 2008 revision of the HFE Act and the 2011 revision of the Bioethics Law explicitly reiterated the prevention of a slippery slope as a key legislative goal. See for instance, Great Britain Parliament, House of Commons, *Parliamentary Debates (Hansard): House of Commons Official Report* (London: H.M. Stationery Office, 2007) at 39, 1277; Assemblée Nationale Constitution Du 4 Octobre 1958 Treizième Législature Enregistré À La Présidence De L’assemblée Nationale Le 20 Janvier 2010. Rapport D’information Fait Au Nom De La Mission D’information Sur La Révision Des Lois De Bioéthique Président M. Alain Claeys, Rapporteur M. Jean Leonetti, Députés, at 217-220 online : http://www.assemblee-nationale.fr/13/rap-info/i2235-t1.asp#P2055_549938

³⁸ See for instance, House of Commons Science and Technology Committee “Genomics and Genome-Editing : Future Lines of Inquiry Sixteenth Report of Session 2016–17 Report, together with formal minutes relating to the report (London : HMSO, 2017) at 7 ; Conseil d’État, “Étude du Conseil d’État à la demande du Premier ministre, Ass. Gén., Révision de la loi de Bioéthique : Quelles options pour Demain ? ”, (28 juin 2018) at 143-146. See also a recent commentary by the former French Minister of Health who led the development of the Bioethics law about its 2020 revision. Jean-François Mattei, “La loi de Bioéthique : Ses Sources, Ses Évolutions, Son Avenir” (2019) 67 :1 Laennec 6-26.

Jean-François Mattei, a professor of pediatrics and genetics, is frequently referred to as the “father of the Bioethics law” due to his extensive involvement in the development of the Bioethics law (see Vincent *infra* note 926). Mattei explains that the Bioethics law’s main objective of preventing neo-eugenics is more relevant today than ever before due to recent advances in gene editing technologies, genomics and artificial intelligence assisted bioinformatics. In the context of prenatal genetic interventions, novel biotechnologies are more capable than ever before in producing the kinds of neo-eugenic misuse the act seeks to prevent.

The Risk of Future State Involvement in Market-Driven, Neo-Eugenic Practices

With a growing number of child genetic traits offered on the market, the state is freer to incentivize interventions that supposedly align with public interests. Nikolas Rose expands on Foucault's bio-governance thesis,³⁹ arguing that states have a vested interest in reproductive techniques that would make its future citizens healthier, more productive and law-abiding.⁴⁰ Eminent political philosophers warn that the potential involvement of the state in market-driven, neo-eugenic practices would constitute a problematic form of social control as the state would promote the birth of future citizens with physical and mental traits that seemingly benefit a statist conception of the "greater good".⁴¹

The growing genetic intervention market enables the state to intervene on it by incentivizing and nudging prospective parents towards genetic choices that seemingly serve goals such as improving public health and the productivity of future citizens. As the legal change broadens the range of genetic traits offered on the market, so is the state freer to incentivize interventions that supposedly align with public interests.⁴² Overextensive legal change gradually erodes the very safeguards that could have prevented the state from intervening on a broadening range of physical, mental and cosmetic genetic traits offered in the market.

³⁹ Michel Foucault's biopower thesis asserts that we live in an age in which states have a growing interest in employing a vast number of techniques to achieve "the subjugations of bodies and the control of population. National politics takes interest in the regulation of various bodily functions a features of its citizenry: including the size and the quality of the population, reproduction and human sexuality, health and disease, birth and death." See Michel Foucault, *Naissance de la Biopolitique. Cours au Collège de France* (Paris : Gallimard, Seuil Hautes Etudes, 1978) at 234-235.

⁴⁰ See Nikolas Rose *supra* note 7.

⁴¹ Bertrand Russell, "ICARUS or the Future of Science" (New York: E.P. Dutton & Company, 1924); Jürgen Habermas, *The Future of Human Nature* (Oxford: Wiley, 2014); Francis Fukuyama, *Consequences of the Biotechnology Revolution* (London: Profile Books, 2017).

⁴² United Kingdom, Government Office for Science, Foresight Mental Capital and Wellbeing Project (London: The Government Office for Science, 2008) 58; Barbara J Shakian et al., Academy of Medical Science; British Academy; Royal Academy of Engineering, *Human Enhancement and the Future of Work* (London: The Royal Society, 2012).

Legal Change's Growing Risk of Inconsistency with Ethical and Human Rights Norms

The legal change pattern potentially brings the regulatory system closer to *prima facie* inconsistency with its own underlying ethical and human rights principles. While this thesis does not assess whether the legal change pattern is in contravention with the ethical and human rights norms underlying the relevant laws,⁴³ it explains that such risks could intensify if this pattern continues. In particular, the potential regulatory trajectory to licensing contentious interventions such as certain human genetic enhancements has a growing potential of being at odds with international human rights law instruments such as the Oviedo Convention and the UNESCO Universal Declaration of Human Rights and the Genome. These international instruments, as well as British and French legal norms, regard such genetic interventions as potentially derogating from liberty, human dignity and freedom from discrimination. Furthermore, human genetic enhancement poses novel risks to health,⁴⁴ society, and, as some eminent life scientists⁴⁵ and jurists assert — to the future of the human species.⁴⁶ The risk of inconsistency with ethical and human rights norms could intensify if legal change continues to trend in the direction of trait selection that has little or nothing to do with medical harms and more to do with children's mental or physical genetic enhancement.

⁴³ A detailed human rights evaluation of the legal change is outside of the scope of this thesis as the topic requires an extensive unpacking of normative arguments. There is already an extensive body of literature dedicated to examining the human rights and ethical implications of genetic intervention technologies. In this thesis, I will argue that the human rights and ethical risks already identified by the legal system are likely to intensify as the legal changes weaken the safeguards put in place and the system's overall ability to set effective legal limits.

⁴⁴ A key rationale behind the legally restrictive approach to human genetic modification is not only direct clinical risks (such as cancers resulting from off-target mutations) but genetic modification unpredictable long-term outcomes). See the discussion in chapter 7.

⁴⁵ A number of geneticists, Noble Laureate James Watson, Lee Silver, Gregory Stock, and Leroy Hood all agree that human genetic modification ultimately means greater control over the course of the future evolution of the human species. See John Campbell et al, "A Panel Discussion" in Gregory Stock & John Campbell eds. *Engineering the Human Germline: An Exploration of the Science and Ethics of Altering the Genes We Pass to our Children* (Oxford: Oxford University Press, 2000) 83-89.

⁴⁶ For a discussion of the medical, human rights, ethical, societal risks arising from human genetic enhancement and transcending the biological limits of the human species, see chapters 2, 7 and 8.

The Illusory Narrative of Robust Legal Boundaries and Its Implications on Public Discourse and the Democratic Governance of Genetic Interventions

A prevalent narrative amongst regulators, academics and journalists could create an incorrect impression and a belief that the legal boundaries are robust when evidence shows otherwise. Chapter 8 explains that this narrative has become a dominant narrative⁴⁷ amongst regulators, decision-makers, and academics. This is despite lacking any concrete support that the regulatory regimes are in fact robust, or that they have prevented the slippery slope to eugenics. French and British regulators, which initially warned of the slippery slope, have turned in recent years to argue that they have effectively prevented the slippery slope to eugenics,⁴⁸ a rather bold claim. British regulators have also attempted to gain support for legalizing inheritable genetic modification by claiming there is absolutely no risk that the regulations would allow for genetic enhancement.⁴⁹ Academics have made similar arguments, rejecting claims that there is a slippery slope at present, and trying to argue that plans to make the legal boundaries laxer will not result in a slippery slope in the future.⁵⁰ Furthermore, while media coverage reflects both negative and positive biases towards genetic

⁴⁷ For more about the study about legal narratives, their use in telling incredible stories about the legal system, and their role in reshaping adjudicative discourse, See Peter Brooks, “Narrativity of the Law” (2002) 14:1 L & Lit 1.

⁴⁸ See for instance CCNE, “Opinion n° 105 Questions for the Estates General on Bioethics” (2008) P 4-5; CCNE, Opinion No. 107, Opinion on Ethical Issues in Connection with Antenatal Diagnosis: Prenatal diagnosis (PND) and Preimplantation Genetic Diagnosis (PGD) Paris: 2009, at 19 online: http://www.ccne.ethique.fr/sites/default/files/publications/avis_107_eng.pdf; HFEA, Authority Decision on PGD Policy - Statement on use of Preimplantation Genetic Diagnosis (PGD) for Inherited Cancer Susceptibility, 10 May 2006 (London: HFEA, 2006).

⁴⁹ National Academy of Sciences and National Academies of Sciences, Engineering, and Medicine, Committee on Human Gene Editing Human Gene Editing (Washington, DC: National Academies Press, 2017). See also United Kingdom, House of Commons, Science and Technology Committee: Oral Evidence: Genomics and Genome editing, HC 854, 29 March 2017 online <http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/genomics-and-genomeediting/oral/49725.html>; Joyce Harper & Helen O’Neil, “Scientists Edit Human Embryos to Safely Remove Disease for The First Time – Here’s how they did it” *The Conversation* (August 2, 2017), online: <http://theconversation.com/scientists-edit-human-embryos-to-safely-remove-disease-for-the-first-time-heres-how-they-did-it-81925>.

⁵⁰ See Annelien L Bredenoord et al., “PGD to Reduce Reproductive Risk: The Case of Mitochondrial DNA Disorders” (2008) 23:11 Human Reproduction 2399; Pierre Gosset, “Diagnostic Préimplantatoire: des Évolutions à Prévoir?” (2012) 40 :11 Gynécologie Obstétrique & Fertilité 675 ; Israël Nisand, “Le Diagnostic Préimplantatoire (DPI) : entre Fantasma et Imprécation !” (2007) 35:12 Gynécologie Obstétrique & Fertilité 1271; Rosario Isasi, Erika Kleiderman & Bartha Maria Knoppers, “Editing Policy to Fit the Genome?” (2016) 351 : 6271 Science 337.

interventions, it nearly exclusively promotes the narrative that the regulation has created a robust control system.⁵¹

The incorrect belief that the legal boundaries are robust could hinder a reform to rectify this growing problem. A key problem in the democratic governance of genetic intervention technologies is that the public, which is mostly concerned about the slippery slope to eugenics,⁵² lacks the necessary awareness about the critical shortcomings in setting legal limits. Such awareness is needed to have an informed democratic discourse and generate sufficient political pressure on governments to reform the law to address its critical shortcomings and set effective legal limits. However, the public and decision-makers are exposed to the illusory narrative in the media, academia and in policy circles, which stresses that the regulatory system is robust and has successfully prevented the slippery slope to eugenics. This unfounded belief that the regulation is robust could hinder a law reform to rectify the growing problem of overextensive legal change. Without reform, the combination of overly malleable regulations and rapidly advancing technologies threaten to exceed the pace of democratic debate⁵³ while increasingly setting the course for how these powerful biotechnologies continue to evolve.

⁵¹ See for instance, Paul Benkimoun & Cécile Prieur, "Par De L'assistance Médicale à La Procréation aux Tests Génétiques: Les Questions en Débat", *Le Monde* (31.05.2012), online:https://www.lemonde.fr/societe/article/2008/11/26/de-l-assistance-medicale-a-la-procreation-aux-tests-genetiques-les-questions-en-debat_1123311_3224.html; "Des Moyens Pour Le Diagnostic Pré-Implantatoire", *Libération* (1 July 2009), online: http://www.liberation.fr/societe/2009/07/01/des-moyens-pour-le-diagnostic-pre-implantatoire_567916. James Gallagher, "UK Approves Three-Person Babies", *BBC News* (24 February 2015), online: <http://www.bbc.com/news/health-31594856>.

⁵² *Infra* notes 1138-1140.

Certain academic commentators commonly portray the public's negative response to novel genetic interventions as based on an inherent fear of the unknown and of new technologies. In contrast to these portrayals, qualitative opinion studies reveal members of the public do reflect, reason, and grapple with the ethical dilemmas and challenges and reproductive genetics. Participants can often articulate specific concerns about genetic intervention technologies' ethical and the socio-economic implications typically mentioned in the academic literature. See the discussion in chapter 8.

⁵³ Elie Azria & Gilles Grangé, "Diagnostic Préimplantatoire : Considérations D'ordre Éthique" (2007) 35 :6 *Gynécologie Obstétrique & Fertilité* 506.

Challenges with Slippery Slope Arguments

On a normative level, slippery slope arguments face a set of hurdles as they encounter disagreements whether new developments are ethically undesirable and constitute a slide down a slope.⁵⁴ A growing number of bioethicists reject claims that novel applications of genetic interventions are normatively undesirable and instead argue that such applications are a step in the right direction.⁵⁵ Viewing the problem from a different perspective, philosopher Jürgen Habermas warns that a slippery slope is likely not to be recognized as such because of the increasing normalization of new biotechnologies. The gradual and incremental progress of biotechnology conceals the true revolution these novel techniques bring. A series of precedents legitimizes further technological progress and supports its onward momentum. The march of technological progress in small, gradual steps diffuses public resistance to applications previously considered unacceptable and acts to normalize a growing range of genetic interventions.⁵⁶

The question of whether we are sliding down a slippery slope to eugenics is considerably challenging to answer definitively. Given how the ethics literature defines the problem, researchers face difficulties in factually demonstrating a slide down the slippery slope. Critics argue that proponents of the slippery slope argument would find it hard to decisively demonstrate that the slope leads to eugenic outcomes because the notion of eugenics itself is vague and subject to different interpretations.⁵⁷ Without further defining what such eugenic outcomes would entail, proponents of the slippery slope would not be able to decisively

⁵⁴ Wibren Van der Burg, "The Slippery Slope Argument" (1991) 102:1 *Ethics* 64-67.

⁵⁵ See John A. Robertson et al, "Conception to Obtain Hematopoietic Stem Cells" Helga Kuhse et al. *Bioethics: An Anthology* (Sussex, UK: Wiley, 2015) 149. See also Stephen Wilkinson, "How Worried Should We Be About the 'Slippery Slope to Designer Babies?'" 714 *Bionews* (November 07, 2013) online: https://www.bionews.org.uk/page_94221; and see Elizabeth Fenton & John D Arras, "Wrong Again—Rejoinder to Annas" (2010) 19:1 *Cambridge Q Healthcare Ethics* 142-143.

⁵⁶ Jürgen Habermas, *The Future of Human Nature* (Cambridge, UK: Polity Press, 2003) at 19.

⁵⁷ See David Enoch, "Once you Start Using Slippery Slope Arguments, You're on A Very Slippery Slope" (2001) 21:4 *Oxford J Leg S* 643-645. See also Wibren van der Burg, "Slippery Slope Arguments" (2009), *Social Science Research Network*, online: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1445308.

demonstrate that such outcomes have in fact come to exist. Moreover, slippery slope arguments have been notoriously difficult to study and measure because little consensus exists regarding which methodology to follow, which system to study, how to establish a pattern of change, and which changes can qualify as a slippery slope.⁵⁸ Critics often point out that some slippery slope arguments are logically fallacious because they do not explain the causes of the slippery slope phenomenon.⁵⁹ Not surprisingly, academics have repeatedly dismissed arguments about a slippery slope to eugenics because of the lack of factual proof that a slide down the slippery slope has in fact occurred.⁶⁰

A key problem with arguments about whether the slippery slope has occurred is that the literature has not produced systemic and concrete evidence to either prove or to disprove the slippery slope. Academics have repeatedly tried to critique slippery slope arguments by suggesting there is no factual proof to demonstrate claims⁶¹ that the slippery slope has occurred.⁶² However, what is the proof to the contrary, that the slippery slope to eugenics did not occur or that regulators were successful in preventing the notorious slippery slope? After all, for a central issue with long-term impacts on individuals and society, policymakers and citizens alike may want certain factual guarantees that there is no slippery slope to eugenics and that

⁵⁸ Trudy Govier, "What's wrong with Slippery Slope Arguments?" (1982) 12:2 Can J Phil 304-305.

However, note that there are various versions of the slippery slope argument and some are sounder than others. For more about the different versions of the slippery slope, see Eugene Volokh, "The Mechanisms of the Slippery Slope" (2003) 116:4 Harvard L Rev, 1026-1137. See also Volokh's discussion about the slippery slope argument's heuristic function.

⁵⁹ David Lamb, *Down the Slippery Slope: Arguing in Applied Ethics* (Oxford: Routledge, 2003) at 61.

⁶⁰ See for example: Han Somsen, 'Regulating Technologies: Legal Futures, Regulatory Frames and Technological Fixes'), in Roger Brownsword & Karen Yeung, *Regulating Technologies: Legal Futures, Regulatory Frames and Technological Fixes* (Bloomsbury Publishing, 2008) at 221, 224–231. And see Andrea L. Kalfoglou, et al., "Ethical Arguments for and against Sperm Sorting for Non-Medical Sex Selection: A Review" (2013) 26:3 Repro Biomed online 235-256. See also Sheila A. M McLean, *First Do No Harm: Law, Ethics and Healthcare* (Oxford: Routledge, 2016) at 401.

⁶¹ For claims in the literature that certain genetic interventions constitute an indication that the slippery slope is occurring, See Scottish Council on Human Bioethics, Consultation response to the Human Fertilisation and Embryology Authority, Choices & Boundaries: Should People Be Able to Select Embryos Free from an Inherited Susceptibility to Cancer? (Edinburgh : Scottish Council on Human Bioethics 2006), at 2 online : http://www.schb.org.uk/downloads/publications/consult_choices_and_boundaries_jan06.pdf ; Roberto Andorno, "Le Diagnostic Préimplantatoire Dans Les Législations des Pays Européens : Sommes-Nous Sur Une Pente Glissante ?" (2008) 1:2 Bioethica Forum at 96; See also Marcy Darnovsky, "A Slippery Slope to Human Germline Modification" (2013) 499:7457 Nature 127.

⁶² See Han Somsen supra note 60. See also Andrea L. Kalfoglou et al., supra note 60. Sheila A M & M McLean supra note 60.

regulators were truly successful in achieving this key goal.⁶³ The literature has not produced any concrete and systematic evidence to either prove or disprove a slippery slope to eugenics is occurring. Furthermore, virtually no attempts have been made to assess the strength of the regulatory requirements in setting effective limits. The literature did not attempt to evaluate how the unclear and malleable regulatory standards could have been changed over time as genetic technology progresses and societal expectations rise. A deeper examination of the literature reveals there is no significant evidence to support the rather bold claims that the “robust” laws and regulatory systems have prevented a slippery slope to eugenics.

A Method to Re-Examine the Problem— Legal Change Analysis

The state of research on the slippery slope to eugenics raises a perplexing question: Why have slippery slope arguments failed, even though the uses of genetic intervention technologies have been rapidly expanding? Since slippery slope arguments are prone to several considerable challenges, relying on slippery slope arguments might not be the most effective way forward in studying developments in genetic intervention technologies, especially in the legal context. Thus, this thesis proposes to focus on a more modest, yet plausible alternative: the comprehensive study of the legal changes to genetic intervention laws.⁶⁴ The comprehensive study of these changes to the existing laws will reveal key trends and the patterns in which the regulation of this field has been transformed over the years.⁶⁵

⁶³The Nuffield Council on Bioethics has indicated that given the persistent concerns of a slippery slope occurring, the public may seek even further reassurances that effective legal safeguards are put in place. Nuffield Council on Bioethics, Genetic Screening: Ethical Issues (London, Nuffield Council on Bioethics, 1993) 90 online: http://nuffieldbioethics.org/wp-content/uploads/2014/07/Genetic_screening_report.pdf

⁶⁴ For a lengthier discussion about empirical methodologies for studying legal change see David Ibbetson, “Comparative Legal History: A Methodology in David Ibbetson, Comparative Legal History, and A Methodology” in A & C Stebbings, eds, *Making Legal History: Approaches and Methodologies* (Cambridge, UK: Cambridge University Press, 2012) at 132-135.

⁶⁵ According to Alan Watson, the term legal change describes the study of how laws change or evolve over an extended period of time. Beyond than providing a chronical account, the academic study of legal change attempts to describe “first the nature of the relationship between society and the rules that operate within it, and second the forces that cause law to change.” See Alan Watson, “Legal Change: Sources of Law and Legal Culture” (1983) 131:5 U Pa L R at 1121.

This thesis offers a comprehensive analysis of the manner in which genetic intervention laws have changed since their inception in the 1980s up to the present day. On a descriptive level, this thesis explains each of the rules and examine the degree to which their interpretation and application has changed over the years. Additionally, this thesis assesses how the changes in the interpretation and the application of the rules⁶⁶ have affected these rules' abilities to set meaningful limits. On a normative level, this thesis asks whether these changes in the laws were consistent with the normative considerations that lawmakers and regulators initially expressed.⁶⁷ More broadly, this thesis discusses whether the legal boundaries successfully accomplished the key legislative goal of avoiding misuses and thus addressed the concern of preventing overextensive legal change.

While this thesis does not attempt to determine whether there is a slippery slope, it nevertheless answers a significant question, one similar to the descriptive task of the slippery slope inquiries—are genetic intervention laws gradually becoming laxer and more permissive over time?⁶⁸ My primary focus on a descriptive, straightforward question stems from the realization that slippery slope arguments could be complex and tend to ask both a factual question (Is there a pattern of change?) and a normative question (Is this pattern ethically acceptable?).⁶⁹ By distinguishing between these two independent questions and answering them separately, this concrete, legal-centric approach can pave a way forward in this line of research after slippery slope to eugenics arguments have been at a standstill for nearly five decades. Hence,

⁶⁶ I will also suggest that the changes in the interpretation and application of the rules could be a signal of the regulators' incremental value shift. I will further examine such potential incremental value shift its possible ramifications in chapter 8.

⁶⁷ Lawmakers, regulators and ethicists tend to use the term 'slippery slope' to refer to the same phenomenon of laws becoming laxer and excessively permissive over time. However, the use they make of the term "slippery slope" is to refer to a general risk that may arise from overly lax regulation rather than to advance claims whether there is a demonstrable a slide down the slope. Whenever I will be quoting or referring to lawmakers, regulators and ethics commissions comments, I will be using their chosen terminology – the "slippery slope". Nevertheless, the conceptual and analytical lens used in this thesis is that of legal change.

⁶⁸ For more about of the significance of providing factual support for arguments such as the slippery slope see Douglas Walton, "The Basic Slippery Slope Argument" (2015) 35:3 Informal Logic 304-205.

⁶⁹ Albert Musschenga explains that the normative aspects of the argument (that the outcomes of the slope are negative) cannot be validated through research alone. However, factual, empirical research can support claims that a strict law has become laxer over time. Producing such factual accounts considerably strengthen the argument. See Albert W Musschenga, "Empirical Ethics, Context-Sensitivity, and Contextualism" (2005) 30:5 J Med & Phil 475-476.

my first and foremost objective, independent from normative evaluations, is to describe the extent and nature of the legal change to genetic intervention laws over the past two decades. Although answering a reframed question, this inquiry will nevertheless produce findings regarding whether genetic intervention laws in the UK and France are becoming more permissive over time.

Original Contributions

1) A Comprehensive Chronology and Analysis of the Legal Changes

This thesis endeavours to contribute to the discussion by addressing four key gaps in the literature. The first essential step is to demonstrate a consistent pattern of change in the laws. Several issues have so far hindered the systematic study of legal change. First, the literature has almost exclusively focused on slippery slope arguments while neglecting the study of legal change. Second, when the literature does discuss the topic of legal change (which is not clearly designated as such), it does so in a fragmented manner. Instead, the literature nearly always discusses particular instances of change (such as screening for a “saviour sibling” donor)⁷⁰ while failing to provide a complete chronological account of all such changes from the inception of the laws through to the present day. The literature has yet to put forward an account that accurately describes the significant transformation that genetic intervention laws have undergone over the course of their entire history.

This thesis offers a comprehensive legal change analysis of each of the four main rules on the books (regarding untreatable conditions, the degree of genetic risk, the seriousness of the condition and inheritable genetic modification).⁷¹ This methodological shift from focusing on particular cases to examining general patterns enables revealing the extent of the legal change and its effects such as the weakening of the rules’ ability to set meaningful boundaries. Such a systematic evaluation of the rules has not been performed. For

⁷⁰ Cordelia Thomas, “Preimplantation Genetic Diagnosis: Development and Regulation” (2006) 25 Med & L 368.

⁷¹ I will explain the meaning and purpose of these four rules in the four respective chapters that analyze the legal change to these rules. Here, I am only referencing the four rules I will analyse later in the thesis for the purpose of explaining the analytical steps and showing that such analysis has not been conducted in the literature so far.

instance, the regulatory requirement that interventions are only allowed for untreatable conditions has barely ever been discussed in detail, let alone been systematically assessed. The rules restricting interventions to high-risk probability and serious conditions have been discussed in the literature, but only through case studies and not by examining the general patterns in the regulatory interpretations and application of these rules over the years. Chapters 4-7 offer a systematic analysis of these rules and explain that rather than the problem being with the approval of a few specific contentious cases (such as intersex and congenital deafness), the problem is with the rules themselves. The thesis explains that the extensive changes in the interpretation and application of the “high risk” and the “serious condition” requirements have consistently expanded these unclear rules’ scope to the point of significantly compromising their boundary-setting function.

This inquiry contributes to the concurrent, high-profile discussion about the governance of inheritable genetic modification by critically examining the emerging regulatory model’s ability to set effective limits for this highly transformative technology. With the commercialization of genetic modification technology on the horizon, key countries such as the United States,⁷² the UK,⁷³ and the Netherlands⁷⁴ are in the process of considering reversing their legal bans. National reports have argued that genetic modification will be tightly regulated to prevent these potent technologies’ misuse.⁷⁵ Similarly, a prevalent narrative has

⁷² A US spending act currently bars the FDA from reviewing requests to approve any clinical trial “in which a human embryo is intentionally created or modified to include a heritable genetic modification.” See Consolidated Appropriations Act of 2016, Pub. L. No. 114-113, 129 Stat. 2242, 2283 (2015).

See National Academy of Medicine, National Academy of Sciences & the Royal Society, *Heritable Human Genome Editing* (Washington, DC: The National Academies Press, 2020).

⁷³ Ibid, see also The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

⁷⁴ See Netherlands, Commission on Genetic Modification (COGEM) and the Health Council of the Netherlands. *Editing Human DNA: Moral and Social Implications of Germline Genetic Modification*, COGEM (March 2017) at 60-61 online: <https://www.cogem.net/index.cfm/en/publications/publication/editing-human-dna-moral-and-social-implications-of-germline-geneticmodification?order=relevance&q=genome+editing&category=&from=30-09-1998&to=29-06-2018&sc=fullcontent>.

⁷⁵ See Committee on Human Gene Editing *supra* note 72. See also United Kingdom, House of Commons, Science and Technology Committee: Oral Evidence: Genomics and Genome-editing, HC 854, (March 29, 2017) online: <http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology/committee/genomics-and-genomeediting/oral/49725.html>

emerged in the academe that genetic modification regulation is certain to remain confined to only carefully approved, legitimate therapeutic uses.⁷⁶ In contrast, I will show how the proposed regulatory model (the genetic diagnosis model) is ill-adapted to govern novel heritable genetic modification technologies.⁷⁷ The use of genetic diagnosis's unclear and overbroad regulatory requirements will import a number of line-drawing weaknesses to the more ethically contentious context of heritable genetic modification. In particular, such line-drawing weaknesses would enable the potential approval of heritable genome editing of genes linked to mild and treatable conditions. Moreover, I will identify and describe two previously unflagged loopholes in the proposed regulatory model. These two loopholes are likely to enable, under the pretense of therapy, human genetic enhancement — the very same eugenic practices the proposed regulatory model seeks to prohibit. Closing these two loopholes would be profoundly challenging because of the difficulty in developing a legal test to effectively distinguish between genetic therapy and enhancement. This analysis shows the regulatory model is likely to be unsuccessful in setting effective legal limits to prevent genetic enhancement and eugenic misuse.

2) An Evaluation of the Legal Change Pattern and an Analysis of its Potential Ramifications

This thesis evaluates the extensive legal changes and shows how it is *prima facie* inconsistent with the overarching normative considerations behind genetic intervention laws. Academics have frequently argued that the specific rules (such as early age of onset or high risk) are arbitrary, serve no useful function,

⁷⁶ Rosario Isasi et al. *supra* note 50 at 337. See also Israël Nisand *supra* note 50; see also Nuffield Council on Bioethics “Genome Editing” (London: Nuffield Council on Bioethics, 2016) online: <http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf> and also Helen O’Neil & Joyce Harper *supra* note 49.

⁷⁷ The proposed regulatory model, the one used for genetic diagnosis, is the main model recommended in key countries such as the US, Western European and other developed nations. *Supra* notes 72-75. See also the discussion in chapter 7.

and needlessly impede market access.⁷⁸ Various commentators, including Wertz and Knoppers,⁷⁹ Bredenoord et al.,⁸⁰ and Boyle and Savulescu⁸¹ praise the “relaxation” in the manner the rules are applied.⁸² In contrast, the thesis shows that these changes are *prima facie* incompatible with the laws underlying normative considerations of preventing these technologies misuse and the associated ethical, societal and medical risks. This work helps to fill the gap regarding the laws and the specific rules’ overarching normative considerations and the manner in which the legal changes have sharply deviated from the key legislative goals. Furthermore, the thesis explains challenges and the ramifications of the overextensive legal change pattern such as ineffectiveness in accomplishing the key legislative goal, lack of awareness of the laws’ current flaws and the growing risk of state involvement in neo-eugenic markets.

3) Theoretical and Evidence-based Insights into the Potential Drivers of the Legal Changes

This thesis provides insights into the potential drivers for the rapid change of genetic intervention laws. Given the lack of critical inquiry into the legal changes as a systemic problem, little research has addressed the possible drivers of this phenomenon. Jacques Testart briefly indicated that the restriction of genetic diagnosis to only “serious” conditions, without defining what the term “serious” entails, could

⁷⁸ See for example Rosario Isasi et al. *supra* note 50 at 339. See also Annelien L. Bredenoord, et al., “Dealing with Uncertainties: Ethics of Prenatal Diagnosis and Preimplantation Genetic Diagnosis to Prevent Mitochondrial Disorders” (2008) 14:1 Human Repro Update 90. And see Peter Braude, “Preimplantation Genetic Diagnosis for Genetic Susceptibility” (2006) 6 N Engl J Med 541-543.

⁷⁹ Dorothy C. Wertz & Bartha Maria Knoppers, “Serious Genetic Disorders: Can or Should They Be Defined?” (2002), 108:1 Am J Med Genetics 35.

⁸⁰ Annelien L. Bredenoord, et al., *supra* note 50.

⁸¹ Robert J. Boyle & Julian Savulescu, “Prenatal Diagnosis for “Minor” Genetic Abnormalities Is Ethical” (2003) 3:1 Am J Bioethics 60.

⁸² While various normative viewpoints will be briefly discussed, the scope of the thesis does not allow for an extensive examination and appraisal of the wide variety of individual authors’ opinions. Overall, there is no consensus in the literature on the question of whether laws are overly permissive or restrictive. Nevertheless, there is a broad consensus among academics, governments and civil society organizations that legal limits are required to prevent genetic intervention technologies’ misuse. The thesis argues that decision-makers require better tools to address the challenges posed by the overextensive legal change problem.

potentially lead to the regulatory approval of conditions that are less and less serious over time.⁸³ Similarly, David King further implied that unclear language plays a role in broadening the scope of the legal restriction of genetic diagnosis only to “serious” conditions.⁸⁴ However, King only briefly mentioned the unclear language in conjunction with the unstable boundaries and did not advance a complete argument to demonstrate the role of unclear language in the legal change process. While these brief comments do provide useful insights, they are in themselves not sufficient to fill the gap in the literature about the potential drivers of the legal change. Søbirk has commented on this gap, suggesting that a lack of explanation of the causes of this phenomenon casts doubt on its very existence.⁸⁵ To address this gap, this thesis provides insights that can help explain why genetic intervention laws are becoming laxer and more permissive over time. The legal change pattern largely stems from pressures from industry and prospective parents and government entities on the vague, subjective and overly broad legal constructs such as “serious condition” and “therapeutic” to be interpreted more expansively and permissively. This inquiry’s findings that the unclear, malleable lines that were drawn are a potential driver of the overextensive legal change problem also pave the way to reform.

4) A Blueprint for a Reform to Address the Overextensive Legal Change Problem

This thesis proposes a general blueprint for reform to redraw the legal lines with the aim of making them clearer and more durable. The literature has so far failed to offer practical solutions for how to draw lines that would be more durable and effective in setting limits. While a formidable attempt, Jeffery Botkin’s scheme, the only academic proposal to draw a (non-legal) criteria uses the very same constructs of “seriousness,” “risk” and “benefit to the parents,” which are vague, malleable and promote overextensive

⁸³ Jacques Testart, *Diagnostic Génétique Pré-implantatoire (DPI) : Réponse à un Editorial*, (1997) 13 *Medicine/Sciences*, 134.

⁸⁴ David King, “Preimplantation Genetic Diagnosis and ‘Slippery Slopes’” *Bionews* (13 May 2007) online: http://www.bionews.org.uk/page_37933.asp.

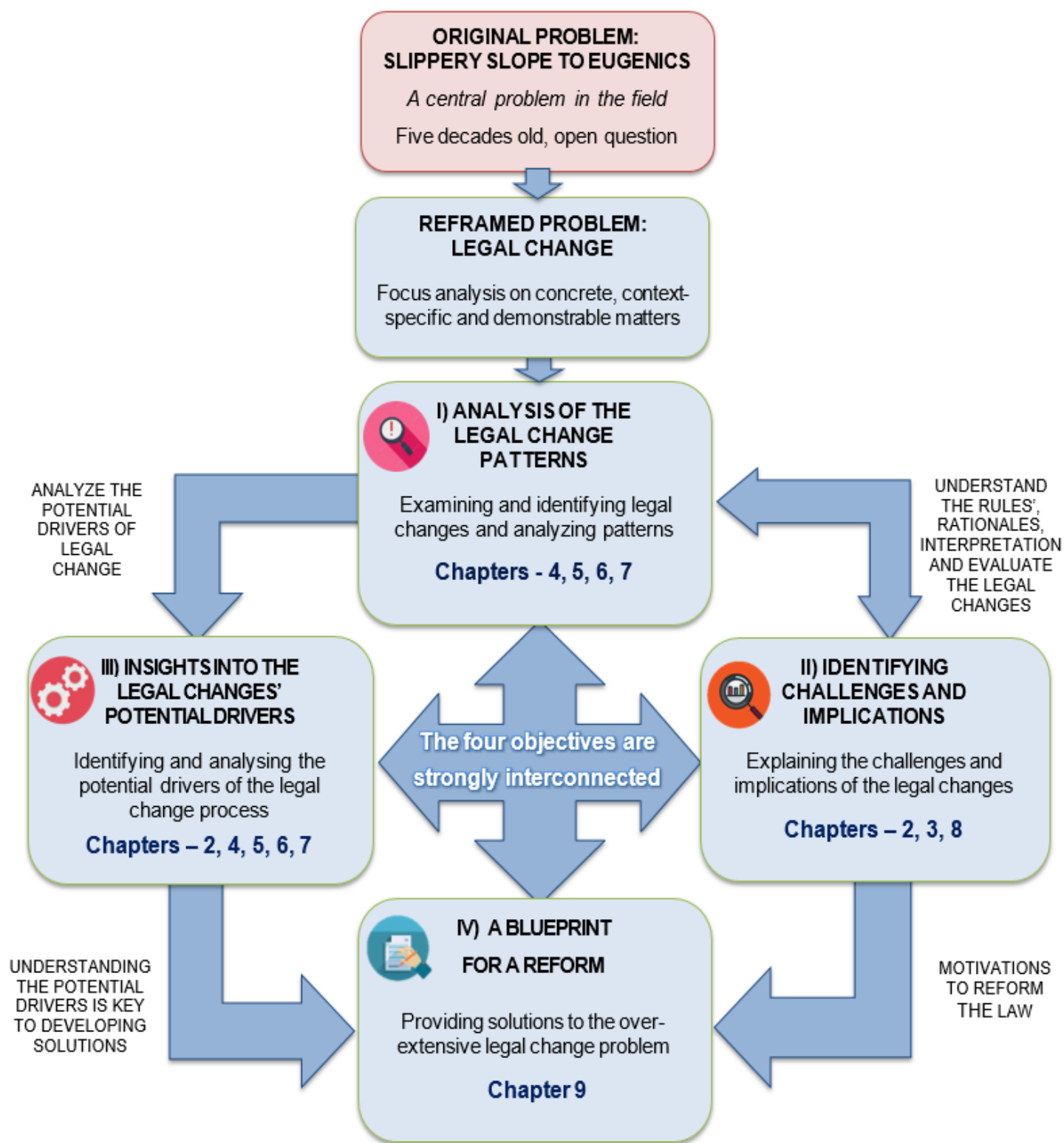
⁸⁵ See Thomas Søbirk Petersen, “Just Diagnosis? Preimplantation Genetic Diagnosis and Injustices to Disabled People” (2005) 31:4 *J Med Ethics* 233.

legal change.⁸⁶ The literature's lack of critical inquiry into the potential drivers of the legal changes did not further the goal of finding effective solutions to remedy this problem. Yet, by drawing on this analysis of the potential drivers of the legal change process, chapter 9 provides operative recommendations in the form of a blueprint for reform. The blueprint provides practical examples for how to draw legal lines for genetic intervention laws that have a certain degree of flexibility while also maintaining certain and effective boundaries.⁸⁷ To improve on the existing rules, the blueprint includes newly developed legal tests, clearer distinctions and proposed legislative amendments to rewrite rules and strengthen genetic interventions' governance.

⁸⁶ For the attempt to devise a set of rules see Jeffrey R Botkin, "Prenatal Screening: Professional Standards and the Limits of Parental Choice (1990) 75 *Obstetrics & Gynecology* 875. See also Jeffrey R. Botkin, "Fetal Privacy and Confidentiality" (1995) 25:5 *Hastings Center Rep* 32.

⁸⁷ I will explain that the main issue at hand is not the perceived tension between flexibility and certainty, but rather it is laws setting effective as opposed to ineffective legal limits. In chapters 4-7, I will discuss in detail how the extensive legal change significantly eroded the ability of laws to set effective limits., In chapter 8, I will further discuss the challenges with current legal limits being overly lax and ineffective such as allowing for regulatory mission creep, technological somnambulism and the closing of the political window of opportunity to reform the law. In chapter 9, I will provide examples of fine distinctions that can be incorporated to allow a certain degree of flexibility for specific hard cases.

Flowchart – Overview of the Project, General Structure and Contributions



The Scope of the Study

This study examines the legal change of genetic intervention laws in France and the UK, two key Council of Europe jurisdictions.⁸⁸ Despite traditional divisions between civil and common-law systems, the laws pertaining to genetic intervention technologies are new developments and a part of larger international legislative efforts. The legislation in these two countries traces some of its origins to the efforts of the Council of Europe's in the 1980s. These efforts later led to the development of the Oviedo Convention, a legally binding international treaty intended to set standards and limits to novel biomedical technologies.⁸⁹ The UK and French Laws originally relied on similar and comparable normative considerations.⁹⁰ Indeed, the regulatory systems in the UK and France have been frequently compared. Regulators themselves in both countries have conducted some of the comparisons.⁹¹ These two regulatory bodies also conducted joint consultations based on the similarities between the laws.⁹² In addition, academic comparative studies stated

⁸⁸ Unlike its British and French counterparts, Canadian genetic intervention laws' short and fragmented history does not make Canada a reasonably good choice for this study of long-term legal change patterns. Moreover, unlike in the UK and France, which regulated the field for more than two decades, the Canadian regulator, the Assisted Human Reproduction Agency (AHRA) was a short-lived institution that only existed between 2007-2013. The AHRA never exercised its regulatory power over trait selection using genetic intervention technologies. For more about the legal situation in Canada see Françoise Baylis & Jocelyn Downie, "The Tale of Assisted Human Reproduction Canada: A Tragedy in Five Acts" (2013) 25:2 Can J of Women & L 183.

⁸⁹ The Council of Europe's Oviedo Convention has become the cornerstone of genetic intervention law in Europe. See Council of Europe, "Closing Declaration of the Eighth Meeting of the Conference of National Ethics Committees (COMETH), Dubrovnik (Croatia) (25-26 April, 2005) online: https://www.coe.int/t/dg3/healthbioethic/cometh/8_Dubrovnik%20Declaration_en.pdf.

⁹⁰ While the ethical premises of the UK and French acts are similar, they are not entirely identical (for example, while the status of human embryos is unclear in the UK, it enjoys greater protection in France) Melanie Latham, *Regulating Reproduction: A Century of Conflict in Britain and France* (Manchester: Manchester University Press, 2002) 195-198.

The Grand Chamber of the ECHR noted that: "At European level, ...there is no consensus on the nature and status of the embryo and/or foetus, although they are beginning to receive some protection in the light of scientific progress and the potential consequences of research into genetic engineering, medically assisted procreation or embryo experimentation. *Vo v. France* [GC] [2004] App No. 53924/00, Judgment of 8 July 2004 at para. 84.

⁹¹ HFEA, "Legal Aspects of PGD Licensing, SCAG/ELC (06/05) 01 Annex A", (London: HFEA, 2005).

⁹² La France au Royaume-Uni HFEA : "Journée De Consultation Pour La Mise À Jour Du Code De Bonnes Pratiques" Ministère de l'Europe et des Affaires étrangères (May 13, 2010) online : <http://www.ambafrance-uk.org/HFEA-journee-de-consulation-pour>

that the two countries possess rather similar substantive laws and regulatory processes.⁹³ Scholars who have compared the Council of Europe regulatory systems often classify the UK and French regulatory regimes as a middle-ground approach to the regulation of genetic intervention technologies that is not overly permissive or restrictive.⁹⁴

Unlike some smaller Council of Europe jurisdictions, France and the UK have produced a sufficient amount of legislative and regulatory documents to discuss the key objectives and the normative considerations underlying the legal restrictions on genetic intervention technologies.⁹⁵ Sufficient documentation is an essential requirement for an extensive inquiry into the relevant legal history and the process of legal change. To produce such analysis, the thesis examines the original parliamentary debates, legislative documents, committee publications and the foundational legal and regulatory policy documents. Additionally, the thesis reviews legal and policy documents, regulatory decisions and relevant court decisions.

The thesis focuses on the study of legal change in the UK and France also given the commonalities in their legal histories and similar timelines of the change process. Both the UK and French legislative and policy discourse exhibited as early as the 1980s a great degree of foresight of developments that are now materializing such as screening for low risk susceptibilities and inheritable genetic modification.⁹⁶ Furthermore, the UK and France are amongst the first jurisdictions in the

⁹³ Joyce C. Harper et al, *Practical Preimplantation Genetic Diagnosis* (Springer: London, 2012) 289. See also Sipra Soini, "Preimplantation Genetic Diagnosis (PGD) in Europe: Diversity of Legislation a Challenge to the Community and its Citizens" (2007) 26 Med & L 309.

⁹⁴ Melanie Latham, "Regulating the New Reproductive Technologies: A Cross-Channel Comparison" (1998) 3:3 Med. L. Int'l 111; See also Allane Madanamoothoo, "Saviour-Sibling and the Psychological, Ethical and Judicial Issues that It Creates: Should English and French Legislators Close the Pandora's Box?" (2011) 18:3 Eur J Health L 295.

⁹⁵ In addition, The UK and France are amongst the most widely discussed countries in the context of the legal governance of genetic interventions given that these two jurisdictions have world-renowned biotechnology industries, binding legislation and extensive regulatory experience. Furthermore, The UK and French regulation of genetic interventions has particular relevance for the Canadian policy discourse as the analysis of these two jurisdictions has been frequently featured in foundational documents produced by the Parliament of Canada, Health Canada and the Government of Quebec. For instance, see *infra* notes 947, 1125 1287, 1288 and 1290.

⁹⁶ There is a long-standing practice in the UK and France of conducting horizon scanning, examining the R&D pipelines and developing foresight-based insights. In the context of genetic interventions, it is important to examine whether new

world to enact legally binding laws⁹⁷ on genetic interventions.⁹⁸ Both countries began officially regulating genetic diagnosis in the 1990s. Many of the legal changes described in the thesis occurred around similar timelines in the two jurisdictions. These commonalities in terms of legal history and timelines make the UK and France prime jurisdictions for the study of legal change of their genetic intervention laws over an extended period of time.

This thesis examines the process of legal change in France and the UK since its inception in the 1980s to the present day. France and the UK began with nearly identical rules. The laws in both countries made use of a main regulatory standard, the seriousness of the condition, which was further narrowed by additional requirements (e.g., that the condition ought to be early onset, high penetrance, and untreatable). In both systems, all of the legal requirements have substantially changed either formally or in terms of their application, in the same order and around similar timelines. The relevant chapters analyze general legal change patterns and show that the relevant rules have become considerably laxer as genetic technology has grown more powerful.

Dividing the Analysis into Four Phases and Evaluating the Patterns of Legal Change

To analyze the legal change with greater accuracy, I divide the chronology into four phases, each corresponding to a specific rule.⁹⁹ These four key rules I analyze are the legal restrictions to 1) untreatable

and emerging technologies are consistent with the key legislative and policy objectives as well as human rights laws and the underlying ethical considerations to make sound decisions. For a general discussion about the importance of foresight studies in technology policy see European Commission *infra* note 135.

⁹⁷ Various other jurisdictions across the globe are not suitable for a legal change analysis as the majority of them lack binding legislation on genetic interventions as well as a dedicated regulatory authority. Moreover, there are additional challenges with a conducting a comparative legal change analysis with many non-OECD countries given the considerable differences in terms of their political systems, policy objectives and a variety of socio-cultural factors.

⁹⁸ The legal situation and legislative history in the UK and France differs from various European and other developed countries that enacted legislation and begun regulating genetic interventions only the first or second decade of this century. See for instance Das Deutsche Referenzzentrum für Ethik in den Biowissenschaften, “Präimplantationsdiagnostik, Rechtliche Aspekte”, DRZE (February 2021) online: https://www.drze.de/im-blickpunkt/pid/rechtliche-aspekte?set_language=de

⁹⁹ I will analyze each of these four phases of change in separate chapters because of the thematic difference between the various issues. These four rules have somewhat different policy and ethical considerations underlying them, different chronologies and timelines as well as a different mix of pressure and motivations from prospective parents, industry and

conditions, 2) high-risk and early-onset conditions,¹⁰⁰ 3) serious conditions and 4) the restrictions on inheritable human genetic modification.¹⁰¹ I examine the legal change of each of these four rules in a respective chapter (in chapters 4-7). The aim of examining each of the four rules in detail is to document and analyze the process of legal change in a thorough and rigorous manner. Beyond the examination of each of the specific rules, I will discuss the common characteristics of the process of legal change as well as explain how these changes are interconnected.¹⁰² The sharp transition from more restrictive to highly permissive interpretations often stands in stark contrast with the rules' initial normative considerations.¹⁰³ Identifying common patterns allows for drawing broader observations about the characteristics of the legal change phenomenon.

Conducting Pattern Analysis by Examining the Patterns of Legal Change Over Time

This thesis examines the legal change process by providing a comprehensive overview of these changes and conducting a detailed review of illustrative case studies. These two examination methods will

political actors to make these particular rules laxer. For instance, the normative issues that could arise from approving genetic diagnosis for a condition such as PKU, which is fully treatable with a special diet, are profoundly different than those raised by inheritable genetic modification.

¹⁰⁰ The regulatory restrictions regarding the age of onset and high risk are technically two distinct rules, but for the sake of clarity of the presentation, I will discuss them together in the same chapter since they are both related to the same topic – the approval of susceptibility conditions. These two rules share a common history as they were both changed at the same time to allow for screening of predisposition to various conditions such as cancers and neurodegenerative diseases.

¹⁰¹ Two other key rules I will not be including in this review of the legal changes are: a) the prohibition on human cloning (as well as the cloning of human eggs and sperm) and b) the prohibition on human-animal gene admixture (to produce genetically modified transgenic human embryos). While these two rules have changed, they have not changed in a sufficiently considerable matter to warrant a comprehensive account of their legal change. I will briefly note that the rule prohibiting the creation of human-animal admixed embryos for research purposes was reversed in the 2008 revision of the HFE act in the UK and the upcoming revision of the French Bioethics Law. Moreover, in 2015 HFEA has approved a technique to genetically modify the mitochondrial (non-nuclear) DNA, which often involves the cloning of human eggs. See José Rafael Blesa et al, “Ethical Aspects of Nuclear and Mitochondrial DNA Transfer” (2016) 83:2 the Linacre Q 179. See also Calum MacKellar, “Differentiating between Human and Non-Human Interspecies Embryos” (2014) 40:4 J Med Ethics 284.

¹⁰² As sociological historian E. Evans-Pritchard rightfully remarked “History is not a succession of events, it is the links between them.” See Edward Evans-Pritchard, *Anthropology and History* (Manchester: Manchester University Press, 1961) at 3. In this thesis, I will go beyond chronologically recording a sequence of relevant events to explain the links between such events, identify trends, analyze patterns and explain the broader ramification of the rapid and extensive legal change of genetic intervention laws.

¹⁰³ A key component and method employed in the legal change analysis is the evaluation of to which extent the change pattern is consistent or inconsistent with key legislative objective and rule-specific rationales identified. As discussed above, this analysis is an important step in the appraisal of regulatory licensing practices over an extended period of time.

portray the legal change phenomenon in both depth and breadth. First, in chapters 4-7, I provide a bird's-eye view of the nature and extent of the changes to the rules. I begin by reviewing the rule's original interpretation and application. I then identify change patterns by examining the regulatory licensing of conditions with special attention to the manner in which such newly approved conditions, physiological and clinical features substantially differed from the original interpretations and the application of the rule. By examining the similarities amongst conditions approved under the later broadened rule, I identify key common patterns that describe the main changes to the four key rules regarding genetic interventions. Drawing on those patterns of change in regulatory licensing, I then explain the manner in which the rules have become laxer and more permissive over the years. For instance, I describe the process of lowering the regulatory bar of risk from the starting point of 90 percent risk of developing a disease prior to 2006, to how it went all the way down to 0 percent risk, the lowest point possible. Overall, this bird's-eye view will show how the gradual transition from rather restrictive to permissive regulatory lines has accumulated over time into a legal change of a considerable scale.

I additionally examine case studies to provide in-depth accounts of the legal change. For each of the four phases of legal change, I review three case studies that vividly illustrate the extent to which the rules have become broader and more permissive.¹⁰⁴ For instance, in regards to the rule restricting genetic diagnosis to serious conditions, I review in detail the case of genetic diagnosis of Klinefelter syndrome. Klinefelter syndrome is a condition that falls under the intersex umbrella diagnosis and manifests in subtle appearance differences such as smaller genitals, enlarged breast tissue and fertility problems.¹⁰⁵ People with Klinefelter

¹⁰⁴ The selected case studies were chosen because they more clearly illustrate the extent of the changes in the interpretation and the application of the rules. These case studies often examine conditions that are milder or overall have less of an impact of the future child's health. However, there are various other worthwhile intermediate cases such as Down syndrome, which I will highlight throughout the thesis.

¹⁰⁵ Fabio Lanfranco et al., "Klinefelter's Syndrome" (2004) 364:9430 *The Lancet* 273.

syndrome may opt for hormone replacement therapies to have a more gender-typical body.¹⁰⁶ In addition, advancements in microsurgical techniques and artificial reproductive technologies have greatly improved fertility rates amongst patients.¹⁰⁷ Chapter 6 shows how the decision to permit genetic diagnosis for Klinefelter syndrome is a stark departure from the earlier interpretation of the serious condition requirement that restricted genetic diagnosis to life-threatening diseases. By examining particular cases and general change patterns, chapter 6 shows that the regulators have reinterpreted the seriousness requirement to apply to conditions that have little or no effect on health but are nonetheless regarded as deviating from a common conception of bodily normalcy.

Theory

The Living Law — Ehrlich's Sociological Theory of Legal Change

This thesis provides insights into the potential drivers of the extensive changes to genetic intervention laws by drawing on scholarly work from the field of legal sociology. I will primarily base my analysis on Eugen Ehrlich's theory of legal change – “the living law”. Ehrlich, who was one of the founding fathers of the sociology of law,¹⁰⁸ contends that legal change predominantly emanates from social change.¹⁰⁹ Ehrlich's theory holds that the “center of gravity of legal development therefore from time immemorial has not lain in the state but in society itself, and must be sought there at the present time.”¹¹⁰ Changing social, cultural, ideological, technological and economic conditions drive the legal system to continually re-adjust its

¹⁰⁶ Jeannie Visootsak & John M Graham, “Klinefelter Syndrome and Other Sex Chromosomal Aneuploidies” (2006) 1:1 Orphanet J Rare Diseases 42.

¹⁰⁷ Ranjith Ramasamy et al., “Successful Fertility Treatment for Klinefelter's Syndrome” (2009) 182:3 J Urology 1108. See also Lise Aksglaede & Anders Juul, “Therapy of Endocrine Disease: Testicular Function and Fertility in Men with Klinefelter Syndrome: A Review” (2013) 168:4 Euro J Endocrinology R67.

¹⁰⁸ Nicholas S Timasheff, *An Introduction to the Sociology of Law* (New Jersey: Rutgers Transaction Publishers, 2002) ix.

¹⁰⁹ Eugen Ehrlich, *Fundamental Principles of the Sociology of Law* (New Jersey: Rutgers Transaction Publishers, 1936) 390.

¹¹⁰ *Ibid.*

rules and doctrines to stay aligned with society's ever-changing common practices and power relations.¹¹¹ The law is therefore forced to adapt to the constantly changing cultural, technological and economic circumstances, many times having to do so within the confines of pre-established and older legal texts.¹¹²

Adjudicators can read in new social norms, sometimes disguised in fictions and subtle distinctions that facilitate legal change. In certain cases, “it might not be necessary on that account to change a single line of written law.”¹¹³ Through this process, adjudicators “put a new picture into an old frame.”¹¹⁴ The open-textured nature of the language provides an opportunity for evolving practices and norms to reshape the law.¹¹⁵

According to Ehrlich's theory, prominent institutions exert pressure on legal structures and norms to accommodate these institutions' social, economic and political interests.¹¹⁶ These institutions put pressure on adjudicators and lawmakers to realign legal norms with changing social circumstances and ever-shifting power relations. Adjudicators adjust the open to interpretation language often in accordance with the changing social circumstances and the realignment of power and institutions' interests.¹¹⁷ According to

¹¹¹ See Ehrlich 1936 *supra* note 109 at 433, 439, and 341–45. In chapter 2, I examine major technological, economic ideological and cultural trends and shifts relating to genetic intervention technologies. I will show that genetic technology is evolving from a medical method to prevent the birth of embryos with congenital malformations to a new commercial service intended for human genetic enhancement purposes. I will also highlight key market, political and cultural forces that may have a role in the growth and the emergence of a consumer market in child trait selection.

¹¹² See Ehrlich 1936 *supra* note 109 at 400–401.

¹¹³ Eugen Ehrlich, “Judicial Freedom of Decision: Its Principles and Objects” in *Science of Legal Method* (Boston: Boston Book Company 1917) at, 57.

Similar to Ehrlich, I will use the term ‘legal change’ not only to denote formal revisions of the law (as those made by parliaments and governments) but also those resulting from changes in the interpretation and the application of rules.

¹¹⁴ See Ehrlich 1936 *supra* note 109 at 397.

¹¹⁵ Mikhail Antonov, “Eugen Ehrlich-State Law and Law Enforcement in Societal Systems” (2013) 44:3 *Rechtstheorie* 301–303.

¹¹⁶ Please note that throughout the thesis, Ehrlich's theory is solely used as a framework for the development of descriptive accounts of the legal change process (rather than to propose perspective accounts). For more about this distinction, see Hans Kelsen, ‘Eine Grundlegung der Rechtssoziologie’, in *Hans Kelsen & Eugen Ehrlich, Rechtssoziologie und Rechtswissenschaft. Eine Kontroverse* (1915/1917) (Baden-Baden, Nomos Verlagsgesellschaft, 2003).

¹¹⁷ Jeremy Webber, “Naturalism and Agency in the Living Law” in *Living Law: Reconsidering Eugen Ehrlich* (Portland: Hart Publishing, 2009) 200–203.

Ehrlich's theory, to properly understand how the law changes, one has to first identify the shifting power dynamics in society and the alignment of institutional interests.¹¹⁸

I will identify three primary sources of institutional pressure: prospective parents, fertility clinics (as a part of the industry) and governmental entities. Regulators often come under pressure by the government bodies that oversee them (mainly health departments) as well as by lobbying by the industry.¹¹⁹ Similarly, Katz and Schweitzer accurately identified a convergence of stakeholder interests in the regulation of genetic diagnosis, which includes the industry (e.g. IVF clinics, medical insurance companies, and the biotechnology industry), prospective parents and government entities.¹²⁰ While government entities may seek to reduce the costs associated with certain genetic traits,¹²¹ the industry is motivated by maximizing profits chiefly through liberalizing and expanding the market for prospective parents to make choices regarding their children's

¹¹⁸ David Nelken, "Law in Action or Living Law? Back to the Beginning in Sociology of Law" (1984) 4:2 Leg S 162. See also Alex Ziegert, "A Note on Eugen Ehrlich and the Production of Legal Knowledge" (1998) 20 Sydney L Rev 106-110.

¹¹⁹ For more about the claims of regulatory capture of the HFEA by the industry see Robert G. Lee, "Look at Mother Nature on the Run in the 21st Century: Responsibility, Research and Innovation" (2012) 1:01 Transnat'l Envtl L, 105 at 115. See also David Morgan, 'Ethics, Economics and the Exotic: The Early Career of the HFEA' (2004) 12:1 Health Care Analysis, 7; and see Therese Callus, 'Ensuring Operational Compliance and Ethical Responsibility in the Regulation of ART: the HFEA, Past, Present, and Future' (2011) 3 L Inno & Tech 85.

Claims about industry lobbying and regulatory capture of the ABM are made by Jacques Testart, the first clinician to ever perform IVF in France, the Honorary Director of the National Research Council - INSERM (Institut National De La Santé Et De La Recherche Médicale) and former member of the ethics commission - CCNE. Testart asserts that:

"The Biomedicine Agency (ABM) is an organization that, as a part of its role of regulating assisted human reproduction is completely dominated by CECOS (fertility and genetics) practitioners ... For everything about assisted reproduction, there is a lobby of technicians who have managed to trump bioethics by imposing their own rules. And in general, the pressures on those who are responsible for developing ethical rules are intolerable. We clearly see the lobbies that act when their interest is at stake, and leave ethical reflection to develop only where their interests are not at stake."

See Jacques Testart & Jean-Marie Le Méné, "L'humanisme Peut-Il Faire Reculer L'eugénisme?" *Génétique* (30 Septembre 2014), online : <http://www.genethique.org/fr/entretien-croise-entre-jacques-testart-jean-marie-le-mene-lhumanisme-peut-il-faire-reculer-62167>. For similar claims about the industry regulatory capture of the ABM, see Christian Godin, "Bioéthique en Europe. Le Sens, Les Enjeux Et Les Évolutions Prévisibles". *La Documentation Française* 12/07/2010, online <http://www.ladocumentationfrancaise.fr/pages-europe/d000449-bioethique-en-europe.-le-sens-les-enjeux-et-les-evolutions-previsibles-par-christian/article>

¹²⁰ Gregory Katz & Stuart O. Schweitzer, "Implications of Genetic Testing for Health Policy" (2013) 10:1 Yale J Health Pol'y, L & Ethics 113-114.

¹²¹ In addition to Katz and Schweitzer's insightful analysis, similar claims made by Rose *supra* note 7.

genetic traits.¹²² Katz and Schweitzer's work focuses on analyzing the regulatory political landscape in the UK and France and does not aim to produce a theory for why the laws change. Nevertheless, their stakeholder analysis correctly identifies the key players in the field, which serves as a starting point for my study of the pressures that such interest groups exert on the malleable boundaries to become laxer and permissive.

As a leading theory, "the living law" provides a useful and comprehensive framework to study and analyze the process of legal change. More than a century after his work first appeared in print, Ehrlich's theory continues to be commonly featured in the legal sociology and legal theory discourse.¹²³ A key reason for Ehrlich's continued relevance is his theory's strong legal and social science foundations, its comprehensiveness and its usefulness for the analysis of legal change in a variety of legal contexts. Ehrlich's work provided a lasting contribution to the field,¹²⁴ particularly given that the theory of legal change remains a highly complex, niche topic with very few alternatives and robust theoretical frameworks. The work of the two prominent theoreticians in the field, Alan Watson and Lawrence M. Friedman is influenced by Ehrlich. Their work is often expressed in less general theoretical terms and deals with legal change on a different level of resolution such as the study of how legal systems evolve over centuries or how legal cultures influence each other in a globalized world.¹²⁵ Ehrlich's theory provides the appropriate level of resolution for the study of the legal change of genetic intervention laws as it focuses on examining key trends in this fast-moving field. Ehrlich's comprehensive theoretical framework gives due consideration to a variety of socio-cultural,

¹²² See Debora L. Spar, *The Baby Business: How Money, Science, and Politics Drive the Commerce of Conception* (Cambridge Mass: Harvard Business Review Press, 2013); Leon Kass in The President's Council on Bioethics, *Beyond Therapy: Biotechnology and The Pursuit of Perfection* (Washington DC: The President's Council on Bioethics, 2003).

¹²³ See for instance David Nelken, "Eugen Ehrlich, Living Law, and Plural Legalities" (2008) 9 *Theoretical Inq. L.* 443. Klaus Ziegert, "Beyond" Living Law": Eugen Ehrlich's General Theory of Law" in Knut Papendorf, Stefan Machura, Anne Hellum eds. *Eugen Ehrlich's Sociology of Law* (Vienna: Lit Verlag, 2014): 17-38; Jean-Louis Halperin, "Law in Books and Law in Action: The Problem of Legal Change" (2011) 64 *Me. L. Rev.* 45.

¹²⁴ See for instance Likhovski's work regarding Ehrlich influence on the legal literature and theory. Assaf Likhovski, "Czernowitz, Lincoln, Jerusalem, and the Comparative History of American Jurisprudence" (2003) *Theoretical Inq. L.* 4: 621. See also Roscoe Pound, "Appreciation of Eugen Ehrlich" (1922) 36 *Harv. L. Rev.*, 129.

¹²⁵ Alan Watson, *Sources of Law, Legal Change, and Ambiguity* (Pennsylvania: University of Pennsylvania Press, 1998), Lawrence M. Friedman, "Is there a Modern Legal Culture?" (1994) 7:2 *Ratio Juris*, 117.

economic and political drivers of legal change. It does so while amply discussing the complex relations between institutions and the various sources of the law, gives attention to the legal text and examines how key players have come to reshape the interpretation of the law over time.

The Limitations of Legal Theoretical Explanations of the Legal Change Pattern

This thesis does not endeavour to fully explain these key players' various social, political, and economic interests in promoting laxer and permissive genetic intervention laws. Such a monumental task far exceeds the scope of this thesis. Instead, my aim here is more modest—to show that the phenomenon of pressure exerted by key players exists and to generally explain how these pressures gradually led to the described legal changes.¹²⁶ While these key players' effects on the regulatory system cannot be examined in full here, the pressure they exert to expand the already malleable regulatory lines will be generally described and explained. I will primarily focus my attention on examining how the unclear drafting of the vague rules allows for expansive and permissive interpretations, which played a role in the process of legal change.

An Examination of the Unclear Legal Language and its Role in Facilitating Legal Change

To develop deeper insights and propose potential solutions, this thesis examines in detail the unclear language genetic intervention laws use and the role it plays in the legal change. This thesis identifies three distinct manners in which the language of genetic intervention laws is unclear: conceptual unclarity, subjectivity, and an overbroad scope.¹²⁷ First, the language of genetic intervention laws frequently refers to

¹²⁶ The social science evidence I have examined, such as interviews with regulators, clinics and prospective parents typically mention stakeholders' pressures on regulators to get a more favourable decision. There is a sufficient amount of evidence to suggest that such pressures by regulators and stakeholders, do in fact exist, and that they could affect regulatory decision-making. In general, there is ample socio-legal literature on stakeholder pressure in other legal fields. See for instance Amitai Etzioni, "The Capture Theory of Regulations—Revisited" (2009) 46:4 *Society* 319-323.

Chapters 4-7 describe the legal change process and specifically the notable regulatory policy changes of giving prospective parents and the treating physicians a significantly expanded role by relying on their interpretations of the otherwise vague regulatory requirements.

¹²⁷ I will rely on theoretical and applied insights about linguistic indeterminacy and the manner in which it enables adjudicators to significantly broaden their margin of discretion. See for instance, Timothy AO. Endicott, "Linguistic Indeterminacy" (1996) 16:1 *Oxford J. Leg Stud.* 667; Ludwig Wittgenstein, *On Certainty* (Oxford: Basil Blackwell, 1996); Kent Greenawalt, *Law and Objectivity* (Oxford: Oxford University Press, 1992); Brian Bix, "Law, Language, and Legal Determinacy" (Oxford: Oxford University Press, 1993); Ken Kress, "Legal Indeterminacy" (1989) 77 *Cal L R* 283-337.

conceptually unclear constructs. Constructs such as a “serious condition” and a “therapeutic” purpose are hard to define, particularly because they refer to concepts that are themselves arguably inherently ambiguous and unclear.¹²⁸ Second, the legal text excessively relies on subjective interpretations of malleable constructs such as “genetic risk” and “serious conditions.” The subjective language allows for flexible interpretations of the malleable constructs in a manner that tends to favour interested parties. For example, despite more objective methods to quantify the statistical probability that a gene will lead to the emergence of a disease (i.e. penetrance), current laws leave such delineations to parents’ subjective opinions on how much risk they are willing to accept (perceived risk). Third, the scope of the rules regarding genetic intervention is often overbroad. These rules do not set any discernable cut-off points or clear minimal thresholds to denote which interventions should be excluded. For example, the “significant risk” requirement does not set any discernable minimal bar to flag genetic risks that are too low or remote to warrant a genetic diagnosis. This thesis will further explain how gradual and consistent changes in the interpretation and the application of the unclear rules have effectively diminished their ability to set meaningful limits. These findings regarding the role of language in the process of legal change will later assist me in developing custom-tailored solutions to address this growing problem of reproductive biotechnologies’ potential misuse and to strengthen their legal governance.

Conclusion

This thesis examines the process of legal change to genetic intervention laws in the UK and France and provides essential insights about the quality of the legal governance of these transformative technologies. It shows that genetic intervention laws in the UK and France exhibit a pattern of continuous legal change

Lawrence M. Solan, "Vagueness and Ambiguity in Legal Interpretation "Vagueness in Normative Texts, Linguistic Insights" (2005) 23 S in Language & Comm 73-96.

¹²⁸ See Isabel Karpin & Roxanne Mykitiuk, "Going Out on a Limb: Prosthetics, Normalcy and Disputing the Therapy/Enhancement Distinction" (2008) 16:3 Med l. rev 413-436; See also Jackie Leach Scully & Christoph Rehmann-Sutter, "When Norms Normalize: The Case of Genetic" Enhancement" (2001) 12:1 Human Gene Therapy 8.

over the past several years to include a broadening range of previously prohibited genetic interventions. Such a legal change pattern is *prima facie* inconsistent with the key legislative objectives and relevant international instruments, which seek to restrict these particular genetic interventions. Furthermore, the legal change pattern raises a number of significant problems such as ineffectiveness in accomplishing the key legislative goal of preventing a pattern in which the legal boundaries would become gradually laxer, the emergence of human heredity improvement practices and the associated human rights, societal and medical impacts. Additionally, the thesis provides insights into the potential drivers of the overextensive legal change. Finally, this thesis provides solutions to address the problem by offering a blueprint for law reform with applicable lessons and practical examples of how to redraw the rules with the aim of developing stronger and more effective legal boundaries. The contributions this thesis makes are essential to understanding the overextensive legal change problem, explaining its impacts, providing insights into its potential drivers and developing appropriate solutions. The task of developing effective legal governance solutions for the growing problem of the misuse of genetic intervention technologies is particularly important in the wake of a brave new world.

Chapter Two – Background

Prenatal Genetic Interventions: Technologies, Markets, and Political Ideologies

The idea of improving the hereditary traits of humankind has captured the imagination of thinkers throughout history. From classic antiquity to modern times, philosophers, authors and political leaders have fiercely debated the notion of directed heredity improvement - eugenics. This chapter clarifies what the often-misunderstood term eugenics entails and explains why it kept perplexing liberal legal systems for over a century. The elusiveness of the term eugenics¹²⁹ owes a great deal to the eugenic movement's complex history of reinvention in the face of an ever-changing political landscape. This chapter reviews the movement's transformation through the lens of intellectual history. This review shows that eugenics is not intrinsically wedded to any particular political ideology (such as authoritarianism, fascism, social democracy or libertarianism); rather, it changes certain tenets to better fit the spirit of the time. Furthermore, the intellectual history examination reveals certain enduring core tenets of eugenic thought, such as the employment of individual methods to pursue the collective improvement of the gene pools, the judgment of people's life's worth based on a hierarchy of bodily and cognitive traits and support at times for illiberal and coercive methods.¹³⁰ These enduring aspects of eugenics reveal some of the central issues that have perplexed liberal legal systems from the early 20th century well into the biotechnology era.

This chapter provides the reader with the essential intellectual, ethical and sociological foundations for understanding the legal restrictions on genetic interventions on the grounds of eugenics risks. First, the chapter explains that despite the current ethos of neo-eugenic practices as being entirely free and

¹²⁹ For more about the elusiveness of the concept see Dianne Paul, "Is Human Genetics Disguised Eugenics?" in D. Hull & M. Ruse, eds, *Philosophy of Biology* (Oxford: Oxford University Press, 1998).

¹³⁰ Like their predecessors, liberal eugenicists, despite what their name implies, still retain many elements of non-liberal, even coercive thinking, which is revealed through the close reading of its proponents' writings, which openly (but not often) advocate for certain forms of legally mandated eugenic programs.

voluntary, a myriad of societal, medical and legal pressures on individuals may veer them in the direction of what is perceived as ‘more desirable choices’ and produce in the long-term eugenic outcomes. Second, this chapter provides a broader context, useful to examining the legislative intent in enacting laws on genetic interventions such as concerns about neo-eugenic laden human rights risks including child commodification, instrumentalization and discrimination. Third, the chapter explains how the realities of growing sovereign debts, lower fiscal capacity and slower GDP growth could drive nations in the future to seek new ways to decrease health and social spending and to increase productivity levels by intervening in the markets for genetic interventions. Finally, this chapter explains the role of genetic intervention laws in either facilitating or preventing neo-eugenic practices, as they control which trait selection and modification are offered on the market. This chapter argues genetic intervention laws have a crucial role to play in either opening the door or preventing states in the future from being potentially involved in market-driven neo-eugenic practices.

I) Genetic Intervention Technologies’ Growing Capabilities of Shaping Reproductive Outcomes

“The advance of genetic engineering makes it quite conceivable that we will begin to design our own evolutionary progress.” – Isaac Asimov, *The Beginning and the End*

Transforming human capabilities through genetic modification may sound as if the idea belongs to the realm of science fiction, but biotechnology’s staggering progression rate is beginning to turn such scenarios into science fact. Genomic sciences are progressing toward understanding human genetic characteristics at a rapid pace that would stagger most spectators. Fertility regulators dismiss scenarios of human enhancement and extensive genetic modification as technologically unfeasible or far remote.¹³¹ Yet,

¹³¹ To illustrate, the HGC (the consulting body to the UK regulator, the HFEA) states that: “it may be the case that most fears of eugenics are unfounded, as they are based on unrealistic expectations of what can be achieved through genetic technology.” The HGC cites “practical limitations” to show that “the anxiety that PGD lies at the top of a slippery slope leading to the possibility of a wide range of potential enhancements, such as intelligence or beauty is misplaced.” United

advances in genetic science and model animal experiments have demonstrated the ability to significantly increase immunity, boost muscle mass and enhance cognitive abilities. Most of these technologies have not been applied to humans yet. Certain applications, such as choosing a child's cosmetic traits (e.g., eye colour, skin colour and height)¹³² are technologically feasible but generally not yet commercially available. Nonetheless, such applications of the technology face a number of legal, ethical and public opinion challenges as well as the various health risks that inheritable human genetic modification entails.¹³³ More potent enhancement options may become technologically feasible as genetic science is moving towards resolving many of the technical limitations, such as a limited understanding of the genome and the adverse effects of inheritable genetic modification. This review focuses on the rapid technological evolution of genetic interventions. It highlights that these technologies' use for "non-medical selection"¹³⁴ or enhancement purposes in the early stages of emergence. The constant developments in the field require a better understanding of emerging genetic intervention technologies as well as foresight about how re-engineering human biology could impact future individuals, families and society at large.¹³⁵

Kingdom, Human Genetics Commission, *Making Babies: Reproductive Decisions and Genetic Technologies* (London: HGC, 2006) para 31.

¹³² Professor, Lord Robert Winston, one of the first clinicians to perform pre-implantation genetic diagnosis warns that:

“We may find that people will want to modify their children, enhance their intelligence, their strength and their beauty and all the other so-called desirable characteristics...That will be a form of eugenics which will actually have all sorts of serious implications for developed societies.”

Quoted in Lyndsay Buckland, “Lord Robert Winston Warning Over Child “Eugenics”, *The Scotsman*, (18 March 2013) online: <http://www.scotsman.com/news/lord-robert-winston-warning-over-child-eugenics-1-2842227>

¹³³ I will discuss these various points in the next chapters and in chapter 8 in particular. The aim of this section is to offer a brief overview of emerging genetic intervention technologies and their potential uses.

¹³⁴ The use of genetic diagnosis for non-medical reasons (such as social sex selection) has initially emerged in countries such as the US, where there are no legal limits regarding trait selection. For more about non-medical sex selection offered by clinics in the US, see Sarah M. Capelouto, et al. "Sex Selection for Non-Medical Indications: A Survey of Current Pre-Implantation Genetic Screening Practices Among US ART Clinics" (2018) 35:3 J Assisted Repro & Genetics 409-416.

¹³⁵ For more about the importance of foresight studies to develop legal and policy solutions to better manage novel challenges raised by emerging technologies, see European Union, European Commission, *Lessons for Policy-making from Foresight in Non-European Countries* (Brussels: European Commission, 2015).

“Choosing Between Lives” – Pre-implantation Genetic Diagnosis

Assisted reproductive technologies have come a long way since the first successful in vitro fertilization in 1978 and are now charting new territories with the advent of advanced genetic technologies. In vitro fertilization (IVF) opened the door for the introduction of a number of assisted reproductive technologies. One of the key technologies that makes use of genetic analysis of the in vitro embryo is pre-implantation genetic diagnosis (PGD).¹³⁶ When the in vitro embryos are only a few days old and are a cluster of cells, one of the cells is removed through a form of biopsy and further analyzed for its genetic composition.¹³⁷ This analysis of the embryonic DNA then enables the lab and the prospective parents to select the most suitable IVF embryo based on its genetic characteristics.

Beyond Lethal Disease

The landscape of genetic intervention technologies has dramatically changed since the first genetic diagnosis was performed in 1990.¹³⁸ In the 1990s and early 2000s, genetic diagnosis was used for detecting lethal chromosomal abnormalities caused by a single gene. However, with the acceleration in the rate of genomic discoveries in the 2000s, genetic diagnosis began charting new grounds. Clinics started using the technology to detect more complex conditions influenced by multiple genes and by various environmental factors. The applications of genetic diagnosis are tied to the scientific endeavour of isolating genes and understanding their role in human physiology. Researchers have discovered gene groups linked with an

¹³⁶ Hereafter, I will use the term genetic diagnosis to refer to PGD.

¹³⁷ Anver Kuliev & Yury Verlinsky, “Thirteen Years’ Experience of Preimplantation Diagnosis: Report of the Fifth International Symposium on Preimplantation Genetics” (2004) 8:2 *Repro Biomed Online* 229.

¹³⁸ For a description of the first preimplantation genetic diagnosis – see Alan H Handyside et al., “Birth of a Normal Girl After in Vitro Fertilisation and Preimplantation Diagnostic Testing for Cystic Fibrosis” (1992) 327:13 *New Eng J Med* 905.

increased susceptibility to develop certain conditions later in life such as obesity,¹³⁹ type 2 diabetes,¹⁴⁰ schizophrenia,¹⁴¹ major depression¹⁴² and bipolar disorder.¹⁴³

Undergoing IVF¹⁴⁴ may no longer be a prerequisite for genetic interventions in the future due to a number of emerging technologies currently in pre-clinical and clinical trials.¹⁴⁵ These IVF bypassing reproductive technologies include the genetic modification of fetuses in the mother's womb,¹⁴⁶ the genomic editing of parents' gamete cells, which would then be reintroduced to their testes or fallopian tubes,¹⁴⁷ and the selection from potentially hundreds of embryos created from the parents' stem cells (artificial gamete

¹³⁹ E M Scott, A M Carter & P J Grant, "Association between Polymorphisms in the Clock Gene, Obesity and the Metabolic Syndrome in Man" (2008) 32:4 *Int'l J Obesity* 658.

¹⁴⁰ Grant FA Struan et al., "Variant of Transcription factor 7-like 2 (TCF7L2) Gene Confers Risk of Type 2 Diabetes" (2006) 38:3 *Nature Genetics* 320.

¹⁴¹ Aswin Sekar et al., "Schizophrenia Risk from Complex Variation of Complement Component 4" (2016) 530:7589 *Nature* 177; Peter Sætre et al., "The Tryptophan Hydroxylase 1 (TPH1) Gene, Schizophrenia Susceptibility and Suicidal Behavior: A Multi-Centre Case-Control Study and Meta-Analysis" (2010) 153:2 *Am J Med Genetics Part B: Neuropsychiatric Genetics* 387.

¹⁴² Naomi R. Wray et al., "Genome-Wide Association Analyses Identify 44 Risk Variants and Refine the Genetic Architecture of Major Depression." (2018) 50:5 *Nature Genetics* 668–81.

¹⁴³ International Schizophrenia Consortium, "Common Polygenic Variation Contributes to Risk of Schizophrenia and Bipolar Disorder" (2009) 460:7256 *Nature* 748.

¹⁴⁴ For more about the emotional, physical and financial costs of undergoing IVF see Chris M Verhaak et al., "Women's Emotional Adjustment to IVF: A Systematic Review of 25 Years of Research" (2006) 13:1 *Human Repro Update* 27-36. Also see Alex K Wu et al., "Time Costs of Fertility Care: The Hidden Hardship of Building a Family" (2013) 99:7 *Fertility and Sterility* 2025-2030.

Nonetheless, an examination of regional registries and IVF utilization data shows that about 5% of live births in Europe are from IVF. Official data from national registries show that over 1.5 million babies in Europe have been born following IVF procedures. See Christian De Geyter, et al. "ART in Europe, 2014: Results Generated from European Registries by ESHRE: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE)" (2018) 33:9 *Human Repro* 1586-1601.

¹⁴⁵ For an overview of these technologies see Sonia M Suter, "The Tyranny of Choice: Reproductive Selection in the Future" (2018) 5:2 *J L & Biosci* 262-300.

¹⁴⁶ See Avery C Rossidis, et al., "In Utero CRISPR-Mediated Therapeutic Editing of Metabolic Genes" (2018) 24:10 *Nature Med* 1513. See also Deepthi Alapati et al., "In Utero Gene Editing for Monogenic Lung Disease" (2019) 11:488 *Science Translational Med* eaav8375.

¹⁴⁷ Antonio Regalado, "Despite CRISPR Baby Controversy, Harvard University Will Begin Gene-Editing Sperm", MIT Tech. Rev. (29 November, 2018) online: <https://www.technologyreview.com/s/612494/despite-crispr-baby-controversy-harvard-university-will-begin-gene-editing-sperm/>

See also Nuffield Council on Bioethics (2018) *Genome Editing and Human Reproduction: Social and Ethical Issues* (London: Nuffield Council on Bioethics) 104-105 online: <http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-and-human-reproduction-FINAL-website.pdf>.

synthesis).¹⁴⁸ Not surprisingly, various experts such as demographers Malcolm Faddy et al.,¹⁴⁹ geneticist Lee Silver,¹⁵⁰ and legal scholar Hank Greely¹⁵¹ predict a significant increase in the percentage of children born as a result of genetic intervention technologies in the coming decades. The rapid evolution of reproductive biotechnology (which could make IVF not necessary in the future) will likely contribute to increased market uptake and consumer demand for new services, including for emerging non-medical applications.

In the past decade, genomic sciences have been moving from a medical research agenda towards the identification of genes that are linked to cosmetic, behavioural and cognitive traits. Notable examples include skin and hair colour in European populations,¹⁵² eye colour,¹⁵³ and height,¹⁵⁴ as well as genes linked to memory formation¹⁵⁵ and cognitive performance.¹⁵⁶ Furthermore, as genomic discoveries link human traits to their genomic origins, they theoretically increase the potential to select for and against certain genes and associated characteristics.¹⁵⁷

¹⁴⁸ For advances in the development of artificial gamete technology see for instance, Zheng, Yi, et al., "Controlled Modelling of Human Epiblast and Amnion Development Using Stem Cells" (2019) 573:7774 *Nature* 421-425.

¹⁴⁹ Malcolm J. Faddy, Matthew D. Gosden, & Roger G. Gosden, "A Demographic Projection of the Contribution of Assisted Reproductive Technologies to World Population Growth" (2018) 36:4 *Repro Biomed Online* 455-458.

Faddy et al's demographic estimate projects that by 2100, 3% of the world's population will be born as a result of IVF and related assisted reproductive technologies. Assisted reproductive technologies are projected to become more prevalent in the future owing to demographic trends such as lower fertility rates and rising maternal age.

¹⁵⁰ Nelly Donnell, *Breeding Out Disease*. In: 60 Minutes: CBS News, (Oct. 26, 2014) online: <https://www.cbsnews.com/news/breeding-out-disease-with-reproductive-genetics-2/>

¹⁵¹ Henry T. Greely, *The End of Sex and The Future of Human Reproduction* (Cambridge: Harvard University Press, 2016).

¹⁵² Patrick Sulem et al, "Genetic Determinants of Hair, Eye and Skin Pigmentation in Europeans" (2007) 39:12 *Nature Genetics* 1443 Hysi supra note 26.

¹⁵³ Richard A Sturm et al supra note 27.

¹⁵⁴ Hana Lango Allen et al supra note 28. See also Avery L Lello et al., "Accurate Genomic Prediction of Human Height" (2018) 210:2 *Genetics* 477-497.

¹⁵⁵ Annette Milnik et al. supra note 29.

Also note that the authors suggest that one of the applications of their study about the KIRBA protein is a better understanding of its role in the potential development of Alzheimer's disease.

¹⁵⁶ See Aysu Okbay et al. supra note 30. See also Max Lam et al., "Large-Scale Cognitive GWAS Meta-Analysis Reveals Tissue-Specific Neural Expression and Potential Nootropic Drug Targets" (2017) 21:9 *Cell Reports* 2597.

¹⁵⁷ Armand Marie Leroi, "The Future of Neo-Eugenics" (2006) 7:12 *EMBO reports* 1185-1187.

Genetic diagnosis technology is presently limited in selecting traits such as eye and skin colour if these traits do not exist in the parental genome. However, a number of established and emerging technologies are able to extend the use of genetic diagnosis for biological enhancement purposes. First, genetic diagnosis has been used in conjunction with egg and sperm donation to produce children with certain desirable traits such as physical characteristics, height and preferred gender.¹⁵⁸ Second, genetic diagnosis can be used in conjunction with genomic prediction technologies to estimate the likelihood of an embryo to have certain cosmetic traits such as a specific chin shape, eye colour and skin tone.¹⁵⁹ In 2018, Dr. Jeffery Steinberg become one of the first clinicians to use genomic prediction technologies in conjunction with genetic diagnosis to offer prospective parents the ability to choose their future children's eye colour.¹⁶⁰ Third, emerging in-vitro gametogenesis technologies could be used to create enhanced children by directly selecting and mating embryos in a controlled lab setting.¹⁶¹

¹⁵⁸ See for instance Carolyn Abraham, "Unnatural Selection: Is Evolving Reproductive Technology Ushering in A New Age of Eugenics?" *Globe and Mail*, (January 7, 2012), online: <http://www.theglobeandmail.com/life/parenting/unnatural-selection-is-evolving-reproductive-technology-ushering-in-a-new-age-of-eugenics/article1357885/?page=3>

¹⁵⁹ Inmaculada de Melo-Martín, "Valuing Reprogenetic Technologies: Bringing Insights from the Philosophy of Technology to Bioethics" In: Laspra B., López Cerezo J. eds *Spanish Philosophy of Technology* (Cham: Springer, 2018) 45-58. Jennifer Couzin-Frankel, "New Company Pushes the Envelope on Pre-Conception Testing" (2012) 338 *Science* 315-316. See also Laura DeFrancesco, "23andMe's Designer Baby Patent" (2014) 32:8 *Nature Biotech* 8.

In the same vein, a US company is currently developing a predictive test to rank embryos based on their estimated IQ score. See Julianna LeMieux, "Polygenic Risk Scores and Genomic Prediction: Q&A with Stephen Hsu", *Genetics, Engineering & Biotechnology News* (April 1, 2019) online: <https://www.genengnews.com/insights/polygenic-risk-scores-and-genomic-prediction-qa-with-stephen-hsu/>

¹⁶⁰ Amy Dockser Marcus, "Is it ethical to Choose Your Baby's Eye Color" *The Wall Street J* (October 2, 2018) online: <https://www.wsj.com/articles/is-it-ethical-to-choose-your-babys-eye-color-1538487936> See also Dr. Steinberg's clinic website: Dr. Jeffery Steinberg, "Choose Your Baby's Eye Color", *The Fertility Institutes* online: <https://www.fertility-docs.com/programs-and-services/pgd-screening/choose-your-babys-eye-color.php>

¹⁶¹ Sparrow describes in vitro gametogenesis as:

"the deliberate breeding of human beings in vitro by fusing sperm and egg derived from different stem-cell lines to create an embryo and then deriving new gametes from stem cells derived from that embryo. Repeated iterations of this process would allow scientists to proceed through multiple human generations in the laboratory. In vitro eugenics might be used to study the heredity of genetic disorders and to produce cell lines of a desired character for medical applications. More controversially, it might also function as a powerful technology of 'human enhancement' by allowing researchers to use all the techniques of selective breeding to produce individuals with a desired genotype."

In Robert Sparrow, "In Vitro Eugenics" (2014) 40:11 *Ethics* 725-731.

Through repeated iterations of mating between chosen in-vitro embryos, labs go through generations of embryos in a rapid process that could produce selective breeding like results of creating genetic gains and improving traits of interests.¹⁶² Yet above all, the key technology that has the potential for producing individuals with an enhanced phenotype is inheritable genetic modification.¹⁶³

Inheritable Modification of the Human Genome

Inheritable genetic modification enables interested parties to customize a newborn's genetic identity to a significantly greater degree by erasing undesirable genetic traits and replacing them with desirable ones.¹⁶⁴ Unlike genetic diagnosis, which only enables passive embryo selection, genetic modification enables deleting traits and inserting new genetic material that does not exist in the parental genome. Children who are genetically modified will have genetic materials inherited outside of the two biological parents. Altering future children's genome to have more than two biological parents' raises psychological, sociological, and ethical questions.¹⁶⁵ The source of genetic materials for more desirable traits would come from outside of the

¹⁶² See Tetsuya Ishii & Mitunori Saitou, "Promoting in Vitro Gametogenesis Research with a Social Understanding" (2017) 23.11 Trends in Molecular Med 985-988; Sonia M. Suter, "In Vitro Gametogenesis: Just Another Way to Have a Baby?" (2016) 3:1 J L & Biosci at 87-119.

¹⁶³ Please note, in this thesis, I will chiefly use the term inheritable genetic modification to refer to the alteration of the human germline genome as opposed to somatic gene therapy.

Somatic gene therapy is a distinct technology, which involves the alteration of genetic materials in somatic cells (a category that comprises of the vast majority of human cells with the notable exception of sperm and ova cells). Unlike germline genetic modification, changes to the somatic DNA are highly unlikely to be inherited by subsequent generations. There are important ethical, legal and medical differences between somatic and germline genetic modification. For more detail, see chapter 9.

As of 2020, a number of companies working on bringing new somatic gene therapies to the market. Such somatic gene therapies would be potentially indicated for congenital diseases, cancers and blood disorders. See Martina C. Cornel et al., "Moving towards A Cure in Genetics: What Is Needed to Bring Somatic Gene Therapy to The Clinic?" (2019) 27:3 Eur J Hum Genetics 484; Alireza Shahryari et al., "Development and Clinical Translation of Approved Gene Therapy Products for Genetic Disorders" (2019) 10:868. Frontiers in Genetics, doi:10.3389/fgene.2019.00868; Annette Bak et al., "Translating Cell and Gene Biopharmaceutical Products for Health and Market Impact Product Scaling from Clinical to Marketplace: Lessons Learned and Future Outlook" (2019) 108:10 J Pharmaceutical Sciences 3169-3175.

¹⁶⁴ Jürgen Habermas suggests that genetic modification will eventually replace genetic diagnosis as the technology of choice. Genetic modification enables the parents to go beyond passive selection between embryos and actively choose traits that do not exist in the genome. Habermas supra note 41 at 69-70.

¹⁶⁵ Françoise Baylis, "The Ethics of Creating Children with Three Genetic Parents" (2013) 26:6 Repro Biomed Online 531.

parental genome. Additional genes can come from a third human parent (or more), but the newly added genes can also come from organisms that are non-human.¹⁶⁶

Picture– A Newborn Transgenic Monkey with Green Fluorescent Protein Genes from a Jellyfish ¹⁶⁷



The above picture shows a transgenic rhesus monkey that was genetically modified to have a green fluorescent protein (GFP) gene from a jellyfish. The GFP gene makes the newborn monkey glow green under UV light. This newborn is one of the few monkeys born as a result of the Oregon State University experiment, as more than 98 percent of the other embryos and fetuses in that experiment failed to develop or died.¹⁶⁸

The first reported case of a genetically modified child reveals the commercial interests in these emerging markets. In September 2016, Darwin Life, an American biotechnology company has modified the

¹⁶⁶ Geneticists are conducting exploratory work on transgenic genetic modification to examine its potential therapeutic applications. For instance, research is conducted to examine if inserting certain genes taken from blue lobsters could have anti-aging properties and genes from salamanders could potentially confer novel regenerative abilities. For more about the potential uses of animal genomics in human health see for instance Ahmed Elewa et al, "Reading and Editing the *Pleurodeles waltl* genome Reveals Novel Features of Tetrapod Regeneration" (2017) 8:1 Nature Comm, 2286.

¹⁶⁷ Picture taken from MIT Technology Review – See Katherine Bourzac, "A Nobel for Illuminating Biology Three Chemists are Honored For Discovering And Developing A Glowing Jellyfish Protein", *MIT Tech Rev* (October 8, 2008) , online: <https://www.technologyreview.com/s/410953/a-nobel-for-illuminating-biology/>

¹⁶⁸ Anthony W. S. Chan, et al., "Transgenic Monkeys Produced by Retroviral Gene Transfer into Mature Oocytes" (2001) 291:5502 Science 309-312.

mitochondrial (non-nuclear) genome of human embryos for reproductive purposes using genetic materials from commercially purchased egg cells.¹⁶⁹ The American team has genetically modified the selected embryo on US soil but implanted the embryo in a woman's womb in Mexico.¹⁷⁰ In an interview with MIT Technology Review, the Head Clinician and the CEO of Darwin Life says he will not stop at treating disease but he intends to use genetic modification to “enable parents to choose their baby's hair or eye colour, or perhaps to improve the child's IQ.”¹⁷¹ He adds “Everything we do is a step towards designer babies...With nuclear transfer and gene editing together, you can really do anything you want.”¹⁷²

Physical Modification

Genetic modification has the potential of changing inborn physical characteristics that are predominantly determined by genetic factors. In order to understand the transformative power of genetic modification technology, consider an example involving a genetically modified mouse from a Harvard research study. The Harvard team originally intended to study how to recreate damaged muscle tissue in humans. To that end, the researcher added two copies of the MSTN gene, encoding the Myostatin inhibitor protein, which regulates muscle growth in various organisms.¹⁷³ The experiment, which knocks out a gene

¹⁶⁹ John Zhang et al., “First Live Birth Using Human Oocytes Reconstituted by Spindle Nuclear Transfer for Mitochondrial DNA Mutation Causing Leigh Syndrome” (2016) 106:3 Fertility and Sterility e375.

¹⁷⁰ As of 2020, US law does not formally prohibit human genetic modification. However, various regulatory approaches are being discussed.

For more on the topic of the American team using the lax Mexican laws to preform genetic modification see Chan, S & M Medina Arellano, “Genome Editing and International Regulatory Challenges: Lessons from Mexico” (2016) 2:3 Ethics, Medicine and Public Health 426; César Palacios-González and Medina-Arellano María de Jesús, ‘Mitochondrial Replacement Techniques and Mexico’s Rule of Law: On the Legality of the First Maternal Spindle Transfer Case’ (2017) 4:1 J L & Biosci 50-69; and Tetsuya Ishii, ‘Mitochondrial Replacement Techniques and Mexico’s Rule of Law: On the Legality of the First Maternal Spindle Transfer Case’ (2017) 4:2 J L & Biosci 384-390.

¹⁷¹ Emily Mullin, “A Pioneering Doctor Wants to use A Three-Parent IVF Technique to ‘Cure Infertility’ In Older Women”, *MIT Tech Rev* (13 June, 2017), online: <https://www.technologyreview.com/s/608033/the-fertility-doctor-trying-to-commercialize-three-parent-babies/>.

¹⁷² *Ibid.*

¹⁷³ Myostatin inhibition is considered to develop through the process of evolution to prevent rampant muscle growth that would consume the body’s satellite cells, which can cause to bodily injury, disease and malnourishment. For example, see

encoding for the Myostatin protein, also more than doubled muscle growth in the mouse,¹⁷⁴ leading the research team to refer to their creation as the “Schwarzenegger” mouse.¹⁷⁵ Other research teams have replicated the outcome of creating animals with abnormal muscle mass in dogs,¹⁷⁶ and non-human primates.¹⁷⁷ Such results could also be reproduced in humans.¹⁷⁸ Aside from increases in muscle mass, researchers were also able to increase overall athletic abilities and running stamina in animal models. By modifying the PEPCK-C metabolic enzyme, the genetically modified mice were able to run nearly two times faster than those in the control group. Once again, the scientists at the Case Western lab nicknamed its PEPCK-C knockout mouse “Mighty Mouse” for its unusual athletic prowess.

Such demonstrations of the potency of genetic alterations make genetic modification a perfect candidate for the creation of high-performing athletes.¹⁷⁹ Dr. Lee, one of the developers of the Schwarzenegger mouse, has since received numerous calls from coaches and athletes asking to volunteer to be patient zero for athletic enhancement.¹⁸⁰ If such a form of genetic modification were to be applied to human embryos, it would dwarf the current ethical debate regarding athlete doping.

Astrid Breitbart et al, “Myostatin from the Heart: Local and Systemic Actions in Cardiac Failure and Muscle Wasting” (2011) 300:6 *Am J Physiology. Heart and Circulatory Physiology* H1973.

¹⁷⁴ Antonio Musaro et al. *supra* note 31.

¹⁷⁵ William J. Cromie, “Gene Boosts Muscle Strength: Mighty Mice Raise Hopes for A Stronger Life,” *Harv Gazette* (February 11, 1999), online: <http://news.harvard.edu/gazette/1999/02.11/muscle.html>

¹⁷⁶ Dana S Mosher et al, “A Mutation in the Myostatin Gene Increases Muscle Mass and Enhances Racing Performance in Heterozygote Dogs” (2007) 3:5 *PLoS Genet* e79.

¹⁷⁷ Janaiah Kota et al, “Follistatin Gene Delivery Enhances Muscle Growth and Strength in Nonhuman Primates” (2009) 1:6 *Science Translational Med* 15.

¹⁷⁸ Eric Smalley, “FDA Warns Public of Dangers of DIY Gene Therapy” (2018) 36 *Nature Biotech* 119-120.

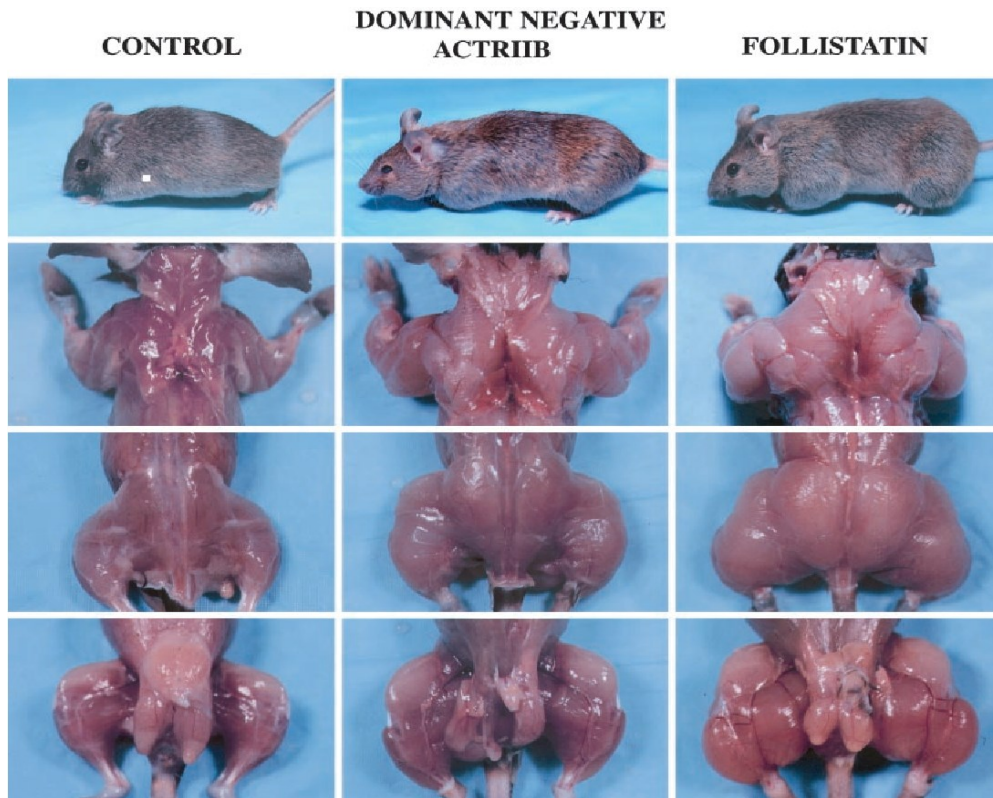
¹⁷⁹ Danielle Simmons, “Genetic Inequality: Human Genetic Engineering” (2008) 1:1 *Nature Education* 2.

¹⁸⁰ Melinda Wenner, “How to Be Popular during the Olympics: Be H. Lee Sweeney, Gene Doping Expert”, *Scientific American*, (August 15, 2008) online: <https://www.scientificamerican.com/article/olympics-gene-doping-expert/>.

Also note that Sweeney has developed another commercial product that can be used and abused by athletes to significantly gain muscle mass. This technology uses a synthetic, lab created gene that encodes the IGF-1 (insulin-like growth factor 1). According to a recent US Supreme Court decision, synthetic genes can be patented. See *Association for Molecular Pathology et al. v. Myriad Genetics, Inc., et al.* 133 S. Ct. 2107 (2013).

Picture – The Genetically Modified, MSTN Knockout “Schwarzenegger Mouse”¹⁸¹

The head of the Harvard research team that created the Myostatin mouse rejects the idea of eventually using such genetic modifications to physically enhance future persons.¹⁸²



Cognitive Modification

Genetic modification can go beyond enhancing physical features to also alter genetically influenced cognitive traits. The prospects of influencing cognitive characteristics increases as scientists study and uncover the role of genetics in neurological function. One study created a transgenic mouse with a gene that increased the amount of type-1 adenylyl cyclase enzyme in the mouse’s forebrain, the location responsible for hippocampus-based recognition memory and long-term memory.¹⁸³ This line of research could

¹⁸¹ Image taken from National Academy of Science, See Se-Jin Lee & Alexandra C. McPherron, “Regulation of Myostatin Activity and Muscle Growth” (2001) 98:16 Proceedings of the National Academy of Sciences 9306.

¹⁸² See William J. Cromie *supra* note 167.

¹⁸³ Hongbing Wang et al, “Overexpression of Type-1 Adenylyl Cyclase in Mouse Forebrain Enhances Recognition Memory and LTP” (2004) 7:6 Nature Neuroscience 635.

potentially be translated to applications in humans since the genetic basis for the cellular machinery of memory appears to have been conserved through the process of mammalian evolution.¹⁸⁴ In another study, a Brown University team, which added an extra pair of the NR2B subunit of the NMDA neuroreceptor (responsible for lower brain plasticity), was able to nearly double the cognitive performance of mice in solving complex puzzles.¹⁸⁵ In a more recent study, a team of British and Canadian scientists attempted to develop therapeutic strategies to combat neurodegenerative diseases such as Alzheimer's by modifying the activity of the phosphodiesterase-4B enzyme (PDE4B) in mice. The genetically modified mice exhibited an increase in their learning ability, memory retention, and problem-solving abilities.¹⁸⁶

Genetic modification of human neurological functions again blurs the distinction between therapy and enhancement. Attempting to treat neurological diseases might seem like a valuable therapeutic endeavour, but it may also prove to be a strategy for cognitive enhancement. For example, to study neurodegenerative diseases, scientists modified rhesus and marmoset monkey genomes by inserting specific human brain genes.¹⁸⁷ The modified monkeys developed human neurodegenerative diseases such as Huntington,¹⁸⁸ Parkinson,¹⁸⁹ and Sporadic Alzheimer's.¹⁹⁰ In another experiment, transgenic human-monkeys were further

¹⁸⁴ Susanne Edelhoff et al, "Mapping of Adenylyl Cyclase Genes Type I, II, III, IV, V, and VI in Mouse" (1995) 6:2 Mammalian Genome 111.

¹⁸⁵ Ya-Ping Tang et al, "Genetic Enhancement of Learning and Memory in Mice" (1999) 401:6748 Nature 63.

¹⁸⁶ Alexander McGirr et al, "Specific Inhibition of Phosphodiesterase-4B Results in Anxiolysis and Facilitates Memory Acquisition" (2015) 41:4 Neuropsychopharmacology 1-2.

¹⁸⁷ The topic of admixed human-monkey hybrids raises a number of important ethical concerns, primarily relating to crossing species boundaries. Nevertheless, this thesis focuses solely on the question of genetic interventions in humans. For additional detail about the ethics of "humanizing" chimeric animal models, see Insoo Hyun, "What's Wrong with Human/Nonhuman Chimera Research?" (2016) 14:8 PLOS Biology e1002535.

¹⁸⁸ Anthony WS Chan et al, "A Two Year Longitudinal Study of a Transgenic Huntington Disease Monkey" (2014) 15:1 BMC Neuroscience 36.

¹⁸⁹ Reona Kobayashi et al, "α-Synuclein Aggregation in the Olfactory Bulb of Middle-Aged Common Marmoset" (2016) 106 Neuroscience Research 55.

¹⁹⁰ Leticia Forny-Germano et al., "Alzheimer's Disease-Like Pathology Induced by Amyloid-B Oligomers in Nonhuman Primates" (2014) 34:41 J Neurosci 13629. See also Danielle Beckman, et al., "Oligomeric Aβ in the Monkey Brain Impacts Synaptic Integrity and Induces Accelerated Cortical Aging" (2019) 116:52 Proceedings of the National Academy of Sciences at 26239-26246.

genetically modified, resulting in reduced rates of development of neurodegenerative diseases. At the same time, these animal models saw a significant increase in cognitive abilities.¹⁹¹ The King's College research team behind the research recognizes that, aside from potential therapeutic benefits such as the prevention of neurodegenerative diseases, these findings can also lead to human cognitive enhancement.¹⁹²

Behavioural Modification

Animal model studies demonstrate the potential for genetic modifications for significant behavioural alteration. Using novel methods, scientists are able to study behavioural neurology with greater precision by examining the particular neural activity patterns in the brains of genetically modified animal models.¹⁹³ For example, by modifying genes related to the hippocampus function, scientists were able to create mice that exhibited false memories, potentially relating to high-stress related events that never existed.¹⁹⁴ In the hope of finding gene therapy for Obsessive Compulsive Disorder, scientists found a way to make mice develop obsessive behaviours.¹⁹⁵ In another study, researchers were able to identify certain sets of genes that increase and decrease mice's aggressive impulses.¹⁹⁶

Genetic modification experiments demonstrate particular success in changing behavioural patterns

¹⁸² Michael R. Johnson et al, "Systems Genetics Identifies a Convergent Gene Network for Cognition and Neurodevelopmental Disease" (2015) 19 :2 *Nature Neuroscience* 4205

¹⁹² *Ibid.*

This deep entanglement of therapy and enhancement is also significant in the legal context. In chapter 7, I will show how genetic modification to potentially reduce the susceptibility to Alzheimer's disease may become a backdoor to approving prohibited genetic enhancements.

¹⁹³ See Karl Deisseroth, "Optogenetics: 10 Years of Microbial Opsins in Neuroscience" (2015) 18:9 *Nat Neurosci* 1213; Elizabeth E Steinberg et al., "Illuminating Circuitry Relevant to Psychiatric Disorders with Optogenetics" (2015) *Curr Opin Neurobiol* 9; Yoav Adam et al., "Voltage Imaging and Optogenetics Reveal Behaviour-Dependent Changes in Hippocampal Dynamics" (2019) 569:7756 *Nature* 413-417.

¹⁹⁴ Steve Ramirez, et al., "Creating a False Memory in the Hippocampus" (2013) 341:6144 *Science* 387.

¹⁹⁵ Kerri Smith, "Compulsive Behaviour Triggered and Treated" *Nature News*, (06/06/2013) online: <http://www.nature.com/news/compulsive-behaviour-triggered-and-treated-1.13144>.

¹⁹⁶ Yanli Zhang-James et al. "An Integrated Analysis of Genes and Functional Pathways for Aggression in Human and Rodent Models" (2019) 24:11 *Molecular Psychiatry* 1655-1667.

arising from the brain reward system (basal ganglia structures), which are more evolutionarily hard-wired, such as sexual behaviour, pleasure-seeking behaviours and tendencies to develop addictions.¹⁹⁷ Genetic modification of the D2 gene, which encodes dopamine receptors responsible for the reward centre in the brain, was able to turn lazy monkeys into “workaholics.”¹⁹⁸ In another study, researchers genetically altered the polygamous meadow vole vasopressin receptor gene allele to a copy of its closely related, but monogamous, prairie vole. The experiment resulted in the polygamous vole becoming monogamous.¹⁹⁹ Genetic modification of the alleles of the vasopressin receptor gene, which is responsible for the brain’s reward centre, may also play a role in human drug addiction and other behavioural patterns.²⁰⁰

Yet even if behavioural genomics becomes fully understood, human behaviour is still hard to control. Human behaviour is an extremely complex result of biological and environmental factors.²⁰¹ Even extensive genetic modification of behavioural genes would not ensure that the child would exhibit the desired behavioural patterns. Habermas, who is aware of this critique, suggests that greater control of future children’s behaviour can be achieved by combining both genetic and behavioural methods simultaneously. Habermas raises an example of a child genetically designed to have both a high aptitude and inclination toward music as well as a tendency toward being a dedicated worker.²⁰² Gregory Stock, a UCLA biophysicist, agrees with Habermas on the point that prospective parents in the future would combine educational and

¹⁹⁷ Vivek R Athalye et al., “Evidence for a Neural Law of Effect” (2018) 359:6379 *Science* 1024.

¹⁹⁸ Zheng Liu et al., “DNA Targeting of Rhinal Cortex D2 Receptor Protein Reversibly Blocks Learning of Cues That Predict Reward” (2004) 101:33 *PNAS* 12336.

¹⁹⁹ Miranda M Lim, et al., “Enhanced Partner Preference in A Promiscuous Species by Manipulating the Expression of a Single Gene” (2004) 429:6993 *Nature* 754.

²⁰⁰ David M. Kaplan, *Readings in the Philosophy of Technology* (Plymouth: Rowman & Littlefield Publishers, 2009) at 419.

²⁰¹ Nevertheless, geneticists estimate that about 50% of personality traits have genetic origins. See for instance a large meta-analysis about the heritability of human personality traits, see Sandra Sanchez Roige et al., “The Genetics of Human Personality” (2018) 17:3 *Genes, Brain & Behav* e12439.

²⁰² Habermas *supra* note 41.

genetic interventions to “behaviourally enhance” their children.²⁰³

Genetic Technologies and Genetic Perfectionism

The possibility of influencing newborn genetic traits before birth is growing as genomic science and technology are charting new grounds, such as the modification of multiple genes simultaneously. The emerging feasibility of the modification of multiple genes simultaneously²⁰⁴ rebuts arguments that complex, multigene traits such as height or IQ cannot be eventually altered. Moreover, advances in synthetic biology are pushing genetic modification research in novel and uncharted ways, to engineering novel genetic traits that do not exist in nature.²⁰⁵ MIT synthetic biologist, Eric Lander, and colleagues write that novel methods of genetic enhancement include: “incorporating new instructions into a person’s genome to enhance, say, their memory or muscles, or even to confer entirely new biological functions, such as the ability to see infrared light or break down certain toxins.”²⁰⁶ The “[f]ather of Synthetic Genomics”, Cal-Tech geneticist Robert Siensheimer, discussed artificial gene synthesis technologies’ potential eugenic uses. Siensheimer stated that “the old eugenics was limited to a numerical enhancement of the best of our existing gene pool, The horizons of the new eugenics are in principle boundless for we should have the potential to create new genes and new qualities yet undreamed...Indeed, this concept marks a turning point in the whole evolution of life.”²⁰⁷ This

²⁰³ See for instance, Gregory Stock, *Redesigning Humans: Our Inevitable Genetic Future* (New York: Houghton Mifflin, 2002), 119-122.

²⁰⁴ For more about new technology to edit the genome at multiple locations, See Bernd Zetsche et al., "Multiplex Gene Editing by CRISPR–Cpf1 using a Single crRNA Array" (2017) 35:1 *Nature Biotech* 31; Meru J. Sadhu et al., "Highly Parallel Genome Variant Engineering with CRISPR–Cas9" (2018) 50:4 *Nature Genetics*, 510.

²⁰⁵ See for instance Eric S. Lander, “Brave New Genome” (2015) 373:1 *New Eng J Med*, 5; George M. Church & Ed Regis, *Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves* (New-York: Basic Books, 2014); See also Antonio Regalado, “Rewriting Life - Plan to Fabricate a Genome Raises Questions on Designer Humans”, MIT Tech Rev, (June 2, 2016) online: <https://www.technologyreview.com/s/601610/plan-to-fabricate-a-genome-raises-questions-on-designer-humans/>

²⁰⁶ Eric S. Lander et al., "Adopt a Moratorium on Heritable Genome Editing" (2019) 567:7747 *Nature* 166.

²⁰⁷ Quoted in Nathaniel Comfort, *The Science of Human Perfection: How Genes Became the Heart of American Medicine* (New Haven: Yale University Press, 2012) at 1983.

Promethean promise of genetic technologies to ultimately “redesign” and “improve” human biology raises novel ethical, legal and societal issues of an unprecedented nature. Emerging biotechnologies’ growing abilities to influence and seemingly improve future generations’ physiological, cosmetic, cognitive and behavioural genetic traits reveal these technologies’ eugenic dimensions.

II) Eugenics and Transhumanism – The Ideologies of Directing Human Evolution

“History does not repeat itself, but it often rhymes” – Mark Twain²⁰⁸

As early as classical antiquity, the Athenian philosopher Plato advocated for schemes of governing the reproduction of the masses to promote the heredity excellence of the city-state. At the apex of the Platonic social order stands the Guardian class, a class of people endowed with the greatest physical and intellectual faculties.²⁰⁹ The hereditary eliteness of the Guardian class serves as the central pillar of a greater political regime, a stratified society ruled by the ablest, most intelligent and competent elites. Such a class of people would eventually be produced if the regime was empowered to direct human reproduction so that the physically and intellectually ablest men and women reproduce exclusively.

The idealized Platonic society would also be free of many weaknesses that plague populations, such as diseases, mental or physical disabilities. Those with weak physical or mental powers would be prohibited from procreation altogether because that weakness runs in their bloodlines.²¹⁰ Plato calls for collective action for the purity of the public blood “that otherwise would have to waste endless effort on sickly and refractory beasts, degenerate by nature and ruined by incompetent breeding.”²¹¹ The “inferior stock” is not just

²⁰⁸ Quoted in James George Eayrs, *Diplomacy and Its Discontents* (Toronto: University of Toronto Press, 1971) at 121.

²⁰⁹ Plato, *the Republic, Book I* (New York: Basic Books, 1991) at 82.

²¹⁰ James Adam, *The Republic of Plato* [vol 1] (Cambridge: Cambridge University Press, 1965) at 357.

²¹¹ See Plato, *The Laws* (Indianapolis: Hackett Publishing Company 1997) at 735–736. For commentary see also CH Güvercin & Berna Arda, “Eugenics Concept: From Plato to Present” (2015) 14:2 Hum Repro & Genetic Ethics 23.

diseased—it should be considered a (*Nosema*) “disease” that is plaguing the “body politic”. The body politic must not be allowed to succumb to the illness, it must cure itself.²¹² The means to cure the societal malaise that affects the masses is through the collective governance of procreation.

Plato was concerned that the masses would reject organized measures to govern their procreation, especially if they knew that the true purpose of such measures would further serve the interests of the aristocracy and entrench a class system. Hence, Plato advised that the public should not be made aware of the true intention of such procreation schemes or even understand the way they are governed.²¹³ For Plato, despite the scheme’s greater collectivist goals, the public must be taught to believe they participate in procreative arrangements on a voluntary basis. To that end, the governing class will spread a “noble lie”, intended to conceal the true intent of procreation governance measures and teach the public to believe they undertake a part in it voluntarily.²¹⁴

Historic eugenic practices, such as infanticide, which were prevalent in Hellenic city-states and Rome, began to lose their traction toward the beginning of the medieval ages.²¹⁵ With the rise of Christianity, new ethics that considered all life sacred has become the dominant mode of thinking in Western societies. For centuries, the once-accepted eugenics worldview faded into the background or was rejected altogether.²¹⁶ However, in Victorian England, the eugenic movement once again found new intellectual foundations essential for its reestablishment.

²¹² *Ibid.*

²¹³ David J. Galton, “Greek Theories on Eugenics” (1998) 24:4 J Med Ethics 263.

²¹⁴ Plato, *supra* note 209 at 84.

²¹⁵ Allen George Roper, *Ancient Eugenics: The Arnold Prize Essay for 1913* (Cookham: Cliveden Press, 1913).

²¹⁶ Mika Ojakangas, “Michel Foucault and the Enigmatic Origins of Bio-politics and Governmentality” (2012) 25:1 Hist Hum Sciences 6.

Survival of the Fittest

In his seminal 1859 work *On the Origin of Species*, Charles Darwin introduced the idea that species evolve according to natural selection, which weeds out disadvantageous traits and leaves advantageous traits, helping organisms to better adapt to their environment.²¹⁷ In 1864, Darwin's peer, Sir Herbert Spencer, coined the phrase "the survival of the fittest," to describe Darwin's theory in its application to both to the animal world and human society alike.²¹⁸ Spencer's theories became the key force behind the intellectual movement of social Darwinism, a movement that aimed at reducing the number of people with "unfit" hereditary traits while increasing those with "fit" traits. The social Darwinism movement sought to recreate the conditions of natural selection in human society so as to put human evolution on a beneficial course. For society and for the species to progress, the birth of the unfit ought to be prevented.²¹⁹ Therefore, benevolent social policies such as extending health care and education to those deemed unfit ironically would end up hurting society. The unfit, who would decrease in number under natural conditions, end up multiplying, consuming more resources, and thus weakening the society that supports them.²²⁰ Hence, society must resist such benevolent urges and let the fittest, the best of human stock, emerge as victorious in the social and

²¹⁷ Charles Darwin, *On the Origin of Species by Means of Natural Selection, Or, the Preservation of Favoured Races in the Struggle for Life* (London: J. Murray, 1859).

²¹⁸ Gregory Claeys, "The 'Survival of the Fittest' and the Origins of Social Darwinism" (2000) 61:2 J Hist Ideas 223.

Darwin himself felt uncomfortable with the application of his theories to humankind. In *The Origin of Species*, Darwin explained that natural selection governed the process of evolution in those that were most capable of adapting to their natural environment. It is important to state that Darwin was also uncomfortable with Spencer's term "the survival of the fittest" or the application of this maxim to human society.

²¹⁹ Herbert Spencer, *The Man versus the State: With Four Essays on Politics and Society* (1884) (London: Penguin Books, 1969). Quoted in RC Bannister, *Social Darwinism: Science and Myth in Anglo-American Social Thought* (Philadelphia: Temple University Press, 1979).

²²⁰ Robert Evans, "In Search of Social Darwinism. The Historiography of the Concept" in M. Berg and G. Cocks eds, *Medicine and Modernity. Public Health and Medical Care in Nineteenth and Twentieth Century Germany* (Cambridge: Cambridge University Press, 1997).

economic competition with the unfit.²²¹

To better govern collective gene pools, scientist and statistician Sir Francis Galton sought to develop a new applied science of human biological improvement.²²² In 1883, Galton coined the term “eugenics” (from the Greek words *Eu*, meaning “good” and *Genos* meaning “birth”) to describe the scientific study of the improvement of the human race.²²³ Ultimately, Galtonian eugenics aimed at realizing the social Darwinists’ goals of improving those “ablest race” traits of health, appearance, intelligence, and moral behaviour.²²⁴ To achieve these ends, Galton chiefly relied on various methods of selective breeding along with population statistics in order to measure and track the progress of human improvement.²²⁵ Central to Galtonian eugenics (and later eugenics) is the concept of “normalcy,”²²⁶ which refers to the idea that qualities can be measured, compared, and ranked according to their position in a hierarchical order of human characteristics. Prospective mates should thus be compared based on their ranking on the scale of human

²²¹ The social darwinistic concept of fitness might seem outdated or harsh, but modern thinkers still embrace such rhetoric. For example, see Ingmar Persson & Julian Savulescu, *Unfit for the Future: The Need for Moral Enhancement* (Oxford: Oxford University Press, 2012).

²²² Galton himself, was deeply influenced by the theory developed by his cousin Charles Darwin. Note that Galton himself was against state coerced eugenic policies. See for instance Francis Galton, “Letter to William Bateson, commenting that knowledge of heredity would be of little practical help to eugenics progress” Wellcome Library (6/12/1904). See also Nathaniel Comfort supra note 207 at 1866-1869.

²²³ Richard Barnett, “Eugenics” (2004) 363:9422 the Lancet 1742.

²²⁴ Nicholas W Gillham, “Sir Francis Galton and the Birth of Eugenics” (2001) 35:1 Ann Rev Genetics, 98. For social Darwinism and Galtonian eugenics, see Robert L. Carneiro, *The Evolution of Society; Selections from Herbert Spencer’s “Principles of Sociology”* (Chicago: University of Chicago Press 1967) at xxix.

²²⁵ See Randall Hansen & Desmond King, *Sterilized by the State: Eugenics, Race, and the Population Scare in Twentieth-Century North America* (New York: Cambridge University Press, 2013) at 33.

²²⁶ Lennard J Davis, *Enforcing Normalcy: Disability, Deafness, and the Body* (London: Verso, 1995) at 30.

For a race-based analysis of the eugenic movement see Zanita E. Fenton, “Disability Does Not Discriminate: Towards a Theory of Multiple Identity Through Coalition” in David Connor, Beth Ferri & Subini Aannamma, *DisCrit: Disability Studies and Critical Race Theory in Education* (New-York: Teachers College Columbia University Press 2016) at 206-208. See also the writings of legal scholar Dorothy E. Roberts on the racial and post-racial aspects of 20th century eugenics and new reproductive genetic technologies - Dorothy E. Roberts, “Opinion- Eugenics is Still a Dangerous Idea” The Philadelphia Inquirer (May 1, 2019) online: <https://www.inquirer.com/opinion/commentary/eugenics-in-america-timeline-medicine-20190501.htm>; and see Dorothy E. Roberts, “Race, Gender, And Genetic Technologies: A New Reproductive Dystopia” (2009) 34:4 Signs: J Women Culture & Soc’y 783-804.

qualities. The median in the distribution of qualities (such as height and IQ) marks normalcy.²²⁷ The “unfit” are those who deviate and are deemed sub-normal. Unfit people often fall below the median score in the ranking of expected normal level capabilities.²²⁸ Negative eugenics ultimately seeks to decrease the number of people with sub-par hereditary traits. The groups commonly targeted for the elimination of their genes from the pool often included people with mental illness, those with mental and physical disabilities, people with substance abuse problems, homeless people and criminals. Positive eugenics, on the other hand, aims to increase the number of people who are above the median in physical and intellectual capabilities. The concepts of positive and negative eugenics are a historical mirror image of the later therapy/enhancement distinction in bioethics, which similarly measures people based on a notion of species-typical functioning. Positive eugenics mirrors the modern concept of enhancement while negative eugenics partially corresponds with therapeutic aims.²²⁹

Social Darwinism and Galtonian eugenics also had their contemporary critics. One of the most famous was biologist Thomas Huxley, a close friend of Darwin and a notable popularizer of his theories.²³⁰ Thomas Huxley enthusiastically supported biological Darwinism but rejected social Darwinism, which he saw as a perversion of Darwin’s theories. For Huxley, human beings cannot be equated to animals, which, in the wild, are subject to harsh evolutionary pressures of natural selection against ill-adapted members.

²²⁷ Francis Galton, *Probability, and the Foundation of Eugenics: The Herbert Spencer Lecture Delivered on June 5, 1907* (Oxford: Clarendon Press, 1907).

²²⁸ David Levy & Sandra Peart, “The Tale of Galton’s Mean: The Influence of Experts” (2002) 113:3 *Public Choice* 357-359.

²²⁹ See Allen Buchanan et al, *From Chance to Choice: Genetics and Justice* (Cambridge, UK: Cambridge University Press, 2001) at 105.

Note that the negative/positive eugenics distinction does not fully mirror the therapy/enhancement distinction. First, genetic diagnosis is arguably not therapeutic because it does not treat, but rather discards embryos. Second, disability scholar Tom Shakespeare opines that genetic diagnosis should not be regarded as a negative eugenics method when it is used to prevent the birth of putative children with early-onset lethal congenital malformations. Putative children with early onset lethal congenital malformations such as Tay-Sachs would even reach an age they can procreate. See Tom W. Shakespeare, “Choices and Rights: Eugenics, Genetics and Disability Equality” (1998) 13:5 *Disability & Soc’y* 671-673

²³⁰ Tim M Berra, *Charles Darwin: The Concise Story of an Extraordinary Man* (Baltimore, MD: Johns Hopkins University Press, 2009) at 71.

Humankind, though, has transcended natural selection—human intellect and civilization have created a sheltered ecosystem akin to a well-tended garden or a greenhouse.²³¹ A sustained human flourishing thus could not be achieved by cultivating a superior strain of humans that would dominate others but rather by improving living conditions for all humanity.²³²

Huxley, a pioneer in evolutionary ethics, further criticized the irresponsibility of the eugenic ideal to direct the course of humankind's evolution and correct human flaws. For Huxley, the idea that the human species could be continuously improved through eugenic methods is misguided to begin with,²³³ and attempts to direct the path of human evolution would end up creating more harm than good.²³⁴ Huxley discusses how leaders would distort the steering force of directed evolution because of their limited intelligence and the pursuit of self-interest. The politics of reshaping humankind are likely to be governed by shortsighted dictums by elites, which could lead the evolution of the species to unintended and undesirable consequences.²³⁵ Thus, human attempts to direct their future evolution would spoil what eons of natural selection had carefully crafted.

Eugenics and the State

The eugenic vision finally came to its political realization in the early decades of the twentieth century, first starting in liberal democracies such as the United States, Canada (in Alberta and British Columbia) and

²³¹ Herbert Spencer, "Social Statistics", in Alan S Weber eds, *Nineteenth-Century Science: An Anthology* (Calgary: Broadview Press, 2000) at 429.

²³² Thomas Henry Huxley, "The Struggle for Existence in Human Society" (1888) 23:16180 *the Nineteenth Century* 195.

²³³ Thomas Henry Huxley, *Evolution and Ethics: And Other Essays* (New-York: D. Appleton, 1902).

²³⁴ Brian K Hall Monroe W. Strickberger & Benedikt Hallgrímsson, *Strickberger's Evolution* (Sudbury Mass: Jones & Bartlett Learning, 2011).

²³⁵ Thomas Henry Huxley Supra note 233.

Scandinavian countries.²³⁶ These Western democracies began to enact laws establishing governmental education and the promotion of “better” mating among fit adults, licensed marriages based on genetic “suitability,” immigration restrictions for unfit populations and coercive sterilizations.²³⁷ Such measures demonstrate how even constitutional democracies derogated from key human rights such as bodily integrity, equality, and dignity in the name of improving the gene pools.²³⁸

Instead of safeguarding essential human rights, notable political and legal figures supported eugenics measures, explaining that the heredity improvement of future generations serves the greater good. This collectivist mindset is reflected in the words of the Alberta Premier in 1929: “The argument of freedom or right of the individual can no longer hold good where the welfare of the state and society is concerned.”²³⁹ The Chairman of the Alberta Eugenics Board, Dr. John A. MacEachran, envisioned the end-goal of eugenic legislation to be the promotion of the Platonic ideal of a perfected society governed by an elite class of the most excellent and intelligent men.²⁴⁰ In a similar vein, in the landmark case of *Buck v Bell*, the US Supreme Court ruled that the Virginia Sterilization Act, which mandated the compulsory sterilization of people with disabilities, was constitutional. Justice Holmes defended his decision, asserting that: “[s]ociety can prevent those who are manifestly unfit from continuing their kind . . . Three generations of imbeciles are enough.”²⁴¹

Nazi Germany took the eugenic ideal to its most radical manifestation to date. Under the Law for the Prevention of Genetically Diseased Offspring 1933 (which was modelled after the California Sterilization

²³⁶ Daniel J. Kevles, “Eugenics and Human Rights” (1999) 319:7207 *Brit Med J* 435. See also Gunnar Broberg & Nils Roll-Hansen, *Eugenics and the Welfare State* (Ann Arbor: University of Michigan Press, 1996) at 108. See also Angus McLaren, *Our Own Master Race: Eugenics in Canada, 1885–1945* (Toronto: University of Toronto Press, 2015).

²³⁷ Kevles *supra* note 2 at 117.

²³⁸ *Ibid.*

²³⁹ Timothy J. Christian & Burke M. Barker, *The Mentally Ill and Human Rights in Alberta: A Study of the Alberta Sexual Sterilization Act* (Edmonton: Faculty of Law, University of Alberta, 1973).

²⁴⁰ Douglas Wahlsten, “Leilani Muir versus the Philosopher King: Eugenics on Trial in Alberta” (1997) 99:2-3 *Genetica* 185.

²⁴¹ *Buck v. Bell*, 274 U.S. 200 (1927).

Act)²⁴² more than 300,000 people with disabilities were sterilized. The rationale behind state coerced sterilizations was that people with disabilities' defective hereditary traits lead to continued and undue burdens on public resources. Still, Nazi Germany carried these policies much further than Western democracies; and actively pursued the death of those who to them, were deemed to be genetically defective. More than 300,000 people were euthanized in the Aktion T4 program²⁴³ and millions lost their lives in acts of genocide.²⁴⁴ The Rome Statute of the International Court stipulates that such eugenic practices amount to crimes against humanity.²⁴⁵

Shocked by the human rights violations of the Nazi regime as well as other Western countries, public opinion turned against the once-accepted movement.²⁴⁶ Since the 1940s, eugenic legislation and practices lost much of their popular support. The appearance of the civil rights movement in the 1950s further contributed to the demise of the eugenic movement, which was viewed as highly contrary to the empowerment of repressed and marginalized groups. Between the 1960s and the 1970s, most Western democracies began abolishing their eugenic legislation.²⁴⁷ Owing to growing public disdain, eugenicists, who once were a part of

²⁴² Stefan Kühl, "The Cooperation of German Racial Hygienists and American Eugenicists Before and After 1933" in the *Holocaust and History the Known, the Unknown, the Disputed and the Reexamined*, Berenbaum and Abraham, eds, (Bloomington: Indiana University Press, 1998) 135-137.

²⁴³ Initially, the Nazi regimen started the Aktion T-4 as a "compassionate" program to ease the suffering of psychiatric patients and people with disabilities by ending their lives. See Henry Friedlander, *The Origins of Nazi Genocide: From Euthanasia to the Final Solution* (Chapel Hill: University of North Carolina Press, 2000).

²⁴⁴ Kevles supra note 2.

²⁴⁵ Gary L Albrecht, *Encyclopedia of Disability* (Thousand Oaks: SAGE Publications, 2005) 492.

Note that Article 7 (1) (g) of the Rome Statute of the International Criminal Court prohibits eugenic practices in general. Article 7 (1) (g) inspired similar prohibitions on eugenic practices (and genetic interventions in particular) in the Oviedo Convention and in the European Union Charter of Fundamental Rights. See Great Britain: Parliament: The Application of the EU Charter of Fundamental Rights in the UK: A State of Confusion House of Commons: European Scrutiny Committee (London: The Stationery Office, 2014).

²⁴⁶ Frank Dikötter, "Race Culture: Recent Perspectives on the History of Eugenics" (1998) *Am Hist Rev* 467; Clare Hanson, *Eugenics, Literature, and Culture in Post-war Britain* (New York: Routledge, 2013), 124-125; Kate Elizabeth Rogers, "Healthy Aspirations? Crypto-eugenics and the Aim to Create Healthy Families in Australia, 1946-1970s" (2018) 23:1 *Hist Fam* 54.

²⁴⁷ Mathew Thomson, "Disability, Psychiatry, and Eugenics" in Alison Bashford & Philippa Levine, eds, *the Oxford Handbook of the History of Eugenics* (Oxford: Oxford University Press, 2010) 124. Paul A. Lombardo, "Medicine, Eugenics, and the Supreme Court: From Coercive Sterilization to Reproductive Freedom" (1996) 13 *J Contemp Health L & Pol'y* 24.

mainstream discourse, went underground.

Eugenics by Other Names: The Birth of Crypto-Eugenics

In the 1950s, the eugenic movement went underground due to strong public discontentment.²⁴⁸ To avoid negative public opinion, eugenicists decided to drop the use of the then scorned word eugenics. General Frederick Osborn was a leading force behind dropping the eugenic moniker and replacing it with scientific, technological or market-oriented labels.²⁴⁹ As Osborn explained, “[e]ugenic goals are most likely to be attained under a name other than eugenics”.²⁵⁰ Osborn’s recommendations were translated into actions. Underground eugenicists have moved in larger numbers into the then-emerging disciplines of social biology, family planning and genetic counseling.²⁵¹ In academic circles, examples of such language change can be seen in the renaming of *Eugenics Quarterly* to the *Journal of Social Biology* and the *Annals of Eugenics* became the *Annals of Human Genetics*.²⁵²

Frederick Osborn laid the foundations for crypto-eugenics, the notion that eugenics can once again be popular if marketed to the masses correctly and by avoiding the damaged brand of eugenics. In a sense, Osborn’s crypto-eugenics echo Plato’s concept of the “Noble Lie” of concealing the intent of eugenics but readapt the concept to fit with modern practices of mass media and consumerism. In his lecture titled

Also note the landmark decision in *E. (Mrs.) v. Eve*, in which the Supreme Court of Canada ruled that the sterilization of intellectually disabled patients for non-therapeutic purposes should never be approved under the *parens patriae* jurisdiction. See *E. (Mrs.) v. Eve*, [1986] 2 S.C.R. 388.

²⁴⁸ Alison Bashford & Philippa Levine, *The Oxford Handbook of the History of Eugenics* (New York: Oxford University Press, 2010) at 164-166; Anne-Emanuelle Birn & Natalia Molina, “In the Name of Public Health” (2005) 95:7, *Am Pub Health J* at 1096.

²⁴⁹ Edmund Ramsden, “Eugenics from the New Deal to the Great Society: Genetics, Demography and Population Quality” (2008) 39:4 *S Hist & Phil Biological and Biomed Sciences* 391.

²⁵⁰ Frederick Osborn, *The Future of Human Heredity: An Introduction to Eugenics in Modern Society* (New-York: Weybright and Talley, 1968) at 25.

²⁵¹ Alexandra Minna Stern, *Eugenic Nation: Faults and Frontiers of Better Breeding in Modern America* (Berkeley: University of California Press, 2005) at 4. Clare Hanson *supra* note 246; Rogers *supra* note 246.

²⁵² Calum MacKellar & Christopher Bechtel, *The Ethics of the New Eugenics* (Berghahn Books: New York, 2014) at 7.

“Galton and Mid-Century Eugenics”, Osborn described the importance of disguising the eugenic intent of the scheme when attempting to convince and market eugenics to the public.²⁵³ The public must not know that their reproductive choices in their children’s hereditary traits further the eugenic agenda. Rather the public must view these as purely individual choices and their very own ideas.²⁵⁴ In his 1968 book *The Future of Human Heredity: An Introduction to Eugenics in Modern Society*, Osborn expressed the view that “[m]easures for improving the hereditary base of intelligence and character can be made effective on a voluntary basis without arousing in the individual any conscious concern for eugenics results.”²⁵⁵

Reinventing a Movement

Public disdain for eugenic ideas has meant that the movement has changed and reinvented itself to regain popularity and validity. In the transition period between historical eugenics and neo-eugenics, key thinkers introduced three main changes to help adapt the movement to the ever-changing social and political zeitgeist. First, neo-eugenicists began focusing on what were then purely experimental genetic interventions on embryos, which they often found to be less ethically problematic.²⁵⁶ Second, neo-eugenicists viewed genetic interventions as a consumer product that supposedly should be free of any state interventions or regulation. Third, transhuman neo-eugenicists view the goal of the movement more broadly than merely improving upon human flaws but utterly transcending the biological boundaries of the species.

²⁵³ Frederick Osborn, “Galton and Mid-Century Eugenics” (1956) 48:1 *Eugenics Rev* 15.

²⁵⁴ Sheldon C. Reed, “The Local Eugenics Society” (1957) 9:1 *Am J Hum Genetics* 1.

²⁵⁵ Osborn, *supra* note 250 at 104.

²⁵⁶ For example, for a discussion about early eugenic proponents of genetic technologies, see Demetrio Neri, “Eugenics,” *Encyclopedia of Applied Ethics, Volume 2* (San Diego, CA: Academic Press, 1998) 161. In particular, note biologist Robert Sinsheimer, who coined the term “new eugenics.” See also Robert L. Sinsheimer, “Prospects for Future Scientific Developments: Ambush or Opportunity?” (1972) *Hastings Ctr Rep* 4.

The Transhumanist Ideology – A Call for Transcending Human Biological Limitations

A key development in the resurgence of neo-eugenic thinking was the introduction of the transhumanist concept. Transhumanism originates from the works of Julian Huxley, a member of the renowned Huxley family²⁵⁷ and the president of the British Eugenics Society.²⁵⁸ In his 1957 book, *New Bottles for New Wine*, Julian Huxley describes the aims of the transhumanist movement as “a deliberate effort [of humankind] to transcend itself—not just sporadically . . . but in its entirety as humanity.”²⁵⁹ While Galtonian eugenics aimed to direct evolution to create the best stock of humans, transhumanism seeks to transcend human limitations by crossing species’ boundaries and forming a new and altogether improved species.²⁶⁰ For transhumanists, evolution has left the human species incomplete, ridden with many inherent defects: disease, intellectual limitations, immoral behaviour, and tendencies toward aggression and mass social upheaval.²⁶¹ Only through conscious, gradual steering of the evolutionary process will our species be cleansed of its inherent defects. In the very long term, genetically enhanced humans will evolve to such a degree biologically that they will have transcended humanity to become a new, post-human species, reaching a new apex in faculties.²⁶²

A Brave New World?

Aldous Huxley, drawing on his brother’s Julian’s eugenic utopian vision, authored the highly

²⁵⁷ Julian Huxley was the grandson of Thomas Henry Huxley. Unlike his grandfather who was an opponent of eugenic policies, Julian Huxley was a notable proponent of eugenics.

²⁵⁸ Jeff Pruchnic, *Rhetoric and Ethics in the Cybernetic Age: The Transhuman Condition* (New York: Taylor & Francis, 2013) 10.

²⁵⁹ Julian Huxley, “New Bottles for New Wine: Ideology and Scientific Knowledge” (1950) 80:1/2 J Royal Anthropological Institute of Great Brit and Ireland 23.

²⁶⁰ Kevles supra note 2 at 176.

²⁶¹ Nick Bostrom, “Human Genetic Enhancements: A Transhumanist Perspective” (2003) 37:4 J Value Inquiry 493.

²⁶² See Stefan Lorenz Sorgner, “Nietzsche, the Overhuman, and Transhumanism” (2009) 20:1 J Evolution & Tech 29; Nick Bostrom, “A History of Transhumanist Thought” (2005) 14:1 J Evolution & Tech 7-8; 19-20.

acclaimed, dystopian novel *Brave New World*.²⁶³ Aside from a celebrated literary career, Aldous Huxley was also a technology theorist.²⁶⁴ In his 1962 Berkeley University lecture, Aldous Huxley warned of future government and corporate involvement in behaviour control and modification technologies that might lead to a rather invisible form of social control.²⁶⁵ In particular, state and corporate involvement in genetic design could steer citizens toward being less antisocial and criminal while increasing their productive output.²⁶⁶ Aldous Huxley has envisioned a future of stratified eugenics, in which different classes would be further differentiated by their use of specific eugenic methods. The lower classes would only be screened for genetic disease, while only a small elite group of people could be fully genetically enhanced to occupy more prominent social positions.²⁶⁷ Unlike his peer, George Orwell, Aldous Huxley's critique of eugenics was less concerned with an authoritarian use of technology to oppress the masses.²⁶⁸ Instead, Aldous Huxley was more concerned with a Platonic ideal of eugenics, in which subtle, indirect, yet powerful messages, well ingrained into cultural, social, and economic structures rather invisibly direct citizens to adopt practices of offspring perfection to serve state and industry interests.²⁶⁹

²⁶³ Aldous Huxley, *Brave New World* (London: Chatto & Windus Publishers Ltd, 1932).

²⁶⁴ See Julian Huxley, "Transhumanism" (2015) 6:1 *Ethics in Progress* 12; Tom Koch, "Enhancing Who? Enhancing What? Ethics, Bioethics, and Transhumanism" (2010) 35:6 *J Med & Philo*, 686-687; 690-692; Hava Tirosh-Samuelson, "Science and the Betterment of Humanity: Three British Prophets of Transhumanism" (2012) *Building Better Humans* 55-56.

²⁶⁵ Aldous Huxley, "The Ultimate Revolution" 269 *Berkeley Language Center—Speech Archive SA* (March 20, 1962).

This situation in which citizens are directed toward having children with more desirable traits oddly resembles the Platonic idea of eugenics as private reproductive choices end up serving the perceived greater good of the society. As Aldous Huxley warned, this brave new world of soft, invisible eugenics is more problematic than state-run eugenics because such reproductive schemes become well normalized and entrenched in social and economic structures, making them, in many senses, harder to resist.

²⁶⁶ Aldous Huxley, *Brave New World Revisited* (New York: Rosetta Books, 2010).

²⁶⁷ States already offer the masses cheaper means (selective abortions) to prevent the birth of children with disabilities.

²⁶⁸ Neil Postman, *Amusing Ourselves to Death: Public Discourse in the Age of Show Business* (New York: Penguin Books, 2006) at xix.

²⁶⁹ Arvin R. Wells, "Huxley, Plato and the Just Society" (1980) *Centennial Rev* 475.

The Consumer Market for Child Genetic Perfection

The neo-eugenic ideology has refocused its efforts on the genetic improvement of the populace by turning to a model of delivery based on consumer markets. Osborn envisioned that the key to reviving eugenics was to move from a statist model to a consumer-driven model.²⁷⁰ Additionally, Osborn emphasized the role of the mass media in influencing consumer tastes to promote the aims of eugenics. Once the public internalizes eugenic values (e.g., designer children) as a consumer good, the aims of the movement will be served by the markets.²⁷¹ The idea of the “genetic supermarket” was championed by Robert Nozick, one of the intellectual forefathers of modern libertarianism. In his 1974 book, *Anarchy, State and Utopia*, Nozick hypothesized that the “genetic supermarket” would emerge once genetic technologies become sufficiently advanced and commercialized.²⁷²

A New Eugenics?

Around the turn of the millennium, the eugenics movement resurfaced openly, adopting a new moniker and a seemingly new ideological tenet: liberal eugenics. Liberal eugenicists maintain that while state involvement in eugenic programs is reprehensible, consumer-led eugenics is morally justifiable (as well as praiseworthy).²⁷³ Contemporary eugenicists often assert their rejection of any form of state involvement and their wishes to empower consumers in their choice for better children.²⁷⁴ Supporters of liberal eugenics and other consumer allies often call for the deregulation of genetic interventions to allow parents to genetically

²⁷⁰ MacKellar & Bechtel *supra* note 252 at 7.

²⁷¹ Frederick Osborn, *Preface to Eugenics* (New York: Harper & Bros., 1951).

²⁷² Robert Nozick *supra* note 5.

²⁷³ See Nicholas Agar, *Liberal Eugenics: In Defence of Human Enhancement* (Cornwall: Blackwell Publishing, 2004); Buchanan et al *supra* note 229; See also Daniel Wilker, “Can We Learn from Eugenics?” (1999) 25:2 J Med Ethics 1. Wilker argues that while historical state coercion was reprehensible, the eugenic goal itself of improving human biological characteristics is commendable.

²⁷⁴ Arthur L Caplan, Glenn McGee & David Magnus, “What is Immoral about Eugenics?” (1999) 171:5-6 West J Med, 336; Ramez Naam, *More Than Human: Embracing the Promise of Biological Enhancement* (New York: Broadway Books, 2005) 27–31; Peter Sloterdijk, *Rules for the Human Park* (Frankfurt am Main: Suhrkamp Verlag, 1999) at 10–13, 25–29.

design their children as they please.²⁷⁵ Having utterly free markets would provide a morally justifiable form of eugenics, as parents could select the appearance, cognitive abilities, and behavioural traits for their children's benefit.²⁷⁶ Liberal eugenicists espouse an ideal of a free market in which consumers make free and autonomous choices. However, is the ideal of reproductive decisions being free of any undue influence or coercion achievable in a more complex reality in which prospective parents are subject to a host of legal, political, economic and cultural pressures to select children with a more "ideal" genetic profile?

III) Neo-Eugenic Ideology and the Pressures to Genetically Intervene

Neo-eugenicists claim that genetically enhanced children will enjoy better education, labour, and life prospects²⁷⁷ as well as having a positional advantage over other, non-enhanced populations.²⁷⁸ Genetically enhanced people will be able to translate their advantageous social and economic position to access still better education, career prospects, and various markets (including the market for further enhancement).²⁷⁹ Furthermore, as with wealth, the genetically enhanced will intergenerationally replicate their advantages bypassing their genetic enhancements directly to the genomes of their offspring.²⁸⁰ Genetic enhancements thus present enormous advantages to the upper echelons of society that will be able to afford these costly

²⁷⁵ John Harris "Taking the "Human" Out of Human Rights" (2011) 20:1 Cambridge Q Healthcare Ethics 9-20; Andy Miah, "Towards the Transhuman Athlete: Therapy, Non-therapy and Enhancement" (2010) 13:2 Sport in Soc'y: Cultures, Commerce, Media, Politics, 221-233; Julian Savulescu & Guy Kahane, "The Moral Obligation to Create Children with the Best Chance of the Best Life" (2009) 23:5 Bioethics 274-290.

²⁷⁶ Collin Gavaghan, *Defending the Genetic Supermarket: The Law and Ethics of Selecting the Next Generation* (Oxford: Taylor & Francis, 2007) at 9.

²⁷⁷ Dov Fox, "The Illiberality of Liberal Eugenics" (2007) 20:1 Ratio 6.

²⁷⁸ Ronald M Green, *Babies by Design: The Ethics of Genetic Choice* (New Haven, CT: Yale University Press, 2007) at 73.

²⁷⁹ Ronald Lindsay, "Enhancements and Justice: Problems in Determining the Requirements of Justice in a Genetically Transformed Society" (2005) 15:1 Kennedy Institute of Ethics J 36-38.

Note that other eugenicists assert that genetic enhancements will not only benefit the enhanced individuals but also society at large. Society stands to gain from this group of people with genetically enhanced intellectual abilities, who will also have a greater aptitude to govern the masses.

²⁸⁰ Peter Singer, "Shopping at the Genetic Supermarket" In S. Y. Song, Y. M. Koo & D. R. J. Macer, eds, *Asian Bioethics in the 21st Century* (Tsukuba: Eubios Ethics Institute, 2003) at 153.

technological advantages.²⁸¹

The promise of genetic enhancement may prove too good to resist, especially because failing to enhance one's child will impair the child's ability to compete with their technologically enhanced peers. When competing against genetically-enhanced children, regular, non-enhanced children will be in a position of relative inferiority. First, such competitive disadvantages would result from the high likelihood that genetically enhanced children might perform better than those who are not physically or cognitively enhanced. The non-enhanced people may end up suffering from reduced social statuses, social mobility, and overall limited prospects as they find it increasingly hard to compete with their enhanced peers.²⁸² Second, in an age of human enhancement, unenhanced children would suffer from the perception that they are less capable than their enhanced peers, which can also lead to discrimination.²⁸³ Both discriminatory attitudes and a possible real gap in capabilities, then, would put the unenhanced in a position of relatively reduced social status, fewer

²⁸¹ Also note that various critiques suggest that the benefits of genetic interventions will be extremely unequally distributed, captured mostly by the very wealthy. See Micheal Mehlman, *Wondergenes: Genetic Enhancement and the Future of Society* (Bloomington: Indiana University Press, 2003).

²⁸² Michael H. Shapiro, "The Impact of Genetic Enhancement on Equality" (1999) 34 Wake Forest L Rev 561. See also Soumya Kannan & Devora Najjar, "Therapeutic Gene Editing Is Here, Can Regulations Keep Up?" (2020) 1 MIT Sci Policy Rev 68.

Even a self-dubbed eugenicist such as Bostrom openly acknowledges the likelihood of genetic enhancement leading to extreme socio-economic gaps. He writes:

"The mobility between the lower and the upper classes might disappear, and a child born to poor parents, lacking genetic enhancements, might find it impossible to successfully compete against the super-children of the rich. Even if no discrimination or exploitation of the lower class occurred, there is still something disturbing about the prospect of a society with such extreme inequalities."

See Nick Bostrom, *supra* note 261 at 505.

²⁸³ See Francis Fukuyama, *Our Posthuman Future: Consequences of the Biotechnology Revolution* (New York: Macmillan, 2003) 97.

The literature has provided evidence that the phenomena of discrimination based on genetics already exist in the present. See Yann Joly et al., "Genetic Discrimination and Life Insurance: A Systematic Review of the Evidence" (2013) 11:1 BMC Med, 25; See also Yvonne Bombard et al., "Beyond the Patient: The Broader Impact of Genetic Discrimination among Individuals at risk of Huntington Disease" (2012) 159:2 Am J Med Genetics Part B: Neuropsychiatric Genetics 217. See also Elizabeth Penziner, et al., "Perceptions of Discrimination among Persons Who Have Undergone Predictive Testing for Huntington's Disease" (2008) 147:3 Am J Med Genet B Neuropsychiatr Genet 320–325.

employment opportunities and diminished prospects.²⁸⁴

Given such negative prospects, even parents who disagree with genetic enhancement might be left with few options but to enhance their children.²⁸⁵ Stock, an avid supporter of neo-eugenics, agrees that parents will choose to enhance their children when faced with the choice of their child being far inferior to their enhanced peers.²⁸⁶ Michael Sandel argues that this looming dynamic of being forced to choose between genetic superiority and being left behind does not represent a free choice between two viable options.²⁸⁷ The situation in which some parents would decide to enhance their children would create a genetic arms race that would draw unwilling parents into a competition they originally sought to avoid but are now strongly compelled to participate in.²⁸⁸

Proactive Beneficence – Liberal Eugenics’ Duty to Have the Best Possible Child

The core assumptions of liberal eugenics are built around the notion that genetic interventions are completely voluntary,²⁸⁹ yet proponents of liberal eugenics claim parents have an obligation to genetically intervene on behalf of their children.²⁹⁰ The parental duty to genetically improve their children’s genetics in order to give them the best available genes is dubbed by Julian Savulescu “procreative beneficence.”²⁹¹

²⁸⁴ United States Congress House Committee on Foreign Affairs Subcommittee on Terrorism, Nonproliferation supra note 9.

²⁸⁵ Lory P Knowles & Gregory E Kaebnick, *Reprogenetics: Law, Policy, and Ethical Issues* (Baltimore, MD: Johns Hopkins University Press, 2007) at 97.

²⁸⁶ Gregory Stock supra note 203 at 147.

²⁸⁷ Michael Sandel, *The Case against Perfection: Ethics in the Age of Genetic Engineering*, 2nd ed. (Cambridge Mass: Belknap Press of Harvard University Press, 2009).

²⁸⁸ Michael J. Selgelid, “Ethics and Eugenic Enhancement” (2003) 1:4 Poiesis & Praxis 259.

²⁸⁹ Nicholas Agar, “Liberal Eugenics” (1998) 12:2 Pub Aff Q 10.

²⁹⁰ Peter Singer supra note 280. See also Julian Savulescu & Guy Kahane supra note 275 at 283. John Harris, John Harris, *Enhancing Evolution: The Ethical Case for Making Better People* (Princeton: Princeton University Press, 2010).

²⁹¹ As I will show later in the thesis, interviews and surveys reveal that a group of prospective parents subjectively feels they have a duty for “procreative beneficence”, creating the best genetic outcomes in their future child. I will further explore how the drive to increase profits and reduce liability promote a state of mind of “procreative duty” among physicians and prospective parents. In chapter 5, I will further link the emerging duty of “procreative beneficence” to

Savulescu argues that the duties of procreative beneficence include customizing children's genomes to give them the best possible health and the greatest cognitive capabilities and behavioural traits. Savulescu suggests that such favourable behavioural traits could include mothering tendencies in girls, along with the selection of gender and even an acceptable sexual orientation.²⁹² More specifically, Jonathan Glover claims that parents have a duty to genetically intervene to prevent the birth of children with disabilities, such as intellectual or sensory impairments, as these children have diminished life opportunities and will not be able to enjoy the same degree of flourishing as an able child.²⁹³ Furthermore, Peter Singer argues that parents who do not avoid having children with impairment should be charged by the state with child neglect.²⁹⁴ The fact that neo-eugenicists call for entirely voluntary participation while simultaneously imposing a duty to participate highlights the contradiction. Liberal eugenicists' imposition of a duty to genetically intervene takes them far from the liberal tradition and brings them considerably closer to the views of their historic counterparts.²⁹⁵

The supposed duty for genetic improvement of children already works on both an individual and an institutional level. The combination of medical professionals' views and the way choice architecture is laid out produces a sense of parental duty to avoid having a child with an abnormal genetic profile. An opinion survey that included more than 3,000 medical professionals found that 74 percent believe they have a duty

pressures by prospective parents to access susceptibility screening even when the likelihood is virtually does not exist or even 0%, out of the concerns their bloodline is tainted by genetic disease.

A study by Kalfoglou et al. indicate an emerging parental feeling of duty as 51.5 percent of respondents agreed with the premise that "parents ought to do everything technologically possible to prevent their child from suffering including using reproductive genetic technologies". See Andrea L. Kalfoglou et al., *Reproductive Genetic Testing: What America Thinks* (Washington: Genetics and Public Policy Center, 2004).

²⁹² See Julian Savulescu, "Procreative Beneficence: Why We Should Select the Best Children" (2001) 15:5-6 *Bioethics* 413; Julian Savulescu & Guy Kahane supra note 275 at 275-276; Julian Savulescu, "Sex Selection: The Case for" (1999) 171:7 *Med J A* 373-375. Brian D. Earp, Anders Sandberg & Julian Savulescu, "Brave New Love: The Threat of High-Tech "Conversion" Therapy and the Bio-Oppression of Sexual Minorities" (2014) 5:1 *AJOB Neuroscience* 4-12.

²⁹³ Jonathan Glover, *Choosing Children: Genes, Disability, and Design* (Oxford: Oxford University Press 2006) at 33.

²⁹⁴ Peter Singer, supra note 280 at 147.

²⁹⁵ Robert Sparrow, "A Not-So-New Eugenics" (2011) 41:1 *Hastings Ctr Rep* 33.

to prevent the birth of children with disabilities.²⁹⁶ Despite guidelines for nondirective advice,²⁹⁷ contradictory practices exist,²⁹⁸ such as genetic counsellors implying desired outcomes through approving and disapproving body language and medical staff providing selective information based on the outcomes they see as most beneficial.²⁹⁹ The patient-physician discourse about genetic interventions serves as a means of socializing prospective parents and attempts to obligate them to make their reproductive choices in light of the knowledge imparted by medical experts,³⁰⁰ who often point out the genetic risks of congenital defects. The mere knowledge of genetic health risks generates a form of “genetic responsibility” and obligations to avoid unwanted conditions.³⁰¹ Physicians’ reassurances reinforce the mother’s obligation to undergo prenatal genetic testing as part of her duty toward her future child’s health.³⁰²

The Greater Collective Goals behind Individual Consumer Eugenics

Despite the consumerist rhetoric that focuses on individual choices and benefits,³⁰³ the writings of neo-eugenicists reveal a much broader goal of the collective improvement of the gene pools. As with Platonic

²⁹⁶ Dorothy C. Wertz, “Eugenics Is Alive and Well: A Survey of Genetic Professionals around the World” (1998) 11:3–4 *Sci in Context* 493.

²⁹⁷ See Council of Europe Comm. of Ministers of the Council of Europe, Recommendation No. R (90) 13 on Prenatal Genetic Screening, “Prenatal Genetic Diagnosis & Associated Genetic Counselling” (1990) 41 *Int'l Dig. Health Legis.* 615.

²⁹⁸ See for instance, Barbara A. Bernhardt, “Empirical Evidence that Genetic Counseling is Directive: Where Do We Go from Here?” (1997) 60:1 *Am J Hum Genetics* 17.

²⁹⁹ See for instance, Helen B., Betty B. Hoskins & Michael Gross, *The Custom-Made Child? Women-Centered Perspectives* (Berlin: Springer Science & Business Media, 2012) at 97-98.

³⁰⁰ Nikolas Rose *supra* note 7.

³⁰¹ Thomas Lemke, “Susceptible Individuals and Risky Rights: Dimensions of Genetic Responsibility” In J. Dumit & V. Burri, eds, *Biomedicine as Culture. Instrumental Practices, Technoscientific Knowledge, and New Modes of Life* (London: Routledge, 2007).

³⁰² Abby Lippman, “Prenatal Genetic Testing and Screening, Constructing Needs and Reinforcing Inequities” (1991) 17 *Am JL & Med*, 22; Health Canada, Discussion Group on Embryo Research, *Research on Human Embryos in Canada: Final Report of the Discussion Group on Embryo Research* (Ottawa: Health Policy Division, Health Canada, 1995) at 22; see also Canadian Fertility and Andrology/Society of Obstetricians and Gynecologists Gynaecologists of Canada (CFAS/SOGC), “Joint Policy Statement: Ethical Issues in Assisted Reproduction” (1999) 21 *J SOGe* 32.

³⁰³ For instance, Daniel Wilker argues that neo-eugenics does not have any collectivist values relating to the improvement of the gene pools. Unlike their predecessors, the neo eugenics movement is committed to value pluralism in genetic design of children. See Daniel Wilker, “Eugenic Values” (1998) 11:3/4 *Science in Context* 461-463.

and Galtonian eugenics before them, neo-eugenic writers demonstrate that their broader aim is not the mere genetic improvement of individuals; individual improvements serve as a means of improving society at large. Furthermore, like their earlier predecessors, various neo-eugenicists still view the births of people who may develop disabilities or mental health problems or might become criminals as obstructing social progress as they unduly strain scarce public resources. By screening against congenital impairments, society can save on the costs of accommodations.³⁰⁴ Screening against genes pertaining to antisocial and aggressive susceptibility ought to play a vital role in the war on terror and crime.³⁰⁵ Screening against intellectual disabilities and mental disorders would help to alleviate poverty, improving overall productivity in an already competitive economy.³⁰⁶ People with enhanced cognition and behaviour would be much more industrious, thereby raising productivity levels.³⁰⁷ Thus, consumers' genetic choices would not only produce children with better genetic qualities but also produce better gene pools in the hope of producing a better society.

Individual Intentions, Eugenic Outcomes

Parents need not assume an ideology of collective genetic perfection for such outcomes to happen. Going forward into the near future, parents might still view the ideology of eugenics as problematic, given its history, and perhaps, simply because many parents view the idea of designing their child's genetic characteristics as reprehensible and even bad parenting.³⁰⁸ Several academics have suggested that individual

³⁰⁴ Buchanan et al. *supra* 229 at 236.

³⁰⁵ Elizabeth Fenton, "The Perils of Failing to Enhance: A Response to Persson and Savulescu" (2010) 36:3 *J Med Ethics* 150. See also Ingmar Persson & Julian Savulescu, "Unfit for the Future? Human Nature, Scientific Progress, and the Need for Moral Enhancement" in Julian Savulescu et al, eds, *Enhancing Human Capacities* (Oxford, UK: Wiley-Blackwell, 2011) 486.

³⁰⁶ Nick Bostrom & Rebecca Roache, "Ethical Issues in Human Enhancement" (2013) *Med Ethics* 237.

³⁰⁷ See for instance, Carl Shulman & Nick Bostrom, "Embryo Selection for Cognitive Enhancement: Curiosity or Game-changer?" (2014) 5:1 *Global Pol'y* 85. See also William Gardner, "Can Human Genetic Enhancement Be Prohibited?" (1995) 20:1 *J Med & Phil* 76-78.

³⁰⁸ Jackie Leach Scully, Tom Shakespeare & Sarah Banks, "Gift not Commodity? Lay People Deliberating Social Sex Selection" (2006) 28:6 *Sociology of Health & Illness* 749. 20:1 *Human Fertility* 22. See also Marie Gaille & Géraldine Viot, "Prenatal

consumers in the child genetics markets will not approach genetic intervention technology from the standpoint of the eugenic ideology.³⁰⁹ When prospective parents approach these technologies, they will approach them as potential consumers seeking to further their interests. Some parents will assume a more altruistic approach, acting from a sense of commitment or duty to give their child the best genes possible, while other parents would seek to confer a competitive advantage for their child in a world that increasingly fights for gaining an advantageous position. Other prospective parents might seek to maximize their own personal interests by genetically enhancing their children to be able to reap some of the benefits from their child's success or to receive better support from them when they are ill, elderly and retired.³¹⁰ Despite these individual motivations, the distinction between public and private interests is far from clear. For example, parental attempts to make their children be more productive workers can also potentially increase the economic output in a certain society if such a genetic enhancement of future citizenry is done on a large enough scale.³¹¹ Regardless of individual motivations, the use of these reproductive technologies to improve human genetics will have in the long-term wider eugenic outcomes.³¹²

Allen Buchanan argues that a combination of state encouragement, vigorous private marketing, and the herd-like impetus of popular culture could eventually direct people's reproductive choices and thus yield in the long-term eugenic outcomes.³¹³ The aggregate choices of consumers in the markets combined with

Diagnosis as a Tool and Support for Eugenics: Myth or Reality in Contemporary French Society?" (2013) 16:1 Med, Health Care & Phil 85.

³⁰⁹ See Pierre Bourdieu "Preface: Advocating for GeneEthics" in Troy Duster, *Back Door to Eugenics*, 2nd ed. (London: Routledge, 2003, vii-xi. See also Ron Amundson & Shari Tresky, "Bioethics and Disability Rights: Conflicting Values and Perspectives" (2008) 5 Bioethics Inquiry 111-123; Marie Gaille & Géraldine Viot *Ibid*.

³¹⁰ See for example Norton, who claims that bringing children with the intention of using their genetic design for the parents own personal or financial benefit amounts to child instrumentalization and commodification. See Vicki G. Norton, "Comment, Unnatural Selection: Non Therapeutic Preimplantation Genetic Screening and Proposed Legislation" (1994) 41 UCLA L. Rev. 1581, 1606.

³¹¹ See for instance, Anders Sandberg, "Cognitive Enhancement" in Julian Savulescu, Ruud ter Meulen & Guy Kahane *Enhancing Human Capacities* (Chichester: Wiley-Blackwell, 2011) 71-91.

³¹² See Merryn Ekberg, "The Old Eugenics and the New Genetics Compared" (2007) 20:3 Social Hist Med 587.

³¹³ Allen E Buchanan, *Beyond Humanity? The Ethics of Biomedical Enhancement* (Oxford: OUP Oxford, 2011) at 187.

social and economic pressures, in addition to the roles states could play, may channel people to certain reproductive choices that are deemed more desirable.³¹⁴ All that the state has to do is to deregulate prenatal genetic interventions and the market will move toward consumer neo-eugenics, which is seemingly free from undue influence.

“Liberal” Eugenics Proponents’ Advocacy for State Involvement in Neo-Eugenics

The liberal eugenic ideology emphasizes the gross immorality of state involvement in the direction of reproductive choices. However, a closer reading shows that many prominent figures in the neo-eugenics movement favour some form of government involvement, including coercive measures. Liberal eugenicists call for increased state involvement via creating a wrongful disability tort, under which parents can be sued for bringing a child into the world with a non-lethal disability, such as Down syndrome,³¹⁵ prosecution for giving birth to a child with a disability,³¹⁶ and a legal ban on knowingly implanting into a mother’s womb an embryo that is likely to develop a disability.³¹⁷ Bostrom likens the prohibition of giving birth to children with disabilities to other medical treatments: “in some cases, we can force needed medical treatment on a child, even against the wishes of its parents.”³¹⁸ Other eugenicists call for partial or extensive mandatory eugenic interventions.³¹⁹ Amongst those who call for certain state-mandated genetic interventions are Bostrom³²⁰

³¹⁴ David King, “Preimplantation Genetic Diagnosis and the ‘New’ Eugenics” (1999) 25 J Med Ethics 182 at 191; Robert Sparrow, “A Not-So-New Eugenics” (2011) 41:1 Hastings Ctr Rep 33.

³¹⁵ Dan Brock, “Preventing Genetically Transmitted Disabilities while Respecting Persons with Disabilities” (2005) *Quality of Life and Hum Difference* 67.

³¹⁶ See Peter Singer *supra* note 280.

³¹⁷ See the discussion in Stephen Wilkinson & Eve Garrard, *Eugenics and the Ethics of Selective Reproduction* (Keele: Keele University, 2013) 18-24.

³¹⁸ Bostrom *supra* note 261 at 499-500.

³¹⁹ It is also interesting to note the interesting relationship between neo-eugenicists and the state. Bostrom appeared before the President Commission on Bioethics and authored a part of their report on genetic technologies. Savulescu and Harris are members of the Hinxton Group, which call to deregulate genetic modification, together with Andrew Greenfield, one of the HFEA’s most senior regulators.

³²⁰ Fox *supra* note 277 at 22.

Appel,³²¹ Savulescu and Persson.³²² As we can see from these examples, the seemingly liberal neo-eugenics movement is not as entirely remote from its intellectual ancestors of the early twentieth century.

Liberal eugenicists do not stop at the prevention of disabilities; many wish the state to facilitate the genetic enhancement of its citizens. For example, Fox calls on the state to legally mandate certain forms of cognitive and behavioural enhancement, arguing that the state has a vested interest in the performance of its citizens. As with mandatory schooling, the state could also require its citizens to genetically enhance their children.³²³ Likewise, Persson and Savulescu call for compulsory state programs for cognitive and moral enhancement. Persson and Savulescu suggest that the world is facing unprecedented risks of blatantly immoral acts, crime, and terrorism as well as global warming that necessitate action. In the face of such catastrophes, the only viable solution is to improve the genetic qualities of our citizenry in the hope of fighting these human-made catastrophes. Thus, the state ought to mandate genetic enhancements so children are less aggressive, more cooperative, and rule-abiding.³²⁴

IV) The Risk of Future State Involvement in Market-Driven, Neo-Eugenic Practices

Presently, governments are not pursuing such neo-eugenics policies, but states across the globe may not always steer away from using such methods in the future. Rose expands on Foucault's bio-governance thesis, arguing that states in the past and at present have a vested interest in reproductive techniques that would make its future citizens healthier, more productive, and law-abiding.³²⁵ The scenario

³²¹ Jacob M. Appel, "Toward an Ethical Eugenics: The Case for Mandatory Preimplantation Genetic Selection" (2012) 14:1 JONA'S Healthcare L, Ethics & Reg 9-11.

³²² Ingmar Persson & Julian Savulescu *supra* note 75.

³²³ Fox *supra* note 277.

³²⁴ Ingmar Persson & Julian Savulescu, "The Perils of Cognitive Enhancement and the Urgent Imperative to Enhance the Moral Character of Humanity" (2008) 25:3 J Applied Phil, 169. See also Ingmar Persson & Julian Savulescu *supra* note 221 at 112.

³²⁵ Nikolas Rose describes future nations' potential interests in intervening in markets in child genetics. Those interests include reducing expenditures on healthcare, social services and disability accommodations, inhibiting criminal tendencies, improving social order and strengthening the elite. These objectives bear an uncanny similarity to the goals of the early

of states becoming eventually more implicated in neo-eugenics is plausible, but not very likely in the short-term because of public opinion.³²⁶ However, neo-eugenics methods and policies could be potentially legitimized and encounter less resistance by framing them as mere means to improve public health and labour productivity.³²⁷ Once the public normalizes and legitimizes genetic interventions, the state might begin to organize private eugenics schemes.³²⁸ Hence, current policy and regulatory choices regarding the genetic intervention technologies of today can have lasting effects on how involved the state might be in future citizen's reproductive choices.

The Politics of Neo-Eugenics

Neo-eugenics is typically portrayed in the literature as either involving abominable state coercion or ascribing to the libertarian ideal of the “genetic supermarket”. However, a more realistic description is a mixed model that accounts for the combined role of the markets and the state.³²⁹ In a mixed system of eugenics, the state would intervene in the markets, using a series of nudges and incentives. These would veer prospective parents towards trait selection that seemingly serves public goals such as improving public health, increasing productivity and reducing budgetary expenditures. Since genetic interventions are already offered

20th century eugenic movement. The key difference between 20th century eugenics and modern era genetics is that more reliable science and new technologies are far more capable of producing offspring with more desirable genetic characteristics. Rose *supra* note 7.

³²⁶ Allen E Buchanan, *supra* note 313.

³²⁷ Further, the Ontario Information and Privacy Commissioner suggested that “governments may inadvertently legitimize the practice of eugenics by forcing choices on individuals for the sake of economy and efficiency” Ontario, Information and Privacy Commissioner, *Submission to the Ontario Law Reform Commission: Report on Genetic Testing* (Toronto: Information and Privacy Commissioner, 1992) at 2.

³²⁸ See SE Evans & Berkeley University of California. *Parental Eugenics: Congenitally Anomalous Newborns and the Continuing Debate over Selective Non-treatment and Neonatal Euthanasia in the United States, 1915-2008* (Berkeley: University of California, Berkeley, 2008). ‘Council for Responsible Genetics *supra* note 10. See also Taylor Telford, “Biomedical Ethics and the Shadow of Nazism” (1976) 6:4 Hastings Ctr Rep 11.

³²⁹ David King notes “It is also important to realize that the line between state eugenics and free-market eugenics is not sharp. It would be perfectly possible for state bureaucracies to intervene in the free market, on grounds of public health or national competitiveness. Such interventions need not be obvious or require coercion.” See David S. King, “Preimplantation Genetic Diagnosis and the “New” Eugenics” (1999) 25:2 J Med Ethics 182.

as market service, the state needs not to use coercion in order to make prospective parents undergo such procedures. General Osborn explained that state coercion of eugenics on its population would only result in fear and alienation. Instead, the public needs to come to think of hereditary traits improvement as something it naturally desires.³³⁰ As such, all the state needs to do is to deregulate the markets and provide incentives for inclined prospective parents to genetically intervene on their future children in a way that aligns with the policy goals it intends to promote.

Parental Reproductive Choices – Are they Entirely Free from State Influence?

Presently, several examples exist for government policies and laws that directly or indirectly affect prospective parents' choices in genetic diagnosis. Despite the lofty libertarian ideals, the state's giant footprint nearly inevitably affects the market for genetic interventions. Financially, limitations on insurance³³¹ and public funding of genetic diagnosis provide economic incentives to prospective parents to prevent selected genetic conditions.³³² The European Union announced in 2008 an ambitious action plan to reduce the disease and disability burden,³³³ by encouraging member states to offer more genetic counseling and genetic diagnosis to prevent the birth of affected children.³³⁴ Further, torts such as wrongful life and wrongful birth³³⁵

³³⁰ Osborn explained that a number of factors are important to market neo-eugenics to the public, harnessing people's competitive tendencies in a capitalistic society and channel it to produce better offspring. According to Osborn's crypto-eugenics thesis, such reproductive practices ought to be framed as legitimate biomedical interventions. Above all, practitioners should strictly avoid any association with eugenics because the label seems to alienate the public. Fredrick Osborn supra 250.

³³¹ Bartha M Knoppers et al., "Preimplantation Genetic Diagnosis: An Overview of Socio-Ethical and Legal Considerations" (2006) 7 *Annu Rev Genomics Hum Genet* 201.

³³² Health Research Board, *Assisted Reproductive Technologies: International Approaches to Public Funding Mechanisms and Criteria. An Evidence Review* (Dublin: Health Research Board Publishing, 2017).

³³³ On the eugenic notion of people with disabilities as being framed as a burden to society and the state see Laurens Landeweerd, "Prenatal Diagnosis and the Trouble with Eugenics" (2009) 30 *L. & Hum Genome Rev* 35-40.

³³⁴ European Commission, "Press Releases - Press release - Top News from the European Commission, 3 November to 30 November 2008", online: http://europa.eu/rapid/press-release_AGENDA-08-38_en.htm

³³⁵ Kate Wevers, "Prenatal Torts and Pre-Implantation Genetic Diagnosis" (2010) 24 *Harv JL & Tech*, 263-266; Paola Frati et al., "Preimplantation and Prenatal Diagnosis, Wrongful Birth and Wrongful Life: A Global View of Bioethical and Legal Controversies" (2017) 23:3 *Hum Repro Update* 338-357. See also 2017 New York Court of Appeal Decision that recognizes wrongful birth claim. *B.F. v. Reproductive Medicine Associates of New York*; *Marie Dennehy v. Alan B. Copperman, M.D.*, No. 126-127 N.Y. (2017). And see the ECHR decision in *A.K. v. Latvia* [2004] App No. 33011/08, Judgment of 24 June 2014.

and medical malpractice³³⁶ veer physicians towards having the “best available child”.³³⁷ In the UK, Section 13 (9) of the HFE Act (as amended in 2008) disallows knowingly implanting an embryo that is likely to develop a serious condition (which is an expanding notion).³³⁸ Gynecologists, obstetricians and fertility clinicians are audited by the HFEA and could be even sanctioned if found to have failed to prevent a “serious condition” they knew about.³³⁹ Such requirements drive clinicians in the direction of practicing defensive medicine in the sensitive context of prenatal genetics. Furthermore, from a relational autonomy standpoint,³⁴⁰ one can argue that clinicians could pressure prospective parents to prevent the birth of children with disabilities due to knowledge asymmetry, ableist views and a widely held notion of procreative beneficence (which is a tenet of neo-eugenic thought).³⁴¹ In the analogous context of prenatal testing, national organizations routinize and encourage screening³⁴² against intellectual disabilities,³⁴³ such as Down

³³⁶ Ana S Iltis, “Prenatal Screening and Prenatal Diagnosis: Contemporary Practices in Light of the Past” (2016) 42:6 J MedEthics 334.

³³⁷ The standard of care is not a static, but a dynamic concept that changes along with advancing technologies, and practices. See Peter Moffett & Gregory Moorem, “The Standard of Care: Legal History and Definitions: The Bad and Good News” (2011) 12:1 West J Emergency Med 109.

³³⁸ Section 13 (9) Human Fertilisation and Embryology Act 1990.

³³⁹ See the sections regarding “Quality of Service and Compliance” and “Learning from Incidents” in - HFEA, State of the Fertility Sector 2016-2017 (2017), 12-19; 23,27 online: https://www.hfea.gov.uk/media/2437/hfea_state_of_the_sector_report_tagged.pdf

³⁴⁰ McLeod and Sherwin explain that relational autonomy involves an “explicit recognition of the fact that autonomy is both defined and pursued in a social context and that social context significantly influences the opportunities an agent has to develop or express autonomy skills.” Relational autonomy accounts employ sociological, political and historical analysis to identify and understand the difficulties agents face in acting autonomously. See Carolyn McLeod & Susan Sherwin, “Relational Autonomy, Self-Trust, and Health Care for Patients Who Are Oppressed” in Cartiona Mackenzie & Natalie Stoljar eds., *Relational Autonomy, Feminist Perspective on Autonomy Agency and the Social Self* (New York: Oxford University Press, 2000) 259-266.

³⁴¹ See Dorothy C. Wertz (1998) *supra* note 296. See also Abby Lippman, “The Genetic Construction of Prenatal Testing” In *Women and Prenatal Testing: Facing the Challenges of Genetic Technology* Karen H. Rothenberg, Elizabeth Jean Thomson eds (Columbus: Ohio State University Press, 1994) at 9. See also Elisabeth Hildt, “Autonomy and Freedom of Choice in Prenatal Genetic Diagnosis” (2002) 5:1 Med, Health Care and Phil 65.

³⁴² See United Kingdom, National Screening Committee (UKNSC). Fetal Anomaly Screening Programme – Screening for Down syndrome: UK NSC Policy recommendations 2007-2010: Model of Best Practice. See also UK National Screening Committee, “The U.K. NSC Recommendation on Fetal Anomaly Screening in Pregnancy” January 2016, online: <https://legacyscreening.phe.org.uk/fetalanomalies>; See also US policies, American College of Obstetricians and Gynecologists. “ACOG Practice Bulletin No. 88, December 2007. Invasive Prenatal Testing for Aneuploidy” (2007) 110: Obstet Gynecol 1459–67.

³⁴³ Authors have argued that routinizing screening against intellectual disabilities is well justified from an economic standpoint. They typically rely on data regarding the economic costs associated with these disabilities. For instance, the

syndrome.³⁴⁴ Despite the intentions, the state's giant footprint could veer prospective parents to make particular reproductive choices using new genetic technologies.

State Involvement in Neo-Eugenics Could Intensify in Dire Economic Times

Research suggests that governments are likely to increase their involvement in encouraging genetic interventions to cut on public expenditures in times of economic troubles. Like with 20th-century eugenic practices that peaked around the height of the great depression, states might be more inclined towards reducing expenditures by using genetic interventions in times of declining fiscal capacity and growing public debts.³⁴⁵ As the state's fiscal capacity gets more constrained, genetic intervention schemes may suddenly appear as a more appealing method to reduce spending on accommodations, healthcare and other social programs associated with conditions with genetic origins.³⁴⁶ The ongoing sovereign debt crisis, lacklustre economic growth, growing welfare and healthcare expenditures on an aging population create “perfect storm” conditions for states to cut on growing public expenditures by encouraging genetic interventions.³⁴⁷ A

Center for Disease Control and Prevention has calculated that without reproductive intervention, each yearly cohort of babies with Down syndrome alone will cost the US economy 51 billion dollars in expenditures and loss of productivity. See CDC, Economic Costs Associated with Mental Retardation, Cerebral Palsy, Hearing Loss, and Vision Impairment—United States, 2003 (2004) MMWR Morb Mortal Wkly Rep 53 at 57–5. In Europe, a comprehensive study of 30 nations estimates that the economic cost of only the direct governmental expenditures on intellectual disabilities at over 43 billion Euros (around 50 billion dollars) See Olesen, J et al., “The Economic Cost of Brain Disorders in Europe” (2012) 19:1 Eur J Neurology 158.

³⁴⁴ European studies show a high termination of pregnancy of fetuses with Down syndrome of over 90 percent. See, ABM, “Rapport Annuel Et Bilan des Activités 2007, Centres Pluridisciplinaires de Diagnostic Prenatal” (Paris : ABM, 2008) 229.

³⁴⁵ The literature suggests there is a connection between governments' likelihood to adopt eugenic measures and fiscal constraints. In the early 20th century, state involvement in eugenics programs has peaked around the height of the great depression, when sovereign debts rose dramatically. Governments often directly cited that the reasons for eugenic programs were reducing the fiscal burden generated by the “unfit”, people with disabilities, mental health and criminals. See Garland E Allen, “The Social and Economic Origins of Genetic Determinism: A Case History of the American Eugenics Movement, 1900–1940 and its Lessons for Today” (1997) 99:2-3 *Genetica* 77. See also Alexandra Minna Stern, “From Legislation to Lived Experience: Eugenic Sterilization in California and Indiana, 1907–79” in Paul A. Lombardo, ed, at a *Century of Eugenics in America* (Bloomington: Indiana University Press, 2011) at 100-104. And see Elizabeth S. Scott, “Sterilization of Mentally Retarded Persons: Reproductive Rights and Family Privacy” (1986) 5 *Duke L Rev* 806.

³⁴⁶ Garland E. Allen, “Is a New Eugenics Afoot?” (2001) 294:5540 *Science* 59.

³⁴⁷ See Linda L McCabe, & Edward R McCabe, “Are We Entering A ‘Perfect Storm’ For A Resurgence of Eugenics? Science, Medicine, and Their Social Context” (2011) in Paul A. Lombardo, ed, *A Century of Eugenics in America: From the Indiana Experiment to the Human Genome Era* (Bloomington, IN: Indiana University Press, 2011) at 193.

European Union report similarly suggests that as economic hardships increase, cost-cutting genetic screening programs may emerge in the future.³⁴⁸ Similarly, a Government of Austria report warns that if an economic crisis or a prolonged depression erupts, states may attempt to reduce costs by encouraging and nudging interested prospective parents to undergo genetic diagnosis that would prevent the birth of people with traits associated with high costs.³⁴⁹

Cognitively Enhancing Future Citizens as Means to Spur Economic Growth

If regulators approve genetic enhancements,³⁵⁰ future governments could view the augmentation of future citizens' cognitive abilities as a way to improve labour productivity, economic growth and international competitiveness.³⁵¹ Buchanan predicts that future governments could eventually encourage the cognitive enhancement of certain segments of its population to bolster economic growth and labour productivity.³⁵² Schulman and Bostrom praise current government policies to deregulate the industry, provide tax incentives³⁵³ and fund genomic research into the genetics of cognitive impairments and enhancement. According to the authors, those states stand to reap long-term benefits from such investment in the form of

³⁴⁸ European Union, *Ethical, Legal and Social Aspects of Genetic Testing: Research, Development and Clinical Applications* (September 2004) at 25-27.

³⁴⁹ Austria, Bundeskanzleramt, Preimplantation Genetic Diagnosis (PGD) - Report of the Bioethics Commission at the Federal Chancellery (Vienna: Bundeskanzleramt, 2004) at 16.

³⁵⁰ In chapter 7, I will explain how weak regulation and pressure on regulators are likely to lead to the approval therapeutic enhancements.

³⁵¹ Singapore has already experimented with policies intended to boost intergenerational intelligence and education attainment levels. In the 1980s and 1990s, Singapore offered university graduates tax breaks for having children. At the same time, it has offered the poor about \$5,000 and housing discounts if they agree to undergo sterilization. See Sharon M. Lee et al., "Fertility Decline and Pronatalist Policy in Singapore" (1991) 17 Int'l F Am Plan. P Ersp. 65, 67.

³⁵² Allen E Buchanan, *supra* note 313.

³⁵³ In 2019, the German Ethics Council report floated the idea that if deemed permissible, the German government can consider giving tax credits to prospective parents who choose to edit their descendants' germline genome to enhance their physiological and cognitive faculties. See Germany, Deutscher Ethikrat, *Intervening in the Human Germline*" (Berlin: German Ethics Council, 2019) 33 Online: <https://www.ethikrat.org/fileadmin/Publikationen/Stellungnahmen/englisch/opinion-intervening-in-the-human-germline-summary.pdf>

If implemented, giving prospective parents tax credits for enhancing the genetic characteristics of their lineage would be a form of governmental intervention on the market in human heredity traits.

more productive, cognitively enhanced population segments that would increase tax revenues and labour productivity.³⁵⁴

The Genetic Arms Race

Presently, a number of state-owned biotechnology companies in newly industrialized countries are leading the world's largest genomics project to uncover the genomic profile of genius-level intelligence. The governments' monumental capital investment in these companies is reported not to be motivated by pure scientific curiosity but by an ambitious long-term plan to encourage cognitive enhancement of certain segments of its populace.³⁵⁵ Such an ambitious long-term project requires state oversight and delivery of genetic intervention services to those populations chosen to be cognitively enhanced by the state. NYU evolutionary psychologist, Geoffrey Miller has suggested that this large-scale biotechnology project to create the foundation for a state-led cognitive enhancement is about to ignite a new global arms race for biotechnological superiority.³⁵⁶

Once genetic enhancement becomes technologically feasible, such state-led programs can eventually draw other nations into a "genetic arms race" for genetic superiority, in which even liberal nations might devise a blueprint for beneficially enhanced citizens and work to serve the greater good. The UK, another leading biotechnology powerhouse, has issued several reports suggesting that the cognitive enhancement of

³⁵⁴ Carl Shulman & Nick Bostrom supra note 307.

The authors explain that the economic advantages would only likely to be reaped if the state would deepen its involvement in support and fostering of cognitive enhancement of large enough segments of its populace over generations. If governments would take an aggressive approach to promote cognitive enhancement, national IQ scores could climb within a number of generations.

³⁵⁵ See Ed Yong, "Chinese Project Probes the Genetics of Genius" (2013) 497:7449 *Nature* 297. See also Gautam Naik, "A Genetic Code for Genius? In China, a Research Project Aims to Find the Roots of Intelligence in Our DNA; Searching for The Supersmart" *The Wall Street Journal*, (February 15, 2013) online: <http://online.wsj.com/news/articles/SB10001424127887324162304578303992108696034#printMode>. See also, G Owen Schaefer, "China May Be the Future of Genetic Enhancement", BBC, (April 8, 2016) online: <http://www.bbc.com/future/story/20160804-china-may-be-the-future-of-genetic-enhancement>.

³⁵⁶ Geoffrey Miller, "Chinese Eugenics", *Edge*, (January 14, 2013) online: <https://www.edge.org/response-detail/23838/>

Britons can strengthen the competitive position in the future economic world order.³⁵⁷ A US Congress report suggests such an intensifying competition creates a “genetics arms race”, in which biotechnologically developed nations would fight for dominance in the new field of improving upon the human genetic blueprint.³⁵⁸ Amongst the key features of the “genetics arms race”, is an anticipated “race to the bottom” to deregulate inheritable genetic modification and adopt a more liberal stance towards the genetic enhancement of its citizenry.³⁵⁹ However, is cognitive enhancement a way for nations just to get a better grip on the economy or the mental characteristics of its future citizens?

Choosing Citizens: Genetic Engineering as a Tool for Social Control

Future states’ potential attempts to direct people’s reproductive choices to serve policy goals such as improving public health, productivity and reducing criminality would constitute an invasive, yet rather an invisible form of social control. As early as 1924, renowned philosopher Bertrand Russell warned of such social control endeavours, explaining that states in the future might use novel eugenic methods to influence the mental characteristics of future generations to create a population that would be more convenient to govern.³⁶⁰ In modern times, Jürgen Habermas contends that the social control element in state involvement in neo-eugenics distorts the relationship between those governing and those governed. The intent of the state to impose upon its governed an “optimal” genetic profile gives the state an excessive degree of control that threatens the very assumptions of liberal democracy.³⁶¹ A Harvard Law Review editorial warns about the dangers of the state endorsement of neo-eugenic measures, arguing that:

³⁵⁷ Supra note 42.

³⁵⁸ United States Congress House Committee on Foreign Affairs Subcommittee on Terrorism Nonproliferation supra note 9.

³⁵⁹ Tetsuya Ishii, “Potential Impact of Human Mitochondrial Replacement on Global Policy Regarding Germline Gene Modification” (2014) 29:2 *Repro Biomed Online* 145; See also William Gardner supra 307.

³⁶⁰ Bertrand Russell supra note 41.

³⁶¹ Habermas supra note 41.

These are not activities the government should be endorsing, much less planning and subsidizing. The real trouble with eugenics is not that it can be coercive; it is that the state can use it to create the citizens it wants to govern. This idea is deeply offensive to democracy and liberalism, which posit that the state exists to serve the needs of its members — that is, individual humans — not vice versa. It is axiomatic to liberal democracy that the governed should choose the government, not vice versa.³⁶²

The public may fail to fully fathom such a subtle form of social control, making it harder to delegitimize and prevent state involvement in neo-eugenic markets. Political theorist Herbert Marcuse explains that subtle, invisible forms of social control are powerful governance tools to direct people's actions towards desired outcomes. This is especially true because the populace often fails to discern how social and economic realities redirect their behaviours, and how those later serve the greater goals of those in power.³⁶³ In our context, prospective parents will not necessarily discern the system's broader eugenic goals of improving future citizenry hereditary traits, but will simply see incentives for individuals to have seemingly healthier, more productive children. Such schemes have an uncanny resemblance to Plato's concept of the "Noble Lie" and Osborn's "Crypto-Eugenics", which asserts that the best way to convince the public to undertake eugenics measures is to convince them they are not partaking in any kind of eugenics. Sociologist Pierre Bourdieu commented on how Crypto-Eugenics was successful in socially framing genetic reproductive technologies as fully legitimized preventive medicine³⁶⁴ methods, while such framing conceals how these

³⁶² Editorial, "Regulating Eugenics" (2008) 121:6 Harv L Rev 1578.

³⁶³ Herbert Marcuse, *Eros and Civilization* (Boston: Beacon Press, 1966).

³⁶⁴ The framing of genetic diagnosis as a medical tool is particularly interesting given the technology does not treat, but merely destroys an embryo. Evolutionary biologist and geneticist Richard Lewontin critiqued the framing of genetic diagnosis, stating "to conflate . . . the *prevention* of disease with the *prevention* of lives that will involve disease, is to traduce completely the meaning of preventative medicine." See Richard Lewontin, "Billions and Billions of Demons" (review of *The Demon-Haunted World: Science as a Candle in the Dark* by Carl Sagan, 1997), *The New York Review*, (9 January 1997) 31.

could be easily used to serve eugenic goals.³⁶⁵ Therefore, if neo-eugenic policies are socially framed as mere means to improve public health and labour productivity, they could be legitimized,³⁶⁶ and encounter less resistance. Through framing neo-eugenics as mere public health and economic policies, one can fail to discern the potential emergence of the bio-governance of people's bodies and minds.³⁶⁷ The utopian allure of governing reproduction to improve the human genome, individuals and society has already proven itself historically to shift attention away from certain semi-dystopian elements.

A Possible Future of Stratified Eugenics

Political scientist Francis Fukuyama criticizes future states' potential involvement in neo-eugenics as a seemingly illiberal endeavour that could ultimately lead to further erosion of the liberal elements of society and of the state. Fukuyama draws parallels between 20th-century eugenics to neo-eugenics, by explaining in both periods liberal democracies have become increasingly involved in administering what initially were private initiatives because of the view that state's governance of reproduction is necessary to achieve the long-term goals of improving the heredity qualities of its populace.³⁶⁸ However, unlike in the 20th century, modern genetic intervention technologies are particularly potent in choosing and altering the genetic characteristics of future generations. Still, economic factors would greatly shape the possible role of states in neo-eugenic practices. The transhuman vision of universal access to genetic enhancement is unrealistic because states lack the fiscal capacity to fund grandiose, highly expensive and complicated projects of genetic enhancement of

³⁶⁵ Pierre Bourdieu *supra* note 309.

³⁶⁶ The Ontario Information and Privacy Commissioner *supra* note 327.

³⁶⁷ See for instance Michel Foucault's warning about how genetic technologies can be used as a tool for bio-governance of future citizens' bodily and mental function to serve state goals. See Foucault *supra* note 39.

Nikolas Rose further explains how governments in the 20th century worked to reframe eugenic methods to control reproduction as valid health, economic and criminal policies. Central to this reframing of eugenics was the popularisation of the ideas that human faculties can be accurately measured, converted into figures and statistics and ripe for tailored government intervention on those with sub-par biological functioning who impede social progress. See Nikolas Rose, *Powers of Freedom: Reframing Political Thought* (Cambridge: Cambridge University Press, 1999) at 209-210.

³⁶⁸ Fukuyama *supra* note 41.

its entire future citizenry. Instead, the economics of neo-eugenics dictate that future state involvement will be limited in fiscal terms, and likely to result in stratified eugenics and ability divide, rather reminiscent of Aldous Huxley's vision in *Brave New World*. The lower classes might be able to access selective abortions (using technologies such as non-invasive prenatal testing - NIPT) to prevent disease and disabilities while the highest classes will have access to very expansive genetic enhancement technologies.³⁶⁹ The genetic enhancement of society's wealthiest could further cement the highest classes' position of dominance in the economy and politics. The growing ability divide between the lower and higher classes could further intensify the already high levels of inequality and growing social conflict that are regarded by political scientists as responsible for the gradual erosion of the liberal foundations of society and the state.³⁷⁰ If future states become less liberal, they might see even fewer impediments to increasing their involvement in the governance of the genetic characteristics of its future populace.

Overextensive Legal Change Erodes the Key Safeguards from State Involvement in Neo-Eugenics

Genetic intervention laws are some of the most effective safeguards³⁷¹ from future state potential involvement in market-driven neo-eugenic practices.³⁷² Genetic intervention laws provide effective safeguards as they were devised to prevent contentious traits selection from even being offered on the market in the first place. If contentious genetic interventions are not approved by regulators, the state cannot then encourage them by creating incentives and disincentives. The state cannot incentivize segments of the market

³⁶⁹ *Ibid.*

³⁷⁰ *Ibid.*

³⁷¹ It is important to note that Article 3(2) of the European Charter of Human Rights, which prohibits "eugenic practices" at large, does not apply to market eugenics but only to state coerced eugenic programs. See The EU Network of Independent Experts on Fundamental Rights "Commentary of The Charter of Fundamental Rights of the European Union" European Commission, (June 2006) online: <https://sites.uclouvain.be/cridho/documents/Download.Rep/NetworkCommentaryFinal.pdf>

See Article 3(2), European Union, *Charter of Fundamental Rights of the European Union*, 26 October 2012, 2012/C 326/02.

³⁷² I will introduce and discuss genetic intervention laws and the phenomenon of legal change in the next chapters. In this chapter, I only focus on the more general point that a more permissive regulatory stance that allows screening for a greater selection of genetic traits frees up the state to potentially intervene in these emerging markets. Genetic intervention laws act as a gate and can either block the access or open up new opportunities for the state to intervene in the market.

if the market does not offer such trait selection. Hence, genetic intervention laws can fulfill a key role in safeguarding the public from the state becoming once again involved in promoting eugenic practices. However, these safeguards are being gradually eroded through the process of rapid legal change. As a result, future states would become freer to discourage the birth of people with disabilities and other disfavoured traits and encourage the birth of people with physical and cognitive performance deemed better.

Conclusion

Neo-eugenics is distinctively different from its early twentieth-century predecessor, and yet similar in various ways. As this canvassing of the intellectual history and the politics of eugenics has shown, the movement has proven to be spectacularly resilient, changing its political ideology (most recently to *laissez-faire* capitalism) to match the zeitgeist. Neo-eugenicists suggest that the movement has been reformed and now adopts liberal free market ethics. Certainly, the movement is committed to expanding the markets in child genetic customization. By examining its intellectual history, I have provided reasons why despite its seemingly free market ideology, the modern incarnation of eugenics continues to perplex liberal legal systems at the present. Eugenic thought maintains a number of problematic core tenants including the collective improvement of gene pools, critical judgments about life with disfavoured bodily and cognitive traits and at times support for illiberal and coercive methods.

This chapter provided essential background to understanding key issues relating to legal change, the motivations behind enacting genetic interventions laws and the specific regulatory rules to prevent a slippery slope to eugenics. Amongst other things, this chapter provided a broader context to the discussion about the potential drivers of legal change by examining several key societal, technological and ideological trends that shape the rapidly changing landscape of genetic interventions.³⁷³ In particular, the rapid evolution of genetic

³⁷³ According to Ehrlich's theory of legal change, these greater social, ideological and technological transformations drive the legal system to continually readjust its rules and doctrines to stay aligned with society's ever-changing power relations and institutional interests. Ehrlich *supra* note 109 at 433, 439, and 341–45.

intervention technologies into tools to select more “desirable” traits is a central theme in later discussions about the ethical challenges and the difficulties with maintaining the regulatory distinctions over time. Furthermore, as choices in child genetics rapidly expand, prospective parents are subject to a host of economic, psychological and societal pressures to produce children with more “optimal” genetic characteristics. The novel abilities of genetic customization are likely to raise issues with prospective parents feeling compelled to design their children in conformity with the ever-shifting of standards of normalcy and performance. Examining these problematic market dynamics provides a broader context to later discussion about the ethical and human rights risks the legal system flagged as concerns about neo-eugenics. The risks market eugenics entail include creating a discriminatory climate, its impacts on people with disabilities, child commodification, and impacts on the children’s autonomy. That is, if genetic intervention laws, which have a key goal of preventing neo-eugenic practices, continue to pave the way for the emerging market of child genetics.

Chapter Three

The Origins and Objectives of Genetic Intervention Laws

Genetic intervention laws present a classic dilemma in science and technology governance, the attempt of lawmakers to pre-emptively prevent harmful outcomes versus increasing pressures to “liberalize” the technology as it develops.³⁷⁴ By examining the legislative and regulatory history, I will show that the prevention of a slippery slope to eugenics is one of the key goals underlying the legislation of the UK and French genetic intervention laws.³⁷⁵ Since, the early 1980s, the British and French governments recommended prohibiting genetic modification and strictly regulating genetic diagnosis. One of the key risks repeatedly highlighted in government reports and debates was that of genetic intervention technology evolving from a tool to prevent lethal congenital malformation to selecting physical, cosmetic and behavioural traits deemed desirable. Without proper boundaries, prospective parents will increasingly seek to exploit the real and perceived benefits of genetic interventions, resulting in a gradual transition to eugenic practices. Regulators were tasked with developing and maintaining regulatory restrictions that would allow genetic diagnosis of certain life-endangering conditions while preventing the slippery slope.

I) The Historical Origins of Genetic Intervention Laws

Genetic intervention laws’ origins can be traced back to a time of social, political and technological transitions. The removal of compulsory sterilization acts from the books in the 1970s marks for historians

³⁷⁴ See Braun et al. who also argues that this dilemma is particularly obvious in the regulation of genetic technologies in the UK and France. See Kathrin Braun et al., “Science Governance and the Politics of Proper Talk: Governmental Bioethics as A New Technology of Reflexive Government” (2010) 39:4 *Econ & Soc’y* 510.

³⁷⁵ Michael Mulkay, *The Embryo Research Debate: Science and the Politics of Reproduction* (Cambridge: Cambridge University Press, 1997) 142. See also Cour de Cassation, *L’innovation Technologique – Rapport Annuel 2005*, Paris, 2006 at 122, online, http://www.courdecassation.fr/IMG/pdf/cour_cassation-rapport_2005-3.pdf; Stéphane Viville & Deborah Pergament, “13 Ethical Perspectives and Regulation of Preimplantation Genetic Diagnostic” in *Preimplantation Genetic Diagnosis* Joyce C. Harper, Joy D. A. Delhanty & Alan H. Handyside, eds, (Chicester: John Wiley & Sons, 2001) at 238.

the end of early 20th-century eugenics.³⁷⁶ At the end of this historic eugenic era, keen observers already foresaw the dawn of a new eugenic era, ushered by advances in reproductive genetic technologies. Academics, clinicians and jurists have begun discussing the then hypothetical scenario that new reproductive technologies will eventually evolve into a tool for selecting children with more desirable traits.³⁷⁷ A major catalyst for the academic and the legal discourse was the first child born through IVF in the UK (and in the world) in 1978 and in France in 1982.³⁷⁸ Governments performed an exercise in foresight by considering how genetic intervention technologies would evolve and hence what kind of legal response would be required.³⁷⁹ On the supranational level, the Council of Europe³⁸⁰ launched pan-European negotiations of a treaty on new

³⁷⁶ See Paul A. Lombardo, *Three Generations, No Imbeciles: Eugenics, the Supreme Court, and Buck V. Bell* (Johns Hopkins University Press, 2008); Alexandra Minna Stern, "Eugenics and Historical Memory in America" (2005) 3:1 Hist Compass 7-8; Erica Dyck, *Facing Eugenics: Reproduction, Sterilization, and the Politics of Choice* (Toronto: University of Toronto Press, 2013) 219-222.

³⁷⁷ See Charles Frankel supra note 16; Ted Howard & Jeremy Rifkin, *Who Should Play God? The Artificial Creation of Life and What It Means for the Future of the Human Race* (Ann Arbor: University of Michigan Press Press, 1977); Robert H Blank, *The Political Implications of Human Genetic Technology* (Boulder: Westview Press, 1981) 201.

While it is widely considered that compulsory sterilizations of people with disabilities belong in the past, it was revealed in 2000 that 15,000 French women with intellectual disabilities have been forcefully sterilized in mental institutions. The French Supreme court has found the appeal inadmissible. See the ECHR litigation in *Gauer and Others v. France* [2012] App No. 61521/08, Judgment of 23 October 2012.

³⁷⁸ See Anne Fagot-Largeault, "In France, Debate and Indecision" (1987) 17:3 Hastings Ctr. Rep. at 11.

In an interesting turn of events, the clinical geneticist who performed the first IVF in France, Jacques Testart also became one of its biggest critics. In the 1980s, Testart participated in efforts to lobby the parliaments in the UK and France and explain to legislators the eugenic potential of genetic intervention technologies. See France, Assemblée Nationale Rapport D'information Fait Au Nom De La Mission D'information Sur La Révision des Lois De Bioéthique N° 2235 M. Jean Leonetti, 20 Janvier 2010, 218 online : <http://www.assemblee-nationale.fr/13/pdf/rap-info/i2235-t1.pdf>

³⁷⁹ Attempts to set rules many years before technologies become feasible require a great deal of foresight. For more detail about the need for foresight to regulate emerging technologies, see comments by the chair of the parliamentary appointed commission that has set the foundations of the HFE act Mary Warnock, "Reflections on the New United Kingdom Legislation on Human Fertilization and Embryology" (1991) 42:2 Int'l Digest of Health Legislation 346-50. See also CCNE, Opinion No.3 supra note 24. See also Michael Mulkay supra note 375 at 72.

³⁸⁰ The Council of Europe is a supranational organization, which was founded after WWII to promote human rights protection in Europe and Eurasia. The Council of Europe has 46 members, out of which 29 signed the Oviedo Convention. See Martyn Bond & Council of Europe, *The Council of Europe and Human Rights* (Strasbourg: Conseil de l'Europe, 2013). Council of Europe – Treaty Office, Chart of signatures and ratifications of Treaty 164 Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, [hereafter: The Oviedo Convention] online: <https://www.coe.int/en/web/conventions/full-list/-/conventions/treaty/164/signatures>

biomedical innovations, including genetic diagnosis and inheritable genetic modification.³⁸¹ On the national level, both the UK and French governments established in the 1980s a number of commissions and committees to study the then largely uncharted territory of assisted human reproduction technologies. These commissions and committees were assigned the key task of recommending appropriate regulatory responses to prevent the misuse of reproductive genetic technologies.

Committee Studies in the UK – The Warnock Report and White Paper

In 1982, the UK government appointed a committee, chaired by Oxford philosopher Mary Warnock, to study the ethical and legal challenges with novel assisted reproductive technologies and recommend an appropriate regulatory response.³⁸² The establishment of the Warnock committee was in large a response to the growing public concerns at the time regarding the misuse of novel reproductive technologies. The Warnock Report directly cited public anxiety as a motivation to examine the ethical landscape of novel reproductive technologies and to consider placing appropriate restrictions.³⁸³ Baroness Ruth Deech, the former Chair of the HFEA suggests that the Warnock Report and the subsequent legislative response “initially arose from the widespread fears expressed by politicians, the media, the public and the professions about embryo research, its morality and its direction.”³⁸⁴

The Warnock Report laid out a number of foundational ethical principles pertaining to genetic interventions. First, human embryos generally have a right to life (albeit not without exceptions). Second, the embryo should be accorded, a sui generis status under British law (albeit lower than that of human adults or

³⁸¹ In 1982, The Council of Europe called on European nations to negotiate an international agreement that would regulate genetic diagnosis and prohibit human genetic modification. See Council of Europe, Consultative Assembly Recommendation 934 (1982) on Genetic Engineering S.2.

³⁸² Mary Warnock, Committee of Inquiry into HFE. Report of the Committee of Inquiry into Human Fertilisation and Embryology. 1984 *Department of Health and Social Security (UK)* London: HMSO, at para 1.2 [Hereafter: Warnock Report]

³⁸³ Warnock Report supra note 24 at 70.

³⁸⁴ Ruth Deech, “The HFEA: 10 Years On” in J. Gunning & H. Szoke, eds, *The Regulation of Assisted Reproductive Technology* (Aldershot: Ashgate, 2003) at 21.

children). Third, embryos cannot give consent to experimentation as they are not yet rational agents. Fourth, embryos must be guarded against any unwarranted and eugenic experimentation, which is a distinct possibility given the manner in which genetic sciences could evolve. Fifth, embryos' moral worth outweighs the potential benefits to society from certain types of scientific research.³⁸⁵

Based on these key ethical principles, the report recommends several regulatory measures regarding genetic intervention technologies. First, genetic diagnosis ought to be restricted to the prevention of genetic conditions (a notion the Warnock Report acknowledged as elusive and potentially requiring further elaboration).³⁸⁶ Second, the report recommended that in order to strictly control the application of genetic technologies, a responsible regulatory authority ought to be established to set controls.³⁸⁷ Third, the report further proposed that in order to deter undue experimentation, unauthorized research on in vitro embryos should constitute a criminal offence.³⁸⁸ Finally, the report recommended prohibiting inheritable genetic modification due to the ethical unacceptability of changing future generations' genomes and the high likelihood of its eugenic abuse in an attempt to improve upon human hereditary traits.³⁸⁹

The Thatcher government decided to commission a subsequent study, which culminated in the publication of the 1987 White Paper.³⁹⁰ The position of the White Paper reflected similarities to the 1984 Warnock Report. The White Paper was a direct response to the post-Warnock Report polarized parliamentary debate on whether genetic diagnosis should be banned or regulated. In light of the polarized parliamentary debates, the White Paper recommended either banning genetic diagnosis entirely or strictly

³⁸⁵ *Ibid* at para 11.10-11.19.

³⁸⁶ *Ibid* at para 11.10.

³⁸⁷ *Ibid* at para 13.3-13.4

³⁸⁸ *Ibid* at para 11.18.

³⁸⁹ *Ibid* at para 12.15-12.17.

³⁹⁰ United Kingdom, House of Commons. The Parliamentary Debates (Hansard), Official Report. Sixth series. Session 1987-88. London, HMSO, Vol. 123, Written Answers, 26 November 1987, col. 330-1; See also HFEA, Strategy and Information Directorate. "How Legislation on Fertility Treatment Developed" (London: HFEA, 2009).

limiting its use to the detection of serious conditions.³⁹¹ The White Paper again restated the risk that genetic diagnosis could be eventually misused to detect and select embryos on the basis of non-pathological traits such as hair and eye colour. Strict parameters and constant monitoring are required to ensure a slippery slope would not occur.³⁹² The White Paper reiterated the recommendation of the Warnock Report to establish a responsible regulatory body to ensure that the technology is not misused.³⁹³ Furthermore, the White Paper recommended prohibiting inheritable genetic modification on the grounds of safety risks, unforeseeable negative consequences of altering the human genome and concerns about eugenic misuse. The White Paper emphasized that:

“One of the greatest causes of public disquiet has been the perceived possibility that newly developed techniques will allow the artificial creation of human beings with certain pre-determined characteristics through the modification of an early embryo’s genetic structure. The technical prospects for achieving this are in fact extremely remote, even if anyone wished to undertake such work. Nevertheless, it is a procedure which society would clearly regard as ethically unacceptable, and the Bill will prohibit it.”³⁹⁴

The Formation and Guidance of the French National Consultative Ethics Committee

In 1983, the Mitterrand government decided to establish a national consultative ethics committee [Comité Consultatif National d'Éthique' (CCNE)] to examine the ethical ramifications arising from advances in biomedical technologies.³⁹⁵ The mission of the CCNE is to “give opinions on ethical problems raised by

³⁹¹The White Paper *supra* note 36 at S 6.

³⁹² *Ibid.*

³⁹³ *Ibid.*

³⁹⁴ *Ibid* at para 37.

³⁹⁵ The President of the Republic, François Mitterrand, established in a decree the Comité Consultatif National d'Éthique pour les Sciences de la Vie et de la Santé (CCNE) See Décret du 25 Février : 1983, 'Portant création d'un Comité Consultatif National D'éthique Pour Les Sciences De La Vie Et De La Santé', J Officiel de la République Française.

the progress of knowledge in the fields of biology, medicine and health, and to publish recommendations on these proposed topics.”³⁹⁶ The role of the CCNE was later recognized by the 1994 Bioethics Law³⁹⁷ as having a moral authority over guiding the development of biomedical advances in light of ethical principles, the paramount of which is human dignity.³⁹⁸

One of the first opinions the CCNE issued addressed the ethical issues raised by genetic intervention technologies. The 1986 CCNE Opinion no. 8 reviewed inheritable genetic modification technology and critiqued it as both being unethical (as it alters the germline genome and thus the gene pools) and redundant - because of the inherently safer alternative of genetic diagnosis.³⁹⁹ Furthermore, the CCNE’s opinion no. 8 addressed both prospects of genetic diagnosis and its potential misuse. The CCNE opinion voiced the concern that when contrasted with selective termination, genetic diagnosis could have a greater potential for eugenic abuse.⁴⁰⁰ According to the CCNE opinion, abortion presents a trying decision for the prospective mother, involving a great physical and mental trauma that could result in self-regulating behaviour. Genetic diagnosis, however, does not involve the same degree of trauma and requires choosing which of the embryos best satisfies the selection criteria. As time passes by and as genomic sciences unlock new trait selection possibilities, parental decision-making is far likelier to exhibit growing degrees of eugenic elements.⁴⁰¹ The

³⁹⁶ Raymond De Vries et al., “The Moral Organization of the Professions Bioethics in the United States and France” (2009) 57:4 Curr Soc 55.

³⁹⁷ Loi no. 94-653- Relative Au Respect Du Corps Humain, Au Don Et À L'utilisation Des Éléments Et Produits Du Corps Humain, J.O. 30 juillet 1994, 1994 art. 23.

³⁹⁸ The CCNE issues opinions that play a major role in determining and guiding regulatory policy. The CCNE has policymaking authority that is much closer to the HFEA, than the equivalent ethics commission in the UK, Human Genetic Commission (HGC). See Alireza Bagheri et al, *Global Bioethics: The Impact of the UNESCO International Bioethics Committee* (Dordrecht: Springer, 2015) 129.

The French Bioethics law stipulates that “the law ensures the primacy of the person, prohibits any assault on a person’s dignity, and guarantees respect for the human being from the beginning of his or her life.” Code Civil, Article. L. 16-1.

³⁹⁹ CCNE, Opinion No. 8 supra note 36.

⁴⁰⁰ *Ibid* at 30.

⁴⁰¹ *Ibid* at. 30-31

CCNE's opinion further explained that a slippery slope to eugenics is ethically problematic because it involves attempts to predetermine the child's traits based on parental preferences and their personal convenience. Technologies such as genetic diagnosis pose a risk that parents will come to expect the birth of children with "normal" bodily and mental traits. Prospective parents would select against "abnormal" traits associated with vulnerable groups, such as people with disabilities.⁴⁰² The CCNE recommended a moratorium on genetic diagnosis, due to its then experimental nature and the risks of its misuse.⁴⁰³

In its 1990 opinion, the CCNE decided to extend the moratorium on genetic diagnosis but suggested that the moratorium could eventually be replaced with strict regulations. The CCNE recommended regulating genetic diagnosis in a manner that would limit the use of the technology only to the detection of serious and untreatable conditions.⁴⁰⁴ The CCNE made this recommendation in order to allow parents to detect certain congenital problems prior to implantation and thus to avoid the dilemma of choosing between abortion and giving birth to a child with a lethal genetic condition. Nevertheless, the CCNE commented that a key risk with removing the moratorium is that the practice would shift over time to non-medical traits selection to satisfy parental and societal desires.⁴⁰⁵ To avoid such outcomes, the CCNE recommended setting clear rules and a control system that would prevent the slippery slope from occurring. The CCNE further recommended periodic reviews of the regulatory controls to ensure that the act's goal of preventing the slippery slope is continually respected as time passes and reproductive biotechnologies advance.⁴⁰⁶

⁴⁰² *Ibid.*

⁴⁰³ *Ibid* at 35.

⁴⁰⁴ CCNE, Opinion No. 19, on Embryo Research Aiming to Achieve Pre-Transfer Genetic Diagnosis for Which a Moratorium Was Declared in 1986 (Paris: CCNE 1990), 1.

⁴⁰⁵ *Ibid* at 4.

⁴⁰⁶ *Ibid* at 3.4.

These periodical evaluations have ended after the CCNE itself has stated in 2009 that the slippery slope was prevented by the regulatory system and hence no further periodical evaluations are needed.

Two Key Committee Studies in France: The Braibant and the Lenoir Reports

The French government appointed three special commissions to study options for regulating advances in the rapidly evolving field of reproductive technologies. The Braibant Commission produced a report in 1989. The Lenoir Commission was appointed after changes in the composition of the Mitterrand government. While the two reports came from the opposite sides of the political spectrum, the Braibant and the Lenoir reports were rather univocal on the policy prescription they recommended for genetic interventions. Both reports directly recognized the great concern of employing genetic interventions to further the goals of eugenic selection.⁴⁰⁷ Noëlle Lenoir, who was a Judge at the Constitutional Court at the time, characterized the CCNE's moratorium on genetic diagnosis as "an alarm signal" that we should "prevent the risk of eugenics" and the "possibility of choosing children based on desirability."⁴⁰⁸ The Braibant and Lenoir reports recommended prohibiting inheritable genetic modification and restricting genetic diagnosis only to cases in which there was a high risk of developing a particularly serious congenital malformation such as Duchenne Muscular dystrophy.⁴⁰⁹ The 1991 Lenoir report to the Prime Minister stated that "it seems logical to admit the use of PGD to prevent the transfer of embryos or gametes carrying or transmitters of genetic diseases." Nonetheless, the Lenoir report further asserted that line-drawing should be cautious not to be overly inclusive, because essentially, all embryos either have or asymptotically carry genes linked to genetic disease.⁴¹⁰

⁴⁰⁷ See Noëlle Lenoir. Aspects Juridiques et Éthiques du Diagnostic Prénatal : Le Droit et les Pratiques en Vigueur en France et des Divers autres Pays in *Analyse Génétique et Protection de la Personnalité*. Colloque International. Lausanne, Université de Neuchâtel, 14 avril 1994, 43-47.

⁴⁰⁸ Lenoir quoted in Jeanne Kohli, "Les Diagnostics Anténatals (Préimplantatoire Et Prénatal) : Une Éthique Au Regard De La Pratique", 71 online : http://www.academia.edu/download/38048623/Jeanne_Kohli_memoire_diagnostic_antenatal_19_juin_2015.pdf

⁴⁰⁹ Guy Braibant, *Projet De Loi Relatif Aux Sciences De La Vie Et Aux Droits De L'homme* (Paris : La Documentation Française, 1988) ; Noëlle Lenoir, *Aux Frontières de la Vie / Rapport au Premier Ministre* (Paris : La Documentation Française, 1991) 101-103.

⁴¹⁰ Lenoir *ibid* at 57-60 and 200-201

Note that I have translated the above quote from the Lenoir report.

Parliamentary Debates in the UK

The British Parliament was deeply divided on the issue of genetic diagnosis.⁴¹¹ The 1984 Embryo Protection bill that prohibited genetic diagnosis, which nearly passed in the third reading, was defeated in 1985 due to intense lobbying by industry groups in favour of research and commercialization of new assisted reproductive techniques.⁴¹² After the defeat of the Embryo Protection bill, the concern that genetic diagnosis technology could lead to a slippery slope began to surface more frequently in parliamentary debates. Michael Mulkey has analyzed the speeches after the defeat of the Embryo Protection bill and found the slippery slope argument was explicitly evoked in 33 out of 189 speeches. In these speeches, parliamentarians used similar metaphors including “the thin edge of the wedge” and “the downward path”.⁴¹³ The slippery slope concern was expressed in the words of the Marquess of Reading:

“Your Lordships have been speaking with great effect about experimenting with embryos. Can we not expect, perhaps, that this will lead to juggling with genes? Is it not possible that in time to come people may be able to order their own children? Someone may say, “All right; I’ll have two boys with blue eyes” or, I will have two girls with golden hair”, What a terrible thought!”⁴¹⁴

Against the backdrop of the slippery slope concerns, Baroness Warnock attempted to reassure parliamentarians that regulating genetic diagnosis would prevent the slope to eugenics from occurring. She stated:

⁴¹¹ See for instance, Thomas Benchoff, *Embryo Politics: Ethics and Policy in Atlantic Democracies* (Ithica: Cornell University Press, 2011) 89-93.

⁴¹² Anastasia A Theodosiou, & Martin H Johnson, “The Politics of Human Embryo Research and The Motivation to Achieve PGD” (2011) 22:5 *Repro Biomed* online 457.

⁴¹³ Michael Mulkey *supra* note 375 at 205.

⁴¹⁴ Viscount Buckmaster, House of Lords October 31 1984, col. 540.

“I think your lordships should not be frightened of the slippery slope argument. I am sure you will not be and that the general public may be aware of this fact. We can stop our descent down the slippery slope at any point when we wish to do so and the way of stopping ourselves descending into unknown horrors is by legislation.”⁴¹⁵

Finally, after five long years of debates, an agreement was reached that genetic diagnosis would be legal but strictly regulated. The UK Parliament agreed to adopt the recommendations of the White Paper to restrict genetic diagnosis to serious conditions. MPs were apparently convinced by Warnock style arguments that industry regulation would prevent the slide down the slope.⁴¹⁶ The Parliamentary debates also featured the concern that the approval of genetic diagnosis itself is a slide down the slope to a grossly unethical outcome of inheritable genetic modification. However, parliamentarians were convinced that the approval of genetic diagnosis (and somatic gene therapy)⁴¹⁷ would make the modification of the germline genome redundant, as these two techniques would provide more ethical and safer alternatives.⁴¹⁸

Parliamentary debates raised particular concerns about inheritable genetic modification. Both sides of the house were unified in agreement that the inheritable alteration of the human genome ought to be prohibited by parliament. The view was not only that downstream application of inheritable genetic modification should be prohibited but also the research that paves the way to the technology’s development and its subsequent commercialization. Such research could eventually end up with irresponsible attempts to redesign and to improve upon the human genetic blueprint. Mulkay analyzed the parliamentary debates and

⁴¹⁵ Baroness Warnock, House of Lords January 15, 1988 col. 1471.

This was one of the first instances of the narrative that the legal boundaries could prevent the slippery slope. I will discuss the narrative and show how it has become a dominant narrative of regulatory and academic discourse in chapter 8.

⁴¹⁶ Mulkay, *supra* note 375 at 205.

⁴¹⁷ For more about somatic gene therapy see Cornel et al *supra* note 163.

⁴¹⁸ United Kingdom, House of Commons, the Parliamentary Debates (Hansard), Official Report. Sixth Series, Session 1987-88. London, HMSO, Vol. 140, 14 November 1988, Col. 812-28.

noted that the parliament's key concerns relating to inheritable genetic modification included irresponsible meddling with the human genome, unforeseeable long-term consequences, and the slippery slope to non-medical trait selection.⁴¹⁹

Parliamentary Debates in France

Genetic diagnosis stirred an intense debate in the French Parliament between those in favour of prohibition and those seeking a less restrictive approach.⁴²⁰ Political debates about genetic diagnosis proved to be heated and often polarized. Transcripts of the debates reveal a number of concerns raised by senators and ministers, including that of a slippery slope.⁴²¹ Initially, during parliamentary debates, a provision prohibiting genetic diagnosis was passed in the first reading. The Senate “has relied on the [CCNE] moratorium on genetic diagnosis based on the insufficiency of scientific guarantees and the method and the obvious eugenic risks it entails.”⁴²² The Senate’s prohibitive bill was additionally based on the potential abuses arising from the experimentation on in vitro embryos and the risks of legitimizing selection based on biological traits. Finally, after several attempts to pass the bill were blocked by the Senate, an agreement was reached to maintain the moratorium and to leave the matter of the regulation of genetic diagnosis for further study by a committee chaired by the then Senate MP Jean Chérioux and Conseil D’état MP Jean-François Mattei.⁴²³

⁴¹⁹ Mulkay, supra note 375.

⁴²⁰ See Nan T Ball, “The Reemergence of Enlightenment ideas in the 1994 French Bioethics Debates” (2000) 50.2 Duke L J at 556-557.

⁴²¹ See Anne-Sophie Paquez, “On the Political Side of Gene Therapy, What Can Be Drawn from the French Situation?” (2011) in Jörg Niewöhner, & Christof Tanner eds, *Gene Therapy: Prospective Technology Assessment in Its Societal Context* Amsterdam: Elsevier Science, 2011) 194.

⁴²² Jean-François Mattei, Rapport fait au nom de la Commission Spéciale, sur les Projets de Loi n° 957 et 962 Publications de l’Assemblée Nationale, 30 mars 1994, n° 1057, 140-147.

⁴²³ Anne-Sophie Paquez supra note 423. See also Jeanne Kohli supra note 408; Jean-François Mattei & Jean Chérioux, “Rapport fait au nom de la Commission Mixte Paritaire Chargée De Proposer Un Texte Sur Les Dispositions Restant En Discussion Du Projet De Loi Relatif au Don Et À L’utilisation Des Éléments Et Produits Du Corps Humain, “ À

In 1993, the Mattei-Chérioux Joint Committee was formed to study the regulation of genetic diagnosis, headed by Senator Jean-François Mattei, a professor of pediatrics and genetics.⁴²⁴ The Mattei-Chérioux committee report from 1994 recommended permitting genetic diagnosis only for well-circumscribed health-related purposes in exceptional circumstances when there are no alternatives. The report attempted to find an appropriate balance between two competing interests that were featured in the parliamentary debates: allowing parents to select against embryos that are likely to develop genetic malformations while preventing the slippery slope.⁴²⁵ Finally, the report's recommendations found a position that balanced between the two competing interests, although it gave greater weight to the need to avoid a slippery slope and its associated harms. In its recommendations, the committee stated that a full ban on genetic diagnosis would be overly restrictive, as it would impose on prospective parents the particularly trying choice of either undergoing abortion or ending up encouraging reproductive tourism to more lenient jurisdictions. The Mattei-Chérioux report recommended allowing genetic diagnosis to be used for screening embryos for lethal congenital malformations such as Duchenne Muscular dystrophy. However, the report further stated that genetic diagnosis should only be authorized in exceptional circumstances, recalling that the norm is not to resort to it. Using genetic diagnosis only in exceptional circumstances would set limits that would help avoid the slippery slope to practices such as the selection of the unborn child's sex based on parental and societal preferences. Mattei commented that choices based on parental preferences: "opens the door for the selection of embryos that will be either preserved or eliminated based on arbitrary criteria, which is essentially a eugenic approach."⁴²⁶ Jean Chérioux said that "for once, the law must anticipate the evolution

L'assistance Médicale À La Procréation Et au Diagnostic Prénatal Publications De l'Assemblée Nationale, Juin 1994, n° 1369, 18-19.

⁴²⁴ *Ibid.*

⁴²⁵ *Ibid.*

⁴²⁶ Jean-François Mattei, Rapport A Monsieur Le Premier Ministre Sur L'éthique Biomédicale Deuxième Partie Problèmes Soulevés Par Les Recherches Et Les Pratiques Médicales, at 27 online : http://www.ethique.sorbonne-paris-cite.fr/sites/default/files/2eme_partie.pdf

of science and better control the conditions of its application in order to prevent any eugenic drift.”⁴²⁷

II) The Passage of the Governing Acts in France and the UK

The French and UK parliaments both passed legislation that prohibited inheritable genetic modification and legalized genetic diagnosis. The UK parliament passed the *Human Fertilisation and Embryology Act* [hereafter: the HFE Act] in 1990. After 6 years of debates leading up to the enactment of the HFE Act, an agreement was made to leave the parameters for genetic diagnosis outside of the HFE Act, and instead in the hands of the newly created regulator – the Human Fertilisation and Embryology Authority [HFEA].⁴²⁸ The HFE Act empowers the HFEA to develop licensing parameters for genetic diagnosis, to be published in its guidelines – the Code of Practice.⁴²⁹ The legislative solution adopted in France was somewhat similar to that of the UK. The French Parliament passed in 1994 the *Bioethics Law*. The regulations were to be developed by the government and the then regulator CNMBRDP⁴³⁰ (the previous incarnation of the current regulatory agency, ABM - Agence de la Biomédecine).⁴³¹ Noëlle Lenoir, the Chair of the Parliamentary committee, stated that the future regulations on genetic diagnosis would enshrine the significant scientific, legal, and ethical principles agreed upon by the parliament.⁴³² The French and UK parliaments have thus

⁴²⁷ Mattei and Cherioux report supra note 423.

⁴²⁸ Colin Campbell, “Legislation and Regulatory Bodies: The Interface between Law and Ethics” (1995) N. Ir. Legal Q. 365 46:3-4 365-366.

⁴²⁹ See HFE ACT 1990 (London, HMSO), Sections 2, 3.6, 25.

⁴³⁰ Article R. 2131-27 placed the regulation of genetic diagnosis in the hands of Commissions Nationale de Médecine et de Biologie de la Reproduction et Diagnostic Prénatal (CNMBRDP), a body in the French Ministry of Healthcare and Solidary.

⁴³¹ The responsibility of the CNMBRDP has been transferred in 2004 to the Agence de la Biomédecine (ABM). The ABM has been created under the 2004 revision of the Bioethics Law to concentrate the regulation of several biomedical and reproductive techniques under the authority of one responsible body. See France, Sénat, Projet de Loi de Finances pour 2004 : Santé, Famille, Personnes online : <https://www.senat.fr/rap/103-073-336/103-073-3362.html>

Monpetit et al. compares the ABM’s mission and regulatory responsibilities to those of the HFEA in the UK see Éric Montpetit, et al., *The Politics of Biotechnology in North America and Europe: Policy Networks, Institutions and Internationalization* (Plymouth: Lexington Books, 2006) 126.

⁴³² Noëlle Lenoir supra note 407 at 43-47.

tasked regulators to develop regulations under the respective acts and create criteria to set appropriate limits in this complicated field.

III) The Establishment of the Regulatory Requirements under the Acts

In 1998, both France and the UK established the regulatory requirements under the respective acts related to licensing conditions for genetic diagnosis. In the UK, the regulatory requirements for licensing genetic diagnosis under the HFE Act were first listed in the fourth edition of the HFEA Code of Practice in 1998.⁴³³ In France, the regulatory requirements for licensing genetic diagnosis under the Bioethics Law, 1994⁴³⁴ were first published in article L. 162-17 of the 1998 Public Health Code.⁴³⁵ Both the French and British legislation listed four key requirements that had to be met in order for the regulator to grant a license to screen for a particular genetic condition.⁴³⁶ The French and UK regulations stipulate that permissible genetic diagnosis is restricted to a) a high-risk probability of transmission of b) an early-onset condition that is, c) fatal or seriously debilitating childhood condition that has d) no prospects for treatment.⁴³⁷ These requirements have been later incorporated in the 2004 version of the Bioethics Law and the 2008 HFE act.⁴³⁸

⁴³³ HFEA, Code of Practice 4th ed., (HMSO: London July 1998) - Section 10.6.

⁴³⁴ Code Civil, Issu de la Loi 94-654 du 29 Juillet 1994, Relative Au Don Et À L'utilisation des Éléments Et Produits du Corps Humain, À L'assistance Médicale À La Procréation au Diagnostic Prénatal), Article L. 2131-4.

The law was subsequently amended in 2004 and 2011. See La Loi no 2011-814 du 7 Juillet 2011 Relative à la Bioéthique.

⁴³⁵ See the authorizing government decree - Le diagnostic Préimplantatoire, Diagnostic Réalisé À Partir des Cellules Prélevées *in vitro* (du Code Civil art. L. 162-17 ; Décret n° 98-216 du 24 Mars 1998), Est Autorisé En France Et Les Conditions De Sa Réalisation Sont Précisées.

⁴³⁶ See notes 59, 61.

⁴³⁷ See HFEA and Advisory Committee On Genetic Testing "Consultation Document on Preimplantation Genetic Diagnosis" (London: HFEA, 1999). See also Décret n°98-216 du 24 Mars 1998 relatif au Diagnostic Biologique Effectué À Partir De Cellules Prélevées Sur L'embryon In Vitro Et Modifiant Le Code De La Santé Publique (Deuxième Partie : Décrets en Conseil d'État), Article L2131-4.

The ACGT [Advisory Committee on Genetic Testing] was an ethics committee advising the HFEA, which its responsibilities were later transferred to its successor the HGC [Human Genetics Commission]. See HGC, Meeting of the Genetic Services Sub-group: 23 October 2002 (2002), online: http://webarchive.nationalarchives.gov.uk/20081023094508/http://www.hgc.gov.uk/Client/Content_wide.asp?ContentId=683

⁴³⁸ In 2008, the HFEA has switched from a formal case by case system to a list of approved conditions. Prior to the enactment of the 2008 HFE act, the regulatory decisions were in regard to applications of individual prospective parents.

While at first glance, the restrictions on genetic diagnosis might appear rather technical, they have a broader, more substantive goal – the prevention of the slippery slope to eugenics and the associated ethical risks.⁴³⁹ Similarly, regulators themselves have repeatedly stated in the early days of the regulation that their goal is to give effect to the legislative objective of preventing a slippery slope to eugenics by setting legal limits that would prevent these technologies' misuse.⁴⁴⁰ Biomedical law expert and French Court of Appeals Judge Christian Byk highlights the concern that the ABM's and HFEA's licensing practices could end up eventually clashing with the respective acts' key objective. This scenario could materialize if regulators facilitate the growth of genetic intervention markets by favouring parental interests⁴⁴¹ over their public role of maintaining a robust control system.⁴⁴² Judge Byk explains that in order to meet the key legislative goal of preventing the slippery slope the HFEA and the ABM require constant and continuous vigilance.⁴⁴³

These decisions were administrative in nature and were subject to judicial review. See Jo Samanta & Ash Samanta, *Medical Law* (London: Macmillan International Higher Education, 2015) 219.

⁴³⁹ The next four chapters further explain the rationales of the particular regulatory restrictions. These chapters show that regulators and lawmakers have identified a number of specific concerns that arise from the slide down the slippery slope to eugenics such as the devaluation of lives with people with disabilities, stigmatization of reproductive choices, and in cases where there is no medical purpose at all, child objectification and commodification.

⁴⁴⁰ HFEA and Advisory Committee On Genetic Testing, "Outcome of the Public Consultation on Preimplantation Genetic Diagnosis" (London : HFEA, 2001) ; Ruth Deech, "Aims of the HFEA: Past and Future" (1999) 2:2 Hum Fertility 12; ABM, Diagnostic Prénatal, Interruption Médicale de Grossesse, Diagnostic Pré-implantatoire et Formes Héritaires de Cancers Rapport rédigé à la Demande de l'Agence de la Biomédecine et de l'Institut National du Cancer, Paris 2006, 18; Pierre F. Ray et al., "Diagnostic Préimplantatoire De La Pratique Au Législatif. L'embryon chez l'homme et L'animal" (Paris : INRA/INSERM, 2002). See also C. Rongieres et al. "Le Diagnostic Pré-Implantatoire : De La Théorie À La Pratique" Collège National Des Gynécologues et Obstétriciens Français–TOME XXVI (28.11.2002) at 72 online : http://www.cngof.asso.fr/d_livres/2002_GO_071_rongieres.pdf.

⁴⁴¹ Chadwick et al. commented that excessive facilitation of prospective parents' choice in child genetics bring raise profound ethical concerns that require regulators to set legal restrictions to parental and clinics conduct. Parents and clinics do not have unlimited rights to choose the genetic profile of the child or otherwise, it would risk the underlying the ethical the regulatory system is founded upon See Ruth Chadwick et al., "Genetic Screening and Ethics: European Perspectives" (1998) 23:3 J Med Philos 255-273.

The European Court of Human rights has confirmed more broadly Chadwick et al.'s point that parents do not have unlimited rights in the context of choices in assisted reproduction techniques in a string of decisions. See the ECHR decision in *S.H and Others v. Austria* [GC] [2011] App No. 57813/00, ECHR 87 Judgment of 1 April 2010, at para 82[Hereafter: *S.H and Others v. Austria*]; *Evans v. United Kingdom* [GC] [2008] App. No. 6339/05, Judgment of 10 April 2007 §118-123; *Dickson v. the United-Kingdom* [GC] [2007] App No. 44362/04, Judgment of 4 December 2007.

⁴⁴² Christian Byk, "Chapitre 5 "Preimplantation Genetic Diagnosis: An Ambiguous Legal Status for an Ambiguous Medical and Social Practice" (2008) 19:3 J Int'l Bioéthique 96.

⁴⁴³ *Ibid.*

Conclusion

This examination of the legislative and regulatory history has shown that the prevention of a slippery slope to eugenics is one of the key goals behind the enactment of the UK's and France's genetic intervention laws.⁴⁴⁴ From the beginning of the early 1980s, the British and French governments recommended prohibiting human germline modification and strictly regulating genetic diagnosis. One of the key risks repeatedly highlighted in government reports and debates was that genetic intervention technologies would evolve over time from methods to prevent lethal congenital malformations, to means of selecting future children's physical, cosmetic and cognitive traits deemed more desirable. Without proper boundaries, prospective parents will increasingly seek to exploit the real and perceived benefits of genetic interventions, resulting in a gradual transition to eugenic misuse of these technologies. Regulators were tasked with developing and maintaining regulatory restrictions that would allow genetic diagnosis of certain life-endangering conditions while preventing the slippery slope to eugenics. The remaining question is which course genetic intervention laws have charted over the years. In the next chapters, I will examine this key question and concern that senior legal figures repeatedly raised - are genetic intervention laws becoming more permissive as time goes by?

⁴⁴⁴ Supra note 375.

Chapter Four

“To Treat or Not to Treat?” Legal Change Concerning Treatable Conditions

This chapter describes and analyzes the considerable changes in the interpretation and the application of the rule that prohibits screening of treatable conditions.⁴⁴⁵ Laws in the United Kingdom and France originally prohibited such screenings on the grounds that with a viable treatment course, a child would effectively not suffer from a serious condition. Hence, screening for treatable conditions would not meet the underlying rationale that would warrant genetic diagnosis. Until 2003, the rule prohibiting screening for treatable conditions was maintained in both letter and spirit. However, since 2003 regulators started approving screenings even for the relatively small number of conditions that could be treated in a safe and effective manner. This chapter explains that such changes stem from the absence of a binding definition or evaluation criteria for which conditions qualify as treatable. These issues have contributed to an expansive reading of what are untreatable conditions to now include previously unrecognized considerations such as treatment cost (even those that are relatively low or covered by public health care), parental discomfort and difficulties in caring for the child. Under the broadened interpretations, regulators have read the untreatability requirement so broadly that even conditions widely regarded in the clinical literature as having safe and effective treatment have been classified as untreatable.

I) The Normative Considerations Behind Restricting Screening to Untreatable Conditions

What were the normative considerations behind permitting genetic diagnosis only for conditions that are not treatable? In short, conditions with a viable treatment course would no longer seriously affect the child's health. As such, treatable conditions would no longer satisfy the underlying rationale that would warrant a genetic diagnosis. A detailed answer requires a more in-depth examination of the normative

⁴⁴⁵ Not only that the literature has not examined the legal change to the rule restricting genetic interventions to untreatable conditions, it has discussed this rule very rarely and often briefly. This chapter aims to fill in the gap of the literature with a detailed analysis of the untreatability requirement and the significant legal change that it has undergone over the years.

foundations of the restriction of genetic diagnosis only to screen for serious conditions. Since lawmakers were unable to come to an agreement or to precisely articulate the underlying ethical underpinnings of the legal boundaries, the normative reasoning behind the seriousness standard has been discussed rarely and in broad terms. Nevertheless, regulators have explained that, in principle, the seriousness standard relies on a consequentialist balancing formula between two competing interests.⁴⁴⁶ One is the prospective parents' interest in deselecting an embryo if the resultant child's health will be significantly affected. The competing ethical interest prohibits the unwarranted destruction of embryos and such potential life prevention when the child's health is expected to be affected only in a minor way or not at all.⁴⁴⁷

Hudson et al. further explain how treatment options can tip the balance in favour of either allowing or disallowing genetic diagnosis. When treatment options are poor or nonexistent and the future child is expected to suffer harmful health effects, the balance tips in favour of approving genetic diagnosis. However, when a condition can be treated, and the child's life and health would not be significantly affected, the rationale is not maintained and the balance tips towards prohibiting the potential prevention of life.⁴⁴⁸ Similarly, Baroness Deech, the former chair of the HFEA, explains that when a condition can be successfully treated, it is unlikely to be regarded as serious.⁴⁴⁹

⁴⁴⁶ Baroness Mary Warnock, the chairperson of the Question of Life Report (The Warnock report), suggested that the seriousness standard is based on a mostly utilitarian balance between the harms of life prevention and the benefits "in the reduction of crippling genetic diseases" in Mary Warnock, "Moral Thinking and Government Policy: The Warnock Committee on Human Embryology" (1985) 63:3 *The Milbank Memorial Fund Q Health & Soc'y* 516-517.

⁴⁴⁷ HFEA Ethics Committee, Minutes of the Meeting of the Ethics Committee on Preimplantation Diagnosis, online http://www.hfea.gov.uk/docs/F-2010-00237_release_pack.pdf; See also CCNE "Opinion on Research and Use of in Vitro Human Embryos for Scientific and Medical Purposes" 1986 online: <http://www.ccne-ethique.fr/docs/en/avis008.pdf>

⁴⁴⁸ See Kathy Hudson et al, "Genetic testing of Human Embryos", in G. A.W. Galston, Christiana Z. Peppard eds. *Expanding Horizons in Bioethics* (Dordrecht: Springer 2005) 108.

⁴⁴⁹ Ruth Deech & Anna Smajdor, *Saviour Siblings, Designer Babies, and Sex Selection* (Oxford: Oxford University Press, 2008).

According to this consequentialist logic, a successful treatment would break the link between the inherited gene and the outcomes of the serious condition.⁴⁵⁰ Thévoz demonstrates this logic in which the treatment breaks the link to a serious condition. For example, in the case of phenylketonuria (PKU), a congenital inability to metabolize certain proteins in childhood, the treatment (dietary adjustments) breaks the link between the inherited gene and the outcomes of the disorder.⁴⁵¹ Likewise, Botkin, one of the academics who developed the untreatability requirement, explains that when the treatment breaks the link between the gene and the inherited disease, the ethical rationale for such genetic diagnosis procedures virtually disappears.⁴⁵²

Screening for Treatable Conditions – Societal Motivations and its Tensions with the Rule

What would be the ethical ramifications of moving ahead with genetic screening even when the condition is known to be treatable? An early CCNE opinion briefly explores the question of screening for treatable conditions and highlights some of its potential eugenic implications.⁴⁵³ As medicine and treatment options have advanced, they have contributed to extending the lifespan of people with congenital disabilities to and beyond reproductive age. From the viewpoint of eugenics, the demographic changes brought about by medical advances have effectively halted the process of natural selection.⁴⁵⁴ As the quality of the gene pool deteriorates, society has to confront the consequences of caring for a growing number of people with congenital disabilities and diseases.⁴⁵⁵ Hence, instead of bringing into the world more disabled children and

⁴⁵⁰ This HFEA and ACGT joint report that new treatment options can in effect relieve symptoms and dramatically increase life expectancy thus reducing the seriousness of the condition. See HFEA & AGCT *supra* note 437.

⁴⁵¹ Jean-Marie Thévoz, "L'annonce d'un Destin Tragique au Cœur D'une Vie sans Nuage" (1998) 54 :2 Laval Théo et Phil 247-276.

⁴⁵² See generally Jeffrey R. Botkin *supra* note 86 at 32, 37.

⁴⁵³ CCNE, "Opinion No. 5 on Problems Raised by Prenatal and Perinatal Diagnosis" – (May 13, 1985) at 10-11. Online: <http://www.ccne-ethique.fr/sites/default/files/publications/avis005en.pdf>.

⁴⁵⁴ *Ibid.*

⁴⁵⁵ *Ibid.*

opting for costly postnatal treatments, prenatal genetic interventions would reduce the financial expenditures and the societal consequences associated with caring for large numbers of people who have inherited faulty genes.⁴⁵⁶

The CCNE's opinion critically examines the motivations to screen for treatable conditions. The motivations to screen for treatable conditions go well beyond medical considerations of the quality of treatment, often into emotional, economic, or even policy considerations. The most ideologically inspired motivation of all, the eugenic approach, seeks to prevent the birth of children with treatable diseases and disabilities to save on the cost of treatments and accommodations, as well as to improve the quality of the gene pool.⁴⁵⁷ Prospective parents, however, are unlikely to adopt the eugenic collectivist thinking or be concerned about the long-term effects of their reproductive choices on the gene pool. Instead, prospective parents simply wish to take action that will not negatively affect their familial, emotional, or financial welfare by avoiding the birth of children with genetic disorders.⁴⁵⁸

Genetic diagnosis laws were initially concerned with a much narrower set of considerations—namely, whether the treatment broke the link between the inherited gene and the serious condition.⁴⁵⁹ This rationale reflects an assessment that is medical in nature: the evaluation of the clinical merits of the treatment. But what happens if this medical rationale ceases to be the primary consideration underlying the assessment of treatability? Gunning is concerned that the regulatory decisions to screen for treatable conditions are inconsistent with the medical rationale underlying the untreatability requirement and cross into the prohibited

⁴⁵⁶ *Ibid.*

⁴⁵⁷ Aside from the CCNE opinion, the argument regarding genetic intervention being used methods to cut on national expenditures on healthcare and social programs is also made by Buchanan et al. *supra* note 229 at 171-174.

⁴⁵⁸ Marie Gaille & Géraldine Viot *supra* note 308.

⁴⁵⁹ I will elaborate on the requirement restricting genetic diagnosis to serious conditions in chapter 6.

territory of socially-motivated screening.⁴⁶⁰ Yet the pattern of more socially motivated screening for treatable conditions took time to emerge, as the rule was originally applied in a manner that respected both the letter and the spirit of the law.

II) The Early Application of the Untreatable Condition Rule

From the late 1990s to 2003, the French⁴⁶¹ and UK⁴⁶² rules restricting genetic diagnosis to untreatable conditions were applied in a strict manner. The conditions approved for screening either lacked a viable treatment course or the treatment options showed poor results in mitigating the harmful effects of the disease. The conditions licensed were often those for which treatment and management options did not produce an extensive change in the patient's overall health profile. Notable examples include Tay-Sachs disease, cystic fibrosis,⁴⁶³ spinal muscular atrophy and Duchenne muscular dystrophy.⁴⁶⁴ A common characteristic of these conditions is that they lacked a medically viable treatment at the time of their approval.

III) An Overview of the Legal Change of the Untreatability Requirement

Around 2003, regulators began licensing screening conditions for which treatments were available. Initially, between 2003 and 2006, regulators began approving conditions that were overall treatable, but their

⁴⁶⁰ Jennifer Gunning, "The Broadening Impact of Preimplantation Genetic Diagnosis: A Slide down the Slippery Slope or Meeting Market Demand?" (2008) 14 :1 Hum Repro & Genetic Ethics 36.

⁴⁶¹ Le diagnostic Préimplantatoire, Diagnostic Réalisé À Partir des Cellules Prélévées *in vitro* (Code Civil art. L. 162-17 ; Décret n° 98-216 du 24 Mars 1998), Est Autorisé En France Et Les Conditions De Sa Réalisation Sont Précisées.

⁴⁶² HFEA, Code of Practice 4th ed., (London: HMSO July 1998) - Section 10.6.

⁴⁶³ Note that at the time of approval of genetic diagnosis for Cystic Fibrosis, in the early 1990s, treatment options were considerably more limited than today. Life expectancy of people with Cystic Fibrosis has increased from 31 years in 1990 to 50 years in 2012. See Anne L Stephenson et al., "A Contemporary Survival Analysis of Individuals with Cystic Fibrosis: A Cohort Study" (2015) 45:3 Eur Respiratory J 670. The case of Cystic fibrosis demonstrates how conditions can become more treatable as time goes by. McLean and Elliston suggest that the improvement in treatment options may warrant a re-evaluation of whether the condition should remain screenable if it has become treatable. See Sheila McLean & Sarah Elliston, *Regulating Pre-Implantation Genetic Diagnosis: A Comparative and Theoretical Analysis* (Taylor & Francis: New-York, 2012) 82.

⁴⁶⁴ See for example Rene Frydman et al., "Preimplantation Genetic Diagnosis: Update of the Parisian Group" (2001) 186:5 Bull de l'Académie Nationale De Médecine 865. See also HFEA & HGC, *Outcome of the Public Consultation on Preimplantation Genetic Diagnosis* (London: HFEA, 2001).

treatment course exhibited drawbacks, such as significant adverse effects. Two conditions approved for genetic diagnosis exemplify these drawbacks: retinoblastoma and beta thalassemia.⁴⁶⁵ Beta thalassemia is a blood disorder that requires repeated blood transfusions throughout life.⁴⁶⁶ The repeated blood transfusions can adversely affect the patient's spleen and in cases of spleen enlargement may require a surgical intervention to remove the damaged organ.⁴⁶⁷ Another presently approved (yet ethically contentious) therapeutic option is the creation of a histocompatible "saviour-sibling."⁴⁶⁸ The second notable example, retinoblastoma, is a rare form of eye cancer that often develops in early childhood.⁴⁶⁹ The progression of retinoblastoma, when confined to one eye, can be stopped by removing the affected eye. The removal of the affected eye results in a cure rate that is higher than 95 percent.⁴⁷⁰

From 2006 onwards, regulators began approving conditions that are commonly regarded in the clinical literature as having safe and effective treatment options. Such conditions can be safely and effectively treated with corrective surgeries, hormonal injections and dietary adjustments. For example, regulators approved screening for several inborn metabolic disorders that impair children's ability to metabolize certain

⁴⁶⁵ HFEA, "PGD Conditions Licensed by the HFEA" online: <http://guide.hfea.gov.uk/pgd/> See also ABM, Diagnostic Préimplantatoire -Indications Disponibles Pour Un Diagnostic Préimplantatoire En France 2018, Agence de la Biomédecine, online: <https://rams.agence-biomedecine.fr/sites/default/files/excels/2020-07/TDPI2.xlsx>

A case could be made to classify retinoblastoma and beta thalassemia as either treatable or untreatable. These two examples demonstrate that the process of legal change regarding the untreatability requirement includes intermediate cases.

⁴⁶⁶ Antonio Cao & Renzo Galanello, "Beta-thalassemia" (2010) 12:2 Genetics in Med 61.

⁴⁶⁷ Alain J Marengo-Rowe, "The Thalassemias and Related Disorders" (2007) 20:1 Proceedings 28-30.

⁴⁶⁸ Note that commentators frequently point that HLA typing raises ethical concerns such as instrumentalization. See Svetlana Rechitsky et al. "Preimplantation Genetic Diagnosis with HLA Matching" (2004) 9:2 Reprod BioMed Online 210; Robert G Edwards, "Ethics of PGD: Thoughts on the Consequences of Typing HLA in Embryos" (2004) 9:2 Reprod BioMed Online 223; Thomas Baldwin, "Ethical Issues in a Changing World" (2005) 8:2 Human Fertility 87.

See also a relevant case litigated in the House of Lords involving a UK child with beta-thalassemia in need of a histocompatible donor see. *R (On the Application of Josephine Quintavalle on Behalf of CORE) v HFEA* [2005] UKHL 28.

⁴⁶⁹ Timothy W Corson & Brenda L Gallie, "One Hit, Two Hits, Three Hits, More? Genomic Changes in the Development of Retinoblastoma" (2007) 46:7 Genes, Chromosomes and Cancer 617.

⁴⁷⁰ Murali Chintagumpala et al., "Retinoblastoma: Review of Current Management" (2007) 12:10 The Oncologist 1237.

nutrients. PKU can be effectively treated with a diet that supplements certain types of proteins.⁴⁷¹ Gaucher disease and Hunter syndrome can be successfully treated with enzyme replacement therapies.⁴⁷² Other notable treatable conditions approved for screening include Dopamine Responsive Dystonia, which can be effectively treated with a low dosage of L-DOPA, a medication that contains the missing building block of the neurotransmitter dopamine.⁴⁷³

Primarily after 2006, regulators began approving screening for conditions that are both treatable and could be classified as non-serious, mild conditions given their minor symptoms.⁴⁷⁴ Examples of such mild, treatable conditions are webbed hands, cleft lips, and clubfoot. In France, the ABM approved genetic diagnosis of embryos with Cherubism (excess build-up of jaw tissue).⁴⁷⁵ In the UK, the HFEA approved genetic diagnosis of embryos that have genes linked to Strabismus (cross-eyes).⁴⁷⁶ Approving such conditions creates a great tension with both the requirement that the condition is serious and that it is untreatable. All of the above conditions can be treated with fairly straightforward corrective surgery.⁴⁷⁷

In a 2006 report, the HFEA recognized that it has allowed screening for treatable conditions, but suggested that such approved screening was limited to only a few treatable conditions.⁴⁷⁸ How does the statement that only a few approved conditions are treatable fare when put in context? When the HFEA

⁴⁷¹ Vanessa J Poustie, & Joanne Wildgoose, “Dietary Interventions for Phenylketonuria” (2010) 1 The Cochrane Database of Systematic Reviews CD001304.

⁴⁷² Michael Beck, “Therapy for Lysosomal Storage Disorders” (2010) 62:1 IUBMB life 33-37.

⁴⁷³ Joseph Jankovic, “Treatment of Dystonia” (2006) 5:10 Lancet Neurology 864.

⁴⁷⁴ I will examine the topic of genetic diagnosis for mild conditions in greater detail in chapter 6. I will highlight a number of mild conditions that respond well to treatments such as rather straightforward surgical procedures and hormonal injects.

⁴⁷⁵ ABM Liste des Diagnostics Biologiques Sur L’embryon in Vitro (DPI) 2017 online: https://www.agence-biomedecine.fr/IMG/xlsx/2017_ra_dpi2016.xlsx&sa=U&ved=0ahUKEwjtoqma0unXAhXHWWhQKHdlRCIoQFggXMAE&usg=AOvVaw0M4cSK7L1aUqd09tXCASMq

⁴⁷⁶ HFEA supra note 465.

⁴⁷⁷ See for instance World Health Organization “Birth defects: Report by the Secretariat. Sixty-third World Health Assembly (provisional agenda item 11.7)” (Geneva: World Health Organisation, 2010) 63. See also Raymond J. Fonseca, *Oral and Maxillofacial Surgery-E-Book: 3-Volume Set* (Elsevier Health Sciences, 2017) 466-467.

⁴⁷⁸ HFEA, “Choices and Boundaries Report” (London: HFEA, 2006) 5.

published its report in 2006, the number of conditions approved for genetic diagnosis was around 200. Considering that only a small number of the conditions on the list were regarded as treatable,⁴⁷⁹ permitting screening for only “a few” treatable conditions was quite significant for a rule that, to begin with, applied to only a few conditions.

What was the fate of the untreatability requirement after the legal change? The untreatability requirement was never officially removed from the books in France or the UK. Still, even in the relatively few cases of congenital conditions that could be treated effectively and safely, regulators approved screening. Gunning and Holm question how PKU, for example, was approved for screening in the UK despite that it is clearly a treatable condition.⁴⁸⁰ A similar question about the untreatability requirement was also posed in the context of the French Code of Public Health.⁴⁸¹ Mackellar and Bachtel further suggest that an initial “slide down the slope” has already occurred with the regulatory approval of screening for treatable conditions.⁴⁸² When even the relatively few treatable conditions are legally classified as untreatable, the untreatability requirement is nearing the point of hardly setting meaningful limits.

The Unclear Regulatory Language’s Role in Legal Change: The Transition from Predominantly Objective Assessments of the Treatment’s Merits to Non-Science based Subjective Evaluations

The changes to the untreatability requirement reflect a growing inconsistency between conditions that are medically regarded as treatable and fertility regulators’ classifications of those conditions as untreatable. What could explain how the regulatory and medical evaluations of what is a treatable condition

⁴⁷⁹ For more about the relatively small percentage of congenital disorders that are treatable see Pierre Gosset & Céline Moutou, “Aperçu du Diagnostic Préimplantatoire Actuel en France” (2012) 4 :2 *Revue de Médecine Périnatale* 53. See also Edmund Pellegrino, *Changing Moral Focus of Newborn Screening: An Ethical Analysis by the President’s Council on Bioethics* (Washington DC: DIANE Publishing 2008) 96.

⁴⁸⁰ Jennifer Gunning & Soren Holm, *Ethics, Law, and Society* (Aldershot: Ashgate, 2007) 224.

⁴⁸¹ Maud Lardy, *L’Extension Du Diagnostic Préimplantatoire* (Saarbrücken : Éditions Universitaires Européennes, 2011).

⁴⁸² MacKellar & Bechtel supra note 252 at 85.

have drifted so far apart? Answering this question requires a deeper examination of how the untreatability requirement is defined, assessed, and applied in this regulatory context. Since the interpretation of the untreatability requirement itself has changed, the examination of the rule must consider the changes in its application and interpretation over time.

IV) Change in the Interpretation of the Untreatability Requirement

Initially, the interpretation of the untreatability requirement was based primarily on an objective assessment of the treatment's merits. The objective evaluation emphasized factors of efficacy, availability and to a lesser extent, safety. A CCNE opinion states that the untreatability requirement is concerned with the overall positive and negative impact of the treatment on the child's health and the efficacy and commercial availability of the treatment.⁴⁸³ These same considerations of safety, efficacy, and availability are mentioned in a foundational HFEA report about the screening criteria for genetic diagnosis.⁴⁸⁴ Baroness Deech, the former chair of the HFEA, stated that while the Code of Practice (the regulatory guidelines) was initially being drafted, the determinative factors for the assessment of the treatment were its availability and its effectiveness.⁴⁸⁵

Academics have additionally discussed the original application of the rule based on child-centric normative considerations. Gosset points out that the ABM will deny a classification of a condition as treatable “only for treatments [whose] efficacy is unknown [and] in more or less [the] long-term, the availability of which is uncertain (bone marrow transplants or organs) or with the heavy and/or side effects.”⁴⁸⁶ Similarly, Boddington and Parker explain that the main considerations the HFEA originally used to assess treatability

⁴⁸³ CCNE, Opinion No.5, *supra* note 453 at 7-9.

⁴⁸⁴ HFEA and AGCT, “Consultation Document on Preimplantation Genetic Diagnosis” (London: HFEA, 1998) at 34.

⁴⁸⁵ Ruth Deech, “Infertility and Ethics” (1997) 9 *Child & Fam LQ* 344.

⁴⁸⁶ Pierre Gosset, *supra* note 50 at 676.

were availability and efficacy.⁴⁸⁷ As reflected in the above sources, untreatability was predominantly assessed based on the effects of the treatment on the putative child's health and its ability to negate the serious condition the child might experience.

Nevertheless, both in the UK and France, the laws never included a binding definition of the requirement or what considerations (safety, efficacy, etc.) played a role in the assessment of treatability. A binding definition of treatment could have grounded the interpretation of the vague requirement and potentially prevented an overly broad application.⁴⁸⁸ However, the laws and the regulators themselves rarely, if ever, provided helpful guidance on how to define or evaluate a condition's treatability.⁴⁸⁹ Isasi et al. acknowledge that the concept of untreatability in France and the UK remains vague.⁴⁹⁰ Furthermore, Knoppers and Isasi point out that the untreatability requirement is "extremely elastic" and can include non-medical, individual, and societal considerations.⁴⁹¹

It is this very elasticity that has enabled regulators to broaden the scope of the untreatability requirement. The lack of definition and lack of limits on the scope of the untreatability requirement enabled regulators to read the requirements broadly to include individual and societal considerations. The HFEA has changed its previous policy and decided to place greater attention on individual circumstances and prospective parents' views on the potential treatment options.⁴⁹² A 2013 CCNE opinion points out that in France, although the untreatability requirement can be defined in medical terms, it also incorporates non-

⁴⁸⁷ Paula Boddington & Michael Parker, "Preimplantation Genetic Diagnosis for Familial Hypercholesterolaemia: A Commentary on the Recent HFEA Decision" (2008) 3:3 Clinical Ethics 145-146.

⁴⁸⁸ See Matthias Klatt, *Making the Law Explicit: The Normativity of Legal Argumentation* (New York: Hart Publishing, 2008) 254-258.

⁴⁸⁹ For example, the ABM suggested interpreting the requirement in light of a common sense approach, which would mean that only minor improvement should not qualify as a treatment. See ABM supra note 440.

⁴⁹⁰ Rosario Isasi et al. supra note 50 at 338-339.

⁴⁹¹ Bartha M Knoppers & Rosario M Isasi, "Regulatory Approaches to Reproductive Genetic Testing" (2004) 19:12 Human Repro 2697.

⁴⁹² HFEA, Scientific and Clinical Advances Committee "PGD for Cancer Susceptibility" (London: HFEA, 2004) 4.

medical considerations, such as the family's circumstances and viewpoints.⁴⁹³ Likewise, the ABM states that the evaluation of untreatability would take into consideration the suffering of both the potential children and their families.⁴⁹⁴ As this chapter will later show, regulators have reinterpreted the untreatability requirement in such a broad manner to eventually include factors such as the costs of treatments borne by the parents (even though those costs are very often covered by public health insurance) or the inconvenience to the family (in terms of common activities such as helping the child to maintain dietary restriction). When regulators introduced unqualified emotional, social, and economic considerations to classify a condition as untreatable, they significantly broadened the notion of untreatability.

Even if regulators view individual considerations as relevant assessment factors, they have not demarcated a cut-off point in which these new considerations stop overriding the determination that the condition is medically treatable. Without limits on the scope and the weight individual viewpoints are given, conditions that are overwhelmingly treatable from a medical science viewpoint can still be legally classified as untreatable. This apparent dichotomy stems from the point that individual considerations of costs and difficulties associated with caring for a child with greater needs can be argued for nearly every chronic condition requiring continuous treatment.

V) Review of Illustrative Case Studies of Screening against Treatable Conditions

I now turn to demonstrate how such individual considerations may affect the classification of particular conditions as untreatable by reviewing illustrative case studies of three treatable metabolic disorders: PKU, Hunter syndrome, and Gaucher disease.⁴⁹⁵ In all three cases, safe and effective treatment options are

⁴⁹³ CCNE, "Opinion No. 120 - Ethical Issues in Connection with the Development of Foetal Genetic Testing on Maternal Blood" (Paris: CCNE, 2013) at 33 online: <https://www.ccne-ethique.fr/sites/default/files/publications/avis120vbeng.pdf>.

⁴⁹⁴ ABM, *supra* note 440 at 17.

⁴⁹⁵ As noted in the research plan in chapter 1, I do not pertain to provide a complete account of all the various motivations of prospective parents, clinicians and regulators to go ahead with the particular genetic interventions in question (which here is genetic diagnosis for treatable conditions). Instead, I will review three illustrative that reflect particular motivations

available. These case studies show how the untreatability requirement's vagueness, subjectivity, and lack of limits on its scope have led to interpretations that are so broad they have left the rule with very limited ability to set meaningful limits. Even when the few conditions that are highly treatable from a medical standpoint are legally classified as untreatable, the requirement nears the point where it ceases to perform a meaningful boundary-setting function.

Is PKU Treatable or Untreatable? Arguments about Prospective Parents' Anticipated Difficulty and Discomfort in Supervising the Special Diet

Should PKU be regarded as a treatable or an untreatable condition? Before reviewing the change to the regulatory policy, let us first examine the condition and its treatment course. PKU is a chromosomal metabolic disorder caused by an inability to digest the phenylalanine (PHE), an amino acid, a building block of protein, found for instance in eggs, cheese and poultry.⁴⁹⁶ If left untreated, excessive buildup of PHE can affect infant brain development and can lead to intellectual disability, seizures, and a behavioural pattern on the autistic spectrum.⁴⁹⁷

As an enzyme deficiency, PKU can be treated effectively with a low PHE diet.⁴⁹⁸ Furthermore, an extensive meta-analysis found that the PKU diet is a highly safe and effective treatment method.⁴⁹⁹ Patients who maintain these dietary restrictions live in good health to old age.⁵⁰⁰ PKU is routinely diagnosed as a part

(such as parental discomfort, difficulty and reducing healthcare expenditures), which could be driving the boundaries to expand in the context of the untreatability requirement.

⁴⁹⁶ Robin A Williams, Cyril DS Mamotte & John R Burnett, "Phenylketonuria: An Inborn Error of Phenylalanine Metabolism" (2008) 12 Metabolism 36.

⁴⁹⁷ Bahare Azadi et al., "Executive Dysfunction in Treated Phenylketonuric Patients" (2009) 18:6 Eur Child & Adolescent Psychiatry 361.

⁴⁹⁸ Nenad Blau, Francjan J. Van Spronsen & Harvey L. Levy, "Phenylketonuria" (2010) 376:1417 Lancet 1417-1427.

⁴⁹⁹ Agency for Healthcare Research and Quality, "Adjuvant Treatment for Phenylketonuria (PKU) - Comparative Effectiveness Review" at 12. online: http://effectivehealthcare.ahrq.gov/ehc/products/259/957/executivesummary_CER56_PKU.pdf.

⁵⁰⁰ Susan A Berry et al., "Newborn Screening 50 Years Later: Access Issues Faced by Adults with PKU" (2013) 15:8 Genetics in Med, 591.

of neonatal screenings programs in the UK⁵⁰¹ and France.⁵⁰² As such, PKU is diagnosed very shortly after birth. Yet, even if the treatment begins in early childhood, a low-PHE diet can dramatically reverse symptoms of PKU, including intellectual disability.⁵⁰³ The NIH guidelines suggest that children with PKU will be able to partially relax their dietary restrictions as they grow.⁵⁰⁴ In addition, the EMA⁵⁰⁵ and the FDA⁵⁰⁶ approved Kuvan (sapropterin), a medication that works in conjunction with the PKU diet to further reduce the level of PHE amino acids in the blood. Thus, Kuvan allows children and their parents greater liberties with the dietary choices they make.

The Change in PKU's Classification from a Treatable to a Nontreatable Condition

The HFEA originally rejected the first application for PKU because the low-PHE diet is a safe and effective treatment.⁵⁰⁷ The HFEA's decision not to permit genetic diagnosis for PKU was consistent with much of the clinical literature on the existence of safe and effective treatment for PKU. The decision was also consistent with the NHS's approval of neonatal screening on the grounds that PKU is treatable.⁵⁰⁸

⁵⁰¹ National Health Services (NHS), "UK Newborn Screening Programme Centre a Guide to Newborn Blood Spot Screening for Health Professional Handbook" (2012) online: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390977/Health_Professional_Handbook_2012_v1.0_December_2012.pdf

⁵⁰² Agence de la Biomédecine, "Regards Croisés sur la Qualité de Vie" (2011) Agence de la Biomédecine, online: https://www.agence-biomedecine.fr/IMG/pdf/actes_journees-agence_def.pdf

⁵⁰³ Susan E Waisbren et al., "Phenylalanine Blood Levels and Clinical Outcomes in Phenylketonuria: A Systematic Literature Review and Meta-Analysis" (2007) 92:1 *Molecular Genetics and Metabolism* 63-70.

⁵⁰⁴ National Institutes of Health Consensus Development Panel, "National Institutes of Health Consensus Development Conference Statement" Phenylketonuria (PKU): Screening and Management" (2001) 108 *Pediatr* 972-982.

⁵⁰⁵ European Medicines Agency, "EPAR Summary for The Public Kuvan," Sapropterin Dihydrochloride. EMA/350999/2017 EMA (November 11, 2017) online: https://www.ema.europa.eu/en/documents/overview/kuvan-epar-summary-public_en.pdf

⁵⁰⁶ US Food & Drug Administration, "Drug Approval Package, Kuvan (Sapropterin Dihydrochloride) Tablets" FDA (December 13, 2007) online: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2007/022181TOC.cfm

⁵⁰⁷ Stuart Lavery et al., "Successful Live Birth following Preimplantation Genetic Diagnosis for Phenylketonuria in Day 3 Embryos by Specific Mutation Analysis and Elective Single Embryo Transfer" (2013) 7 *JIMD Reports-Case and Research Reports* 51-55.

⁵⁰⁸ It is interesting to note the discrepancy between PKU being regarded as treatable after the child is born and untreatable before an implementation of an affected embryo. For the NHS classification of PKU as a treatable condition see NHS supra note 501.

Nevertheless, following the second application in 2008, the HFEA reversed its position and decided to permit genetic diagnosis for PKU.⁵⁰⁹ A key argument in the decision to reverse the previous policy was the potential effects of the treatment course on the parents.⁵¹⁰ The HFEA license for PKU asserted that the treatment course, which involved supervising the special protein diet, caused the parents and the whole family a great deal of discomfort and difficulty.⁵¹¹ The HFEA license cited submissions made by a patient group, Genetic Alliance UK, an industry-funded group that was involved in the second application.⁵¹² Lavery, one of the chief medical practitioners at the clinic that first received the license, writes: “[t]he licensing of PGD for PKU in the UK represents a major ethical shift in the application of PGD for chronic treatable conditions.”⁵¹³

Individual Views on the Treatability of PKU

The decision to permit screening hinged on the following question: in the eyes of prospective parents, does the responsibility of supervising a child’s special diet cause a degree of difficulty that would make it preferable to avoid the potential birth of the child?⁵¹⁴ Certainly, supervising a child with dietary restrictions can be a stressful endeavour. Studies about the parental experience with the condition report

⁵⁰⁹ HFEA License Meeting Committee, “Centre 008 (IVF Hammersmith) Variation to add PGD for Phenylketonuria” (London: HFEA, 2009).

⁵¹⁰ Please note that the ABM in France did not make its licensing decisions publicly available. The ABM and HFEA decisions are only publicized sporadically.

⁵¹¹ HFEA License Meeting Committee *supra* note 509.

⁵¹² *Ibid.*

⁵¹³ Stuart Lavery et al. *supra* note 507.

⁵¹⁴ Hens et al. pose a similar question. Prior to genetic diagnosis becoming an option, prospective parents have seen their responsibility as supervising the child’s PKU diet. However, with the introduction of genetic diagnosis, interested prospective parents redefine their responsibility as avoiding the potential birth of a child that may be affected by PKU. Interested prospective parents justify such choices as both beneficial for their future child, their family and their own personal welfare. See Kristien Hens et al., “Parental Responsibility: A Moving Target” in *Parental Responsibility in the Context of Neuroscience and Genetics* (Heidelberg: Springer, 2017) 3.

somewhat elevated stress and anxiety associated with supervising the PKU diet.⁵¹⁵ However, from a policy perspective, should the inconvenience of supervising a child with dietary restrictions be regarded as a sufficient reason to prevent the child from being born in the first place? Parents commonly have children with non-genetic, acquired food allergies, such as peanut allergies, which can have greater health repercussions than PKU. Is it truly preferable as a matter of policy to allow prospective parents to choose to avoid the birth of children with special dietary needs? Or might it also be that new technological capabilities can reshape prospective parents' preferences and expectations?⁵¹⁶

How might prospective parents view care for a child in need of supervision for a PKU diet? This question cannot be answered with a blanket statement as personal viewpoints are a subjective matter. Prospective parents' opinions about having a child with PKU greatly vary.⁵¹⁷ A University of Leeds team conducted a quantitative and qualitative study using semi-structured interviews with 216 British participants to gauge their views on genetic diagnosis for a number of conditions, including for PKU. The participants predominantly considered the perceived seriousness of the condition in question, the associated emotional costs and the participant's ability and knowledge regarding caring for a child with the condition. Overall, PKU was ranked as the least legitimate indication for genetic diagnosis in the study. Only 32 percent of the respondents suggested they would wish to use genetic diagnosis to avoid the birth of a child with PKU.⁵¹⁸

Personal accounts revealed quite different views on having a child with PKU. One respondent commented “[e]rm, on the one that I ticked no for (PKU)... it’s only ‘could cause mental problems if left

⁵¹⁵ See Astrid Fidika, Christel Salewski & Lutz Goldbeck, “Quality of Life among Parents of Children with Phenylketonuria (PKU)” (2013) 11:1 Health and Quality of Life Outcomes 54. See also Alexandre Fabre et al., “Assessment of Quality of Life of the Children and Parents Affected by Inborn Errors of Metabolism with Restricted Diet: Preliminary Results of a Cross-Sectional Study” (2013) 11:1 Health and Quality of Life Outcomes 158-163.

⁵¹⁶ See Leon Kass *supra* note 122 at 33. See also Kristien Hens et al. *supra* note 514.

⁵¹⁷ Chloe Miller, Jenny Hewison & Stephen Morley, “A Comparison of Decisions about Prenatal Diagnosis and Pre-Implantation Genetic Diagnosis” (2012) 30:4 J Repro & Infant Psychol, 381-386.

⁵¹⁸ Chloe Louise Miller, *A Comparison of Attitudes towards Prenatal Diagnosis and Pre-Implantation Genetic Diagnosis*, (Leeds: The University of Leeds, 2010) [unpublished] 62.

untreated' and they've just got, would have, a normal lifespan and they've just got to have diet restrictions which... a lot of people have dietary restrictions. It's not a big thing."⁵¹⁹ Another participant responded less decisively about genetic diagnosis with regards to PKU: "[t]he thought of designer babies, a la Gattaca, is quite horrifying, but I also feel that knowingly birthing a child which is pre-destined to suffer seems cruel. Condition D (PKU) could go either way with me...."⁵²⁰

Howell advocates for a system that puts at the center parental views on whether the condition is still serious after the treatment. Howell writes: "[s]everity [seriousness] estimates are particularly important. For example, for those of us who have been taking care of your children for a long time, we tend to think that, well, you know that, the diet, the PKU is a very straightforward treatment. Families do not think so. It is a big deal; it is very complicated. And so severity will clearly have a very different view depending on whether you're living with it or at a distance".⁵²¹ Yet, one key question remains - can prospective parents' personal viewpoints regarding difficulty and discomfort set clear and effective legal limits?

Could Parental Subjective Views on A Condition's Treatability Set Effective Limits?

Could a system that is based on parental views impose on itself effective limits that would exclude conditions that are obviously treatable? In a system that is geared towards individual parents' considerations, laws cannot implement a test to distinguish between qualified and unqualified difficulty and discomfort. To further illustrate the point, consider the following questions: Is it possible to develop a legal test to distinguish acceptable from unacceptable parental anticipated difficulty and discomfort? Could regulators articulate or demarcate a cut-off point at which the viewpoints of prospective parents stop overriding the medical assessment that the condition is treatable? How can we know that the parents would truly suffer from

⁵¹⁹ *Ibid* at 48.

⁵²⁰ *Ibid* at 48-49.

⁵²¹ Rodney R. Howell, "Systems to Determine Treatment Effectiveness in Newborn Screening" (2009) 19 Health Matrix 160.

difficulty and discomfort if the alleged negative consequences have yet to even materialized? Arguably, every course of treatment is accompanied by a degree of difficulty and discomfort for the parents. Hence, without a way to draw lines, in nearly all cases parents would be able to argue that the anticipated difficulty and discomfort associated with the treatment should take precedence.

At the root of regarding PKU as an untreatable condition lies the difficulty in finding an acceptable point from which individual parents' claims of expected discomfort and difficulty stop overriding the medical assessment that the condition is treatable. The case of PKU illustrates the notion that even a common parental activity such as supervising a special diet provides sufficient grounds to override the medical assessment that the condition is treatable. Supervising a special diet is not an easy task, but then, which pediatric treatment courses are easy for the parents? Expecting a treatment course to barely cause emotional difficulties for the prospective parents would effectively render the untreatability requirement irrelevant. The PKU diet example illustrates how even a condition that is treatable with simple dietary adjustments can be regarded as untreatable. If PKU, a condition treatable with effective, safe, and readily available dietary adjustments, is not regarded as treatable, what condition could potentially meet the law's new high bar of treatability?

Priceless Lives and Pricey Treatments – The Role of Healthcare Expenditures in Assessing Treatability

What role should financial costs play in determining whether a condition is treatable? From the standpoint of the original objectives, the evaluation of treatability depends on a medical question: does the treatment break the link between the gene and the serious conditions? Introducing costs as a factor in evaluating treatability could lead to an outcome in which the lives of otherwise healthy children would be prevented because the costs of caring for them are deemed prohibitive.

Two conditions exemplify the potential role that the high cost of treatment plays in decisions to approve genetic diagnosis for treatable conditions: Gaucher disease (type I) and Hunter syndrome. Both

conditions present clinical similarities in terms of their biological mechanisms and treatment methods. Both conditions are inborn errors of metabolism, related to deficient lysosomal enzymatic function (glucocerebrosidase in the case of Gaucher disease and iduronate-2-sulfatase in Hunter Syndrome.)⁵²² Both conditions respond well to an enzyme replacement therapy treatment.⁵²³

Gaucher disease and Hunter syndrome are both extremely rare diseases. The birth rate in the general population is less than 1:70,000 for Gaucher disease and 1:120,000 for Hunter syndrome.⁵²⁴ The low prevalence of Gaucher disease and Hunter syndrome led the EMA (the European Medicines Agency) to designate the treatments for these two rare disorders as orphan drugs.⁵²⁵ The EMA describes the orphan drug designation as a structure that “allows a pharmaceutical company to benefit from incentives from the European Union to develop a medicine for a rare disease, such as reduced fees and protection from competition once the medicine is placed on the market.”⁵²⁶ The enzyme replacement therapy for Hunter syndrome costs is in excess of €350,000 per year per individual patient. The enzyme replacement therapy for Gaucher disease costs from €30,000 for infants to potentially over €400,000 per year per individual patient.⁵²⁷

Katz considers health economics to be a key reason behind the regulatory decisions in France and the UK to approve screenings for these conditions. Katz and Schweitzer point to the high cost of the

⁵²² See Ashok Vellodi, “Lysosomal Storage Disorders” (2005) 128:4 *Brit J Hematology*, 414-417. See also Ramakrishna S Sista et al., “Multiplex Newborn Screening for Pompe, Fabry, Hunter, Gaucher, and Hurler Diseases Using a Digital Microfluidic Platform” (2013) 424 *Clinica Chimica Acta* 12-14.

⁵²³ Katrina Wyatt et al., “The Effectiveness and Cost-Effectiveness of Enzyme and Substrate Replacement Therapies: A Longitudinal Cohort Study of People with Lysosomal Storage Disorders” (2012) 16:39 *Health Tech Assessment* 1366.

⁵²⁴ Carla EM Hollak et al., “Limitations of Drug Registries to Evaluate Orphan Medicinal Products for the Treatment of Lysosomal Storage Disorders” (2011) 6:1 *Orphanet J Rare Diseases* 17-19.

⁵²⁵ European Medicines Agency, “Relevant Sources for Orphan Disease Prevalence Data” (2014), EMA online: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/07/WC500130297.pdf

⁵²⁶ For more about and the regulation of orphan drugs in the EU and economic consideration in the regulatory decision-making process see Genevieve Michaux, “EU Orphan Regulation-Ten Years of Application” (2010) 65 *Food & Drug LJ* 639. See also Christian A. Gericke, Annette Riesberg & Reinhard Busse, “Ethical Issues in Funding Orphan Drug Research and Development” (2005) 31:3 *J Med Ethics* 164.

⁵²⁷ Erik Tambuyzer, “Rare Diseases, Orphan Drugs and Their Regulation: Questions and Misconceptions” (2010) 9:12 *Nature Reviews Drug Discovery* 922-923.

Genzyme manufactured enzyme replacement therapy for Gaucher disease as a potential factor for approving genetic diagnosis in the UK.⁵²⁸ Likewise, the authors suggest that the approval of the screening for Gaucher disease in France was driven by the high cost of treatment.⁵²⁹ Western European nations frequently cover the cost of essential treatment for children with congenital disorders. The UK and France operate publically funded insurance schemes that cover the cost of medications, including the typically expensive treatments for rare diseases.⁵³⁰ Katz asserts there is a convergence of interests between the parents and the state: the prospective parents wish to have a child free of genetic disease while the state authorities want to reduce public health care expenditures.⁵³¹ Regulators do not ignore their stakeholders' practical motivations; they consider that permitting genetic diagnosis will be aligned with both prospective parental individual interests and the state's economic interest in implementing cost-cutting measures.⁵³²

Israël Nisand, a former board member of the CCNE, confirms that the costs of treatment and accommodations for people with disabilities have driven the policy of expanding the scope of screenable conditions. Nisand explains that in certain cases, the costs of supporting expensive treatments grossly exceed the costs of genetic diagnosis. He notes that in a fiscally tight policy environment, economic challenges can

⁵²⁸ Gregory Katz & Stuart O Schweitzer *supra* note 120.

⁵²⁹ *Ibid.*

⁵³⁰ While lack of access to essential medicine can effectively render a condition untreatable, this is generally not the situation in the UK and France, where residents have access to publically funded treatments. Moreover, the English and French formularies list treatments for Hunter Syndrome and Gaucher disease. See for instance NHS England, "E06/S(HSS)/c 2013/14 NHS Standard Contract for Lysosomal Storage Disorders Service (Children) Particulars, Schedule 2 – The Services, A – Service Specification" (2014) NHS England online: <https://www.england.nhs.uk/wp-content/uploads/2013/06/e06-lyso-stor-dis-child.pdf>

⁵³¹ At the present, genetic diagnosis against rare and ultra-rare diseases would not necessarily be an effective method to control the often high expenditures on rare diseases for a number of reasons. First, the probability of prospective parents undergoing genetic diagnosis to prevent the birth of a child with a rare disorder is itself very low. For instance, both prospective parents know they are carriers (in the case of autosomal, non-sex related inheritance pattern), which is in itself an extremely rare scenario. Second, even if genetic diagnosis could eventually be a successful method to substantially reduce the number of individuals born with certain rare diseases; this would create a disincentive for governments and pharmaceutical companies to keep on investing in developing new orphan drugs. Without investment in research and development, people living with rare disorders would have much less hope of receiving treatment for their condition. See similar points by MacKaller and Bechtel *supra* note 252 at 85.

⁵³² Gregory Katz-Bénichou, "Le Tamisage des Naissances" (2006) 4 *Cités* 90-91.

trump bioethical concerns.⁵³³

Economic calculations of cost-benefit analysis can play a role in decisions to permit genetic diagnosis.⁵³⁴ Katz and Schweitzer suggest it is much more cost-effective for the NHS to fund genetic diagnosis for carriers of rare diseases than to provide insurance coverage for costly treatments.⁵³⁵ NHS policy institutes commissioning genetic diagnosis for parents who are carriers of either Gaucher disease or Hunter syndrome.⁵³⁶ The UK Parliamentary Office of Science and Technology report specifically discusses genetic diagnosis for Gaucher disease. The report states, “[v]ery few genetic disorders have effective treatments available; most health care for genetic disorders is palliative. Gaucher disease, which is a condition licensed for PGD, can be treated with enzyme replacement therapy, greatly improving the quality of life.” However, the report goes on to note that even though Gaucher disease is treatable, a consideration in favour of allowing genetic diagnosis is the treatment’s high cost.⁵³⁷

Screening for Fiscal Soundness

Economic pressures favouring potential disease prevention are not likely to diminish in the future. Indeed, they are expected to increase, potentially opening the door for genetic interventions premised on the notion of cutting on expenditures.⁵³⁸ A European Union study suggests that European nations fund genetic

⁵³³ G  n  thique, “D  nonciation d’un Eug  nisme de Masse dans le Cadre du Diagnostic Pr  natal ”, *G  n  thique* (1 February 2012) online : <http://www.genethique.org/en/denouncement-mass-eugenics-framework-prenatal-diagnosis-61743.html>

⁵³⁴ Shakespeare highlights a typical viewpoint held by eugenicists of looking at people with disabilities as a financial burden borne by society. Shakespeare is concerned about the use of a cost-benefit like calculus will eventually come to determine which children will be brought in to the world and which will not. See Shakespeare *supra* note 229 at 669.

⁵³⁵ Katz & Schweitzer *supra* note 120.

⁵³⁶ NHS, “Clinical Commissioning Policy: Pre-implantation Genetic Diagnosis (PGD)”, England National Health Service (April 2013) online: <https://www.england.nhs.uk/wp-content/uploads/2013/04/e01-p-a.pdf>

⁵³⁷ United Kingdom Houses of Parliament, The Parliamentary Office of Science and Technology, Post Note, Number 445 September 2013 “Pre-implementation Genetic Diagnosis” online: researchbriefings.files.parliament.uk/documents/POST-PN-445/POST-PN-445.pdf

⁵³⁸ See Troy Duster, *Backdoor to Eugenics* 2d ed. (New York: Routledge, 2003) 53-54; See also Abby Lippman, “Eugenics and Public Health” (2003) 93:1 *Am J Public Health*, 11. See also Ralph Snyderman & Jason Langheier, “Prospective Health Care: The Second Transformation of Medicine” (2006) 7 *Genome Biology* 104.

diagnosis because they expect to save the public treasury millions by reducing expenditures on accommodations and treatments.⁵³⁹ States in the future might be more inclined to loosen their regulation of genetic interventions and encourage them in times of fiscal constraints and soaring public debt.⁵⁴⁰ Another European Union report seems to reaffirm the argument about the cost-cutting motivations and suggests that under growing fiscal constraints and mounting sovereign debt, genetic diagnosis schemes may seem like an appealing method to cut the costs of accommodations for health care and other social programs.⁵⁴¹ With growing public health care spending and rising debt levels, more treatable conditions with lower treatment costs may nevertheless be approved for genetic diagnosis. Bailey, who examined the phenomenon in the similar context of newborn screening, suggests that rising health care expenditures can push health care policy toward eliminating the line between treatable and untreatable conditions altogether.⁵⁴² From a narrow fiscal perspective, public expenditures on healthcare and accommodations could become reasons to prevent the potential birth of people in need of such care.

VI) Reflections on the Potential Outcomes of the Legal Change

How might the changes to the untreatability requirement be viewed? Proponents of broader genetic choices would likely view the legal change in a positive light. Scott et al. argue that prospective parents should be allowed to screen for treatable conditions based on familial considerations and the costs of the treatments.⁵⁴³ Similarly to Scott et al., Knoppers and Isasi argue that the costs of medical treatment should be a consideration in favour of permitting screening. Knoppers and Isasi view broad interpretations as

⁵³⁹ Anniek Corveleyn, & European Commission. *Preimplantation Genetic Diagnosis in Europe* (Luxembourg: Office for Official Publications of the European Communities, 2007).

⁵⁴⁰ See for instance the general discussion by Garland *supra* notes 346 and 347.

⁵⁴¹ European Union *supra* note 348 at 26.

⁵⁴² Donald B Bailey Jr, “The Blurred Distinction between Treatable and Untreatable Conditions in Newborn Screening” (2009) 19 Health Matrix 144.

⁵⁴³ Rosamund Scott et al., “The Appropriate Extent of Pre-Implantation Genetic Diagnosis: Health Professionals’ and Scientists’ Views on the Requirement for a ‘Significant Risk of a Serious Genetic Condition’ (2007) 15 Med L Rev at 330-332.

preferable because they can help interested parents to avoid congenital disorders, even if these conditions might be medically treatable.⁵⁴⁴ The authors conclude that the untreatability requirement should be interpreted broadly to keep the market readily accessible to its consumers—the prospective parents.⁵⁴⁵

What might be the cumulative effect of many prospective parents choosing genetic screening for treatable conditions? A CCNE opinion has warned about a push in the direction of more extensive use of genetic diagnosis as a means to reduce health care costs, noting that such a pattern would have negative ethical implications.⁵⁴⁶ Similarly, a report by the national research funding institution INSERM⁵⁴⁷ mentions the concern that genetic intervention would revive eugenic and social Darwinistic ideas of eliminating faulty genes in the hope of reducing the social assistance provided to the sick and the vulnerable.⁵⁴⁸ However, the INSERM report also attempts to reassure readers that the legal boundaries in place will help prevent the misuse of the technology in such harmful ways.⁵⁴⁹ This faith in the legal boundaries is seemingly unfounded when considering how the untreatability requirement has rapidly transitioned from being applied in a strict manner to being applied in a rather lax manner.

Conclusion

This chapter has shown that the restriction of genetic diagnosis to untreatable conditions has been reinterpreted and broadened to include some of the most treatable early-onset conditions. Regulators have approved screening for conditions that can be treated safely and effectively, such as dopamine-responsive

⁵⁴⁴ Knoppers and Isasi *supra* note 50.

⁵⁴⁵ *Ibid.*

⁵⁴⁶ CCNE, Opinion N° 124 “Ethical Reflection on Developments in Genetic Testing in Connection with Very High Throughput Human DNA Sequencing” (Paris: CCNE, 2016), 9.

⁵⁴⁷ INSERM is the national medical funding agency. It performs a similar function to the NIH in the US and MRC in the UK. See Deitmar Braun, *Structure and Dynamics of Health Research and Public Funding: An International Institutional Comparison* (Dordrecht: Springer Netherlands, 2007) 107.

⁵⁴⁸ INSERM, “Tests Génétiques : Questions Scientifiques, Médicales et Sociétales Une Expertise Collective de l’Inserm” (1 Janvier 2009) XXIX online : www.inserm.fr/content/download/917/9351/version/1/file/cp_test_genetique.pdf

⁵⁴⁹ *Ibid.* Also note that similar, broader comments about the strength of the legal boundaries, Council D’etat, See Conseil D’État *supra* note 35.

dystonia, webbed hands and PKU. The approval of treatable conditions demonstrates an extensive change in the rule restricting genetic diagnosis solely for untreatable conditions. This extensive change becomes more apparent when considering that the restriction of genetic diagnosis to untreatable conditions was initially applied only to conditions that had no viable treatment options. The initial application of the law was in line with the original objectives, which aimed to prohibit screening whenever the medical treatment broke the link between the inherited gene and the serious condition. Despite these rationales, from 2006 onwards, the ABM and HFEA have approved screening for treatable conditions. This change resulted from an expansive reinterpretation of the rule's elastic notion of untreatability. The reinterpretation prompted new considerations about costs (such as in the case of Hunter syndrome and Gaucher disease) and family discomfort or difficulty (such as in the case of PKU, a condition that is treated with safe and effective dietary adjustments). The PKU diet provides effective treatment at present, but new advances in cellular, enzymatic and somatic gene therapies may provide additional therapeutic avenues.⁵⁵⁰ In this age of medical and biotechnological breakthroughs, more conditions should eventually be regarded as treatable.⁵⁵¹ Yet, in practice, even the relatively few congenital disorders that are treatable are being legally classified as untreatable.

⁵⁵⁰ See Francjan J. Van Spronsen, "Phenylketonuria: a 21st Century Perspective" (2010) 6:9 *Nature Reviews Endocrinology* 509. See also Pietro Strisciuglio & Daniela Concolino "New Strategies for the Treatment of Phenylketonuria (PKU)" (2014) 4:4 *Metabolites* 1007. See also Naz al Hafid & John Christodoulou, "Phenylketonuria: A Review of Current and Future Treatments" (2015) 4:4 *Translational Paediatrics* 307-309.

⁵⁵¹ Soini *supra* note 93 at 316.

Chapter Five

“Risks for Everyone”: Legal Change Concerning Susceptibility Screening

The detection of a gene linked to susceptibility does not necessarily spell a looming disease. The Human Genome Project’s former director, Francis Collins, explains that susceptibility genes alone do not cause a disease, but the acquisition thereof would rather depend on complex,⁵⁵² often unpredictable interactions between multiple genes and the environment.⁵⁵³ Due to the complex interaction between genetic and environmental factors, studies can often only point to a statistical correlation between a susceptibility gene and an estimated risk probability of developing the disease later in life.⁵⁵⁴ Given the uncertainty of genetic risks, the manner in which regulators approach the challenges of genetic diagnosis of susceptible embryos (hereafter: susceptibility screening) requires attention. Some of these regulatory challenges include the fact that genetic risks are extremely common, many susceptibilities are highly unlikely to ever materialize, and those susceptibilities are contingent upon the unknown, external factors such as the future child’s lifestyle choices.

In this chapter, I will argue that the changes to the rules regarding susceptibility screening have created a highly expansive notion of “genetic risk” that could potentially apply to every single embryo.⁵⁵⁵

⁵⁵² To illustrate these complex interactions, medical geneticist Patricia Baird offers the example of colorectal cancer susceptibility, in which actual health outcomes cannot be simply reduced to genetics, but depend on equally important environmental factors, including pollution levels, dietary choices, and the individuals’ lifestyle habits. See Patricia A Baird, “Genetic Identification of Susceptibility to Common Diseases: A New Era of Preventive Medicine?” (2014) 3 online: <https://open.library.ubc.ca/cIRcle/collections/ubccommunityandpartnerspublicati/47136/items/1.0048451>

⁵⁵³ Francis Collins, *The Language of Life: DNA and the Revolution in Personalised Medicine* (Suffolk: Profile Books, 2010) 27-28.

⁵⁵⁴ Susceptibility conditions differ from single gene disorders such as Tay-Sachs, in the manner in which genetic studies can point to more straightforward cause-effect relations between the gene and the disease. For susceptibility conditions, the numeric percentage assigned to a correlation between a gene and a disease is known in genetics as penetrance. See Baird *supra* note 552.

⁵⁵⁵ Academics and even regulators themselves have warned that without a minimal bar of risk probability, and given that all embryos have genes linked to susceptibility, most, if not all, embryos could potentially be found to be “at risk.” See Mary Rice, “Very Early Detection? British Group Gauges Public Interest in Embryo Testing for Cancer” (2006) 98:3 J Natl Cancer Inst 156-157. William E Stempsey, “The Geneticization of Diagnostics” (2006) 9 Med, Health & Phil 198. See also Hans Galjaard, *Report of the IBC on Pre-Implantation Genetic Diagnosis and Germ-line Intervention* (Paris, UNESCO, 2003) 12. HFEA, Scientific and Clinical Advances Committee PGD for Cancer Susceptibility, (London: HFEA, 2004) at 4.

The existing literature has failed to show and critically appraise the full extent to which the legal change has expanded the notion of being “genetically at risk.” I will examine the significant transformation that the rules originally disallowing susceptibility screening have undergone. The rules initially disallowed susceptibility screening because genes statistically correlated with an increased risk are not necessarily determinative factors that will cause a disease. To that end, the UK and French rules placed two requirements that effectively disallowed susceptibility screening: (a) that the gene in question is linked to a high risk of developing a condition, and (b) that the condition will manifest in early childhood. Yet, after 2006, and in a matter of only a few years, the interpretation and the application of the two rules have taken a sharp turn in the opposite direction. The maximal age of onset rose steeply from childhood-onset, before as the age of ten, to over the age of sixty by licensing screening against prevalent susceptibilities to later-onset diseases such as Parkinson’s. Further, regulators have lowered the bar of risk of developing the condition, which was originally 90 percent, all the way to 0 percent (unaffected gene carriers). Additionally, I will explain the reasons for this rapid legal change of the rules regarding susceptibility screening.⁵⁵⁶ A key contributing factor was the regulatory licensing policy shift away from objective and measurable targets (such as the probability of disease manifestation - penetrance) to the prospective parents’ own subjective risk perceptions. As a result, a small group of prospective parents can put pressure on these very amorphous boundaries to include their own subjective and expansive views on what constitutes a risk. Since virtually every embryo (and person) carries or is genetically susceptible to several diseases later in life, the regulatory

⁵⁵⁶ The literature has virtually neglected explaining the potential drivers of the very sharp turn that the regulation of susceptibility screening has taken in a relatively short period of time. Moreover, academics such as Bredenoord et al. (supra note 50) explicitly rejected what they call a “logical version of the slippery slope” to ever lower risk rates. They have suggested that such a slippery slope is not likely to ever materialize because parents would not undergo the expensive and physically taxing process of IVF when the risk to the child is marginal. In contrast, chapter 5 provides theoretical explanations and evidence to the contrary, showing that a small group of parents have an interest in susceptibility screening even when risk rates are extremely low.

conception of being genetically “at risk” has expanded to the point where it hypothetically could be applied to every embryo.

D) The Initial Normative Considerations behind Disallowing Screening for Susceptibility Conditions

Which normative considerations initially guided the UK and French regulators in opting to disallow susceptibility screening? In short, regulators initially stressed the reasoning that genes statistically linked to susceptibilities are not determinative factors and are uncertain to cause serious disease.⁵⁵⁷ The French Court of Appeals Judge Christian Byk explains that susceptibility genes’ uncertain causal links to health outcomes was one of the two major ethical concerns behind placing restrictions on susceptibility screening in both the UK and France.⁵⁵⁸ The second ethical concern stems from the fact that if a susceptibility materializes, it will develop into a disease only at a later point in life. The onset later in adulthood means a person would enjoy many years of good health without being affected by the condition. The possible onset, several decades later, means that advances in biomedical science and technology may make the condition more treatable and preventable. Hence, the potential health risks associated with susceptibility genes may never even materialize.⁵⁵⁹

Uncertain Relations between Susceptibility Genes and Health Outcomes

A 1985 CCNE opinion recommended disallowing susceptibility screening on the grounds that there was no certainty that the susceptibility gene would lead to an actual disease.⁵⁶⁰ A subsequent 1995

⁵⁵⁷ The justification to perform susceptibility screening becomes weaker as risk rates become lower since there is a lower of likelihood the putative child will develop the serious condition. See for example, Council of Europe, DIR/JUR (97) 13 Bis Comité Directeur Pour La Bioéthique (CDBI) Groupe De Travail Sur La Génétique Humaine (Cdbi-Co-Gt4) Strasbourg, 27 Octobre 1997 6.

⁵⁵⁸ Byk *supra* note 442 at 100.

Judge Byk is in a unique position to explain the regulation of genetic diagnosis. Aside from his judiciary role, he is a past president of the UNESCO Bioethics Committee and one of the drafters of the Council of Europe additional protocol to the Oviedo Convention regarding genetic diagnosis, which attempted to set Pan-European standards.

⁵⁵⁹ *Ibid.*

⁵⁶⁰ CCNE opinion no.5 *supra* note 453 at 3, 8-10

CCNE opinion reiterated that position and further asserted that susceptibility screening provides no guarantees that the condition in question would not develop, nor does the lack of susceptibility screening mean that the condition would develop.⁵⁶¹ The CCNE opinion reads: “[s]uch afflictions are not determined by mutations alone; they are the result of an unfavourable combination of a set of factors, genetically determined or otherwise (environmental factors). In such disorders, the determination of genetic characteristics can only provide a probabilistic evaluation of the risk.”⁵⁶² The opinion further warns of a line of thinking that excessively attributes determinative power to genes linked to susceptibilities. With susceptibility genes, the risk is uncertain and is based on statistical correlations. The CCNE opinion further states that even as genomic sciences progress, studies will encounter significant difficulties in fully explaining the complex causal relationship between susceptibility genes and environmental factors. The complex interplay between genes, the environment, and health outcomes creates difficulties in establishing causal relations because human environments, themselves, are constantly changing, with evolving societal values, cultural norms, living conditions, and lifestyle habits.⁵⁶³

The 1987 White Paper, which led to the establishment of the regulatory scheme in the UK, stresses the importance of two requirements: the high risk of developing a serious condition and the condition’s onset in infancy. The White Paper bases the exclusion of screening against late-onset, low-penetrance genes on the grounds that susceptibility screening would be unwarranted as it attempts to avert births when a

⁵⁶¹ CCNE, “Opinion and Recommendations on Genetics and Medicine: from Prediction to Prevention.” Report N°6 October 30th 1995 11 online: <http://www.ccne-ethique.fr/docs/en/avis046.pdf>

⁵⁶² *Ibid.*

⁵⁶³ *Ibid* at 2.

Harvard epidemiologist Walter Willett points to the overvaluation of the statistical correlation between certain genetic polymorphisms and the onset of colorectal cancer. Willett stresses the role of lifestyle choices, especially poor nutrition play a greater role than genes in colorectal cancer susceptibility. See Walter C. Willett, “Balancing Life-Style and Genomics Research for Disease Prevention” (2002) 296:5568 *Science* 695.

Rapport and Smith bring further evidence to show that scientific research into susceptibility genetics tends to excessively estimate the correlation of certain genes to health risks because the studies tend to recruit volunteers from industrialized, Western societies. See Stephen M Rappaport & Martyn T Smith, “Environment and Disease Risks” (2010) 330:6003 *Science* 460.

serious disease may very well never develop.⁵⁶⁴ Following the White Paper, the HFEA ethics committee reviewed the high-risk and infant-onset requirements in light of developments in susceptibility genetics. The committee suggested that susceptibility screening should remain prohibited because of the imbalance between the uncertain health benefits of susceptibility screening and the moral harms of the destruction of embryos and potential life prevention.⁵⁶⁵ In 1999, in joint consultation with the ethics advisory body, the AGCT, the HFEA restated the position that a susceptibility gene is uncertain to cause serious disease.⁵⁶⁶ Even when people do develop a disease related to their susceptibility, the genetic factors are not the sole triggers; there are other significant contributing factors, such as the environment and their lifestyle choices.⁵⁶⁷

Between Risk Mitigation and Genetic Reductionism

Baroness Deech, the then chair of the HFEA and a key person behind the development of the regulatory requirements, explained the practical reasons why genetic diagnosis should not take place in instances when a gene is unlikely to cause disease. Deech first cautioned against reducing people to their genetic properties, explaining that children are not predestined to a certain fate dictated by their genes.⁵⁶⁸ She warned of a scenario where popular discourse about genetic technologies could revive eugenic and genetic reductionist thinking,⁵⁶⁹ which excessively privileges the role of genetics in determining health

⁵⁶⁴ The White Paper *supra* note 24.

⁵⁶⁵ HFEA *supra* note 447.

⁵⁶⁶ The AGCT (the Advisory Committee on Genetic Testing) was the former ethics advisory board to the HFEA. In 1999, the AGCT was disbanded and superseded by the newly created HGC.

⁵⁶⁷ HFEA and AGCT, “Consultation Document on Preimplantation Genetic Diagnosis” (London: HFEA, 2000) 13.

⁵⁶⁸ Ruth Deech, “Family Law and Genetics” (1998) 61:5 *Modern L Rev* 713.

⁵⁶⁹ Pediatrician Jeffery Botkin, one of the academics who developed the core concepts behind the regulatory scheme, warns about the problems genetic reductionism poses to setting limits to susceptibility screening. Botkin explains that popularization of genetic reductionist views may veer parents to susceptibility screening in where the risk is very remote or very low, despite having very questionable medical rationale and clinical benefits. Botkin concludes that screening should not be allowed in cases where the risk is very remote or very low, such as for susceptibility condition with very low penetrance (i.e. the risk rate that the condition would cause disease) or very advanced age of onset. See Jeffrey R. Botkin, “Ethical Issues and Practical Problems in Preimplantation Genetic Diagnosis” (1998) 26:1 *J L Med & Ethics* 20-22.

outcomes. Deech raised concerns that prospective parents will put pressure on the regulator to perform a genetic diagnosis, even when such susceptibilities are to conditions with low penetrance rates and a later age of onset.⁵⁷⁰ Deech further pointed out that without explicit limits on the maximum age of onset and minimal risk rates, prospective parents' pressure could push the regulatory bar of risk lower and lower, leading to a "slippery slope."⁵⁷¹

A 2002 CCNE opinion raises several ethical concerns about the manner in which the practice of susceptibility screening may evolve. Although the CCNE opinion did not officially take a stance on where precisely the appropriate lines should be drawn, it warned that the approval of susceptibility screening could set the regulatory system on a path toward allowing lower and more remote risks.⁵⁷² The introduction of susceptibility screening in the hope of mitigating genetic risks could negatively alter prospective parents' views of the process of reproduction and the notion of an acceptable level of genetic risk. The CCNE opinion reads: "There is still the fear of opening the door to uncharted contingencies. Humanity could go in the direction of seeing itself as a means rather than an end. Or [the] prediction mania for late-onset diseases may become irresistible."⁵⁷³ In addition, the CCNE opinion warned that once the regulator approves late-onset conditions such as Huntington's disease, there is no reason not to screen for later onset diseases such as Alzheimer's disease or those that manifest even later. Such developments would bring the regulatory limits on risk remoteness closer to a state of being irrelevant.⁵⁷⁴ To assess these predictions and potential risks, let us examine the process of legal change to these two regulatory requirements.

⁵⁷⁰ Deech *supra* note 485 at 344.

⁵⁷¹ *Ibid.*

⁵⁷² CCNE, Opinion no. 67, Reflections Concerning an Extension of Preimplantation Genetic Diagnosis (Paris: CCNE 2002), 14-17.

⁵⁷³ *Ibid* at 16-17.

⁵⁷⁴ *Ibid* at 17.

II) The Early Application of the Genetic Risk and Age of Onset Rules

The UK and French laws originally disallowed susceptibility screening by restricting genetic diagnosis to childhood-onset, genetically-caused, single-gene disorders.⁵⁷⁵ Unlike single-gene disorders,⁵⁷⁶ susceptibility genes are linked to a certain statistical probability of developing a disease at a later stage in adult life. The UK and French regulators have effectively prohibited susceptibility screening by restricting the age of disease onset to childhood and the penetrance (i.e., risk) rate to 90% or higher. Notable examples of conditions licensed by the HFEA and ABM before 2002, prior to the legal change, included single-gene disorders such as Duchenne muscular dystrophy, Haemophilia and Sickle cell anemia.⁵⁷⁷

A study by Stéphane Viville using official data by the national IVF registrar data shows that in the year 2000 all genetic diagnosis procedures in the three authorized centres in France (Paris, Montpellier and Strasbourg) were limited to the detection of single-gene disorders and chromosomal translocations.⁵⁷⁸ A follow up by clinicians Moutou and Viville again confirms that in 2002, genetic diagnosis in France was confined to single-gene disorders.⁵⁷⁹ The same was true in the UK, where the HFEA restricted genetic diagnosis to single-gene disorders such as Duchenne muscular dystrophy and

⁵⁷⁵ ABM, supra note 440 4. See also HFEA and AGCT supra note 450 at 2-3. See also HFEA, “Clinical Guidance Letter” (13 August 1999) (London: HFEA, 1999)

⁵⁷⁶ A single gene disorder is caused by a mutation of a gene responsible for a certain bodily function. It often manifests as an illness that begins in childhood. See Janette B Benson & Marshall M Haith, *Diseases and Disorders in Infancy and Early Childhood* (Oxford: Elsevier Science, 2009).

⁵⁷⁷ See Xavier Bosch, “UK Criticized for Embryo Screening Decision” (2004) 10:12 *Nature Med* 1266. See also Philippe Barjot, “Le Diagnostic Pré-implantatoire : entre Espoir Thérapeutique et Menace Éthique” (2004) 4 *Spirale* 45.

⁵⁷⁸ Stéphane Viville, “Le Diagnostic Pré-Implantatoire En France : Bilan D’activité Du Groupe D’étude et de Travail du Diagnostic Pré-Implantatoire (GET-DPI) - Année 2000” (2001) 17 *médecine/science* 919-923.

⁵⁷⁹ Céline Moutou & Stéphane Viville, “Le Diagnostic Génétique Préimplantatoire des Maladies Monogéniques” (2003) 61:5 *Annales de Biologie Clinique* 521-32.

Marfan syndrome prior to 2002.⁵⁸⁰ However, the rules have changed as genetic technology developed further, moving from exclusively detecting single-gene disorders to including susceptibility conditions.⁵⁸¹

III) An Overview of the Legal Change of the Risk and Age of Onset Requirements

The first sign of legal change came in 2001 in the UK and in 2002 in France, with the first approval of an adult-onset condition, Huntington's disease. The average age of onset in Huntington's disease is forty years.⁵⁸² Although the fully penetrant type of Huntington's disease is not regarded as a susceptibility condition, the license to screen embryos for Huntington's disease genes has paved the way for the regulatory approval of susceptibility conditions. The licensing of Huntington's disease created a significant precedent by being the first adult-onset condition to gain approval in contrast to the previous policy of licensing only childhood-onset conditions. Licensing the first adult-onset condition was later cited by the HFEA and the ABM as a precedent for approving genetic diagnoses for susceptibility conditions, which also overwhelmingly manifest in adulthood.⁵⁸³

In May 2006, the HFEA announced that it would allow genetic diagnoses for the BRCA1 and BRCA2 genes, which are linked to a susceptibility to breast and ovarian cancer, respectively.⁵⁸⁴ In announcing its decision, the HFEA stated that "the Authority agreed that we should consider the use of genetic diagnosis embryo testing for conditions such as inherited breast, ovarian and bowel cancers that

⁵⁸⁰ HFEA supra note 447 at 4.

⁵⁸¹ See John A. Robertson, "Ethics and the Future of Preimplantation Genetic Diagnosis" (2005) 10:1 Repro Biomed Online 99. Robertson suggests that the increasing clinical utilization of susceptibility screening is tied to:

the state of genetic and genomic knowledge. The most prevalent single-gene disorders have now been identified, and PGD is available for most of them. With most of the low-hanging genetic fruit now having been picked, scientists will have a harder time identifying other single gene mutations for diseases and non-medical traits that are of potential interest to future parents, particularly since developmental and environmental factors may play a more important role than single genes or clusters of genes in causing the chronic diseases of widest concern.

⁵⁸² Richard H. Myers, "Huntington's Disease Genetics" (2004) 1:2 NeuroRX 255.

⁵⁸³ See HFEA (2006) supra note 478. See also CCNE, Opinion n°107 supra note 48 at 14. See also Veronica English & Peter Braude, "Regulation of PGD in the UK and Worldwide" in *Preimplantation Genetic Diagnosis in Clinical Practice* (London: Springer, 2014) 187.

⁵⁸⁴ HFEA *Ibid.*

given the aggressive nature of the cancers, the impact of treatment and the extreme anxiety that carriers of the gene can experience.”⁵⁸⁵ The HFEA further commented about susceptibility conditions: “[t]hese conditions differ from those already licensed before because people at risk do not always develop cancer, it may occur later in life and some treatments may be available.”⁵⁸⁶

The ABM announced that it would change the risk and age of onset requirements to allow for the previously prohibited practice of susceptibility screening. On October 12, 2006, the ABM published a report on susceptibility screening that concluded:

Records have shown that a small number of PGD and PND have already been performed in France compliant with the current legislative provisions, for hereditary forms of cancer or within the framework of diseases associated with a risk of cancer. One may expect that the (Centres) send more requests in the coming years for this type of indication and that the analysis of the situations to be examined is more difficult.⁵⁸⁷

On March 28, 2008, the Steering Board of the ABM approved the extension of the rules to susceptibility conditions on a transitional basis until the revision of the Bioethics Law.⁵⁸⁸ In October 2008, the French Senate approved an amendment to the Bioethics Law, citing in its reasons similar decisions by the HFEA to approve susceptibility screening for hereditary colon cancer and breast cancer.⁵⁸⁹

⁵⁸⁵ HFEA 2006 *infra* note 753; See also Dr. Jess Buxton, “HFEA Approves Embryo Tests for Hereditary Cancer”, *Bionews* 358 (May 11, 2006) online: https://www.bionews.org.uk/page_90023

⁵⁸⁶ Hereditary breast cancer is amenable to both treatment and prevention, especially if detected early. The early detection and preventative measures for hereditary breast cancer made headlines with the highly publicized story about Angelina Jolie’s double mastectomy after discovering she is a carrier of the BRCA1 gene. See D Evans et al., “The Angelina Jolie effect: How High Celebrity Profile Can Have a Major Impact on Provision of Cancer Related Services” (2014) 16:5 *Breast Cancer Research* 1. See also Kalina Kamenova, Amir Reshef & Timothy Caulfield, “Angelina Jolie’s Faulty Gene: Newspaper Coverage of a Celebrity’s Preventive Bilateral Mastectomy in Canada, the United States, and the United Kingdom” (2013) 16:7 *Genetics in Med* 522.

⁵⁸⁷ ABM *supra* note 440.

⁵⁸⁸ ABM, Conseil d’orientation, Séance du vendredi 28 Mars 2008, Délibération n° 2008-CO-12 (Paris : ABM, 2008).

⁵⁸⁹ France Sénat, “Étude de Législation Comparée n°188 – 13 Octobre 2008- Le Diagnostic Préimplantatoire Sénat (Octobre 2008) online : <https://www.senat.fr/lc/lc188/lc188.pdf>

Rapidly Shifting Lines

A few years after the changes, the maximum age of onset allowed by regulators climbed considerably. The rising maximal age of onset represents a significant departure from a policy that holds that certain risk potentialities are overly low to a more laissez-faire approach. Under the more liberalized approach to susceptibility screening, the maximal age of onset was increased to a later point in the life of the putative child. Hereditary breast cancer, the first condition to gain a license in France and the UK, has an average age of onset of 41 years.⁵⁹⁰ Both the HFEA and ABM have further gone on to approve genetic diagnoses for familial Alzheimer's disease, a very rare type of the condition linked to certain gene mutations.⁵⁹¹ To illustrate, the APP gene mutation's average age of onset is 51.3 years, and the PSEN2 gene mutation's age of onset is 57.1 years.⁵⁹² The HFEA has gone further to approve genetic diagnoses for several types of Parkinson's and Alzheimer's susceptibility genes, which are associated with an average age of disease onset in the seventh and eighth decades of life.⁵⁹³

Since 2006, the HFEA and the ABM approved various susceptibility screenings in which the penetrance is below 30 percent, which is clinically regarded as lower penetrance rates. The regulatory approval

⁵⁹⁰ Cheng-Har Yip et al, "Clinical and Pathologic Differences between BRCA1-, BRCA2-, and non-BRCA-Associated Breast Cancers in a Multiracial Developing Country" (2009) 33:10 *World J Surgery* 2081-2082.

⁵⁹¹ See also HFEA, PGD "Conditions Licensed by the HFEA" online: <http://guide.hfea.gov.uk/pgd/> See also ABM Liste des Diagnostics Biologiques Sur L'embryon in Vitro (DPI) 2017 online: https://www.agence-biomedecine.fr/IMG/xlsx/2017_ra_dpi2016.xlsx&sa=U&ved=0ahUKEWjtoqma0unXAhXHWWhQKHdIRCIoQFggXMAE&usg=AOvVaw0M4cSK7L1aUqd09tXCASmq

See the somewhat analogous discussion about the limited predictive power of amyloid neuro-imaging based techniques. Alavi Abass, et al. "Suboptimal Validity of Amyloid Imaging-Based Diagnosis and Management of Alzheimer's Disease: Why it is Time to Abandon the Approach" (2019) 47 *Eur J Nuclear Med & Molecular Imaging* 1-6. And see Paula Span, "A Brain Scan May Predict Alzheimer's. Should you get One" *The New York Times* (August 2, 2019) online: <https://www.nytimes.com/2019/08/02/health/alzheimers-brain-scan.html>

⁵⁹² Marc Cruts, Jessie Theuns & Christine Van Broeckhoven, "Locus-specific Mutation Databases for Neurodegenerative Brain Diseases" (2012) 33:9 *Hum Mutation* 1342-1343.

⁵⁹³ For Parkinson's susceptibility age of onset see Matthew James Farrer, "Genetics of Parkinson Disease: Paradigm Shifts and Future Prospects" (2006) 7:4 *Nature Reviews Genetics* 306.

The full list of conditions that HFEA has approved with onset at between the sixth and the eighth decade include Frontotemporal Dementia with Parkinsonism, Frontotemporal Dementia, Parkinson's Type 8, 4 and 1, Frontotemporal Dementia with Parkinsonism, and Lewy body dementia.

for low-penetrant genes reflects a significant change from the previous regulatory policy. Notable examples include Gaucher disease⁵⁹⁴ (a treatable ultra-rare disorder reviewed in the previous chapter), that its penetrance varies but often falls below 30 percent,⁵⁹⁵ Long QT syndrome (type 3-intermediate),⁵⁹⁶ a congenital cardiac disease, is 16 percent penetrant.⁵⁹⁷ Moreover, cystic fibrosis (Class IV, R117H mutation - mild cystic fibrosis)⁵⁹⁸ is only 3 percent penetrant.⁵⁹⁹

The UK and French regulators went further to approve genetic diagnoses for unaffected carriers, effectively lowering the bar or risk of developing the condition to 0 percent. Unaffected carrier children have a 0 percent risk of developing the disease on a genetic basis.⁶⁰⁰ The regulatory policy on unaffected carrier screening took a sharp turn in just a few short years. The 2000 HGC⁶⁰¹ response to the HFEA consultation recommended against detecting the carrier status of unaffected embryos, citing the extreme remoteness of the risk.⁶⁰² Further, a 2002 CCNE opinion stated that eliminating unaffected embryos to avoid the inheritance of such genes amounts to the instrumentalization of the most vulnerable members of society.⁶⁰³ Since 2006, both the UK and France have changed their position from disallowing to

⁵⁹⁴ HFEA, supra note 465, Agence de la Biomédecine supra note 465.

⁵⁹⁵ Shachar Zuckerman et al., “Carrier Screening for Gaucher Disease: Lessons for Low-Penetrance, Treatable Diseases” (2007) 298:11 JAMA, 1281.

⁵⁹⁶ HFEA, ABM supra note 440 at 18.

⁵⁹⁷ John R Giudicessi & Michael J Ackerman, “Determinants of Incomplete Penetrance and Variable Expressivity in Heritable Cardiac Arrhythmia Syndromes” (2013) 161:1 Translational Research 1.

⁵⁹⁸ Class 4 is caused by R117H mutation and is associated with mild symptoms, See Michel Roussey, et al. “Neonatal Screening of Cystic Fibrosis: Diagnostic Problems with CFTR Mild Mutations” (2007) 30:4 J Inherited Metabolic Disease 613.

⁵⁹⁹ Both the HFEA and the ABM’s predecessor, CNMBRDP have given clinics a blanket license to test for all Cystic Fibrosis mutations, without excluding (as it is sometimes the case) certain mild mutations. See ABM and HFEA supra note 41.

⁶⁰⁰ Carole Kenner & Judy Lott, *Comprehensive Neonatal Nursing Care: Fifth Edition* (New York: Springer, 2013) at 840.

⁶⁰¹ HGC [Human Genetics Commission] was the ethics commission tasked to advise the HFEA in its policy and regulatory decisions. The HGC was abolished in 2012 after the decision of the Cameron administration to cut funding to a number of quangos. For more about the HGC, see HGC, “About the HGC” (2012) The National Archives, online: <http://webarchive.nationalarchives.gov.uk/20120504100111/http://www.hgc.gov.uk/Client/Content.asp?ContentId=5>

⁶⁰² HGC, *Response to the Human Fertilisation and Embryology Authority on the Consultation on Preimplantation Genetic Diagnosis*, (London: HGC 2000) 3.

⁶⁰³ CCNE 2002 supra note 572 at 16.

approving and licensing unaffected carrier screening.⁶⁰⁴ In effect, the regulatory decisions to approve unaffected carrier screening have lowered the minimal bar of disease penetrance rate to 0 percent.

In hindsight, what have a few short years of rapid legal change done to the regulatory bars of penetrance and age of onset?⁶⁰⁵ As time went by, the two regulatory bars have shifted, moving the risk lower and later in the putative child's life. These two regulatory bars have both seen a notable change on a measurable scale. From 2002 onwards, the age of onset steeply climbed from the first decade of the putative child's life to the seventh decade and beyond, with susceptibility conditions such as familial Alzheimer's, Parkinson's and dementia. Similarly, the risk probability of developing the disease has sharply dropped from 90 percent before 2005 to 0 percent. In effect, regulators have lowered the minimum values of the penetrance and age of onset bars to a point that they place very little formal limits on risk likelihood and remoteness.

IV) The Role of Unclear Regulatory Language in the Legal Change: The Transition from Bright-Line Rules to Overly Vague Constructs

What explains how two central legal requirements have taken such a sharp turn in only a matter of a few short years? The answer lies in yet another change—a change to how the regulators assess the degree of risk and the age of onset requirements. With the approval of susceptibility screening, regulators have also changed the way they evaluate the degree and the remoteness of the risk. The HFEA and ABM

⁶⁰⁴ Human Genetics Commission [HGC] supra note 131 at 14, 42 and ABM supra note 38.

⁶⁰⁵ By approving lower penetrance, later onset conditions, regulators have also paved the way for the emerging extension of screening to genes linked to susceptibility to develop mental health conditions and “atypical” behavioral characteristics. The emerging extension of genetic interventions to behavioural and cognitive traits represents a significant change from the original regulatory policy that disallowed behavioural genetic intervention due to its potential of abuse by attempting to “normalize” individuals’ behaviours. To illustrate, in chapter 6, I will discuss the case study of genetic diagnosis for autistic spectrum disorder susceptibility. Later, in chapter 7, I will discuss ideas of deleting genes linked to Alzheimer's susceptibility and replacing them with gene variants that both confer greater resistance to neurodegenerative disease as well as enhance cognition. These examples of cognitive and behavioural genetic interventions have not have been possible from a legal standpoint had regulators not first substantially lowered the bars set by the risk rate and age of onset requirements.

have moved away from measurable thresholds into using unclear constructs of “perceived risk” and “late-onset”, which extensively rely on prospective parents’ subjective views.

By moving away from the clear and measurable thresholds to not setting any limits at which a risk is too low or too remote, the regulators have set in motion this tectonic shift in the legal boundaries. The lack of measurable thresholds that set explicit limits enabled regulators to continuously push the age of onset upwards to later ages and penetrance downwards to lower risk rates. With malleable legal constructs such as “late-onset” and “perceived risk,” a group of clinicians and prospective parents were free to push the unclear boundaries to facilitate their expansive notions of genetic risk.⁶⁰⁶ Before I demonstrate how the regulatees were able to use the unclear rules to further their interests, I will first focus on the change in the assessment of the legal requirements of risk and age of onset.

The Change in the Assessment of the Age of Onset Requirement

The rapidly climbing maximal age of onset from before ten years to beyond sixty years originated from the extensive change in the manner in which the age of onset requirement is assessed. Before 2002, in the UK and France, laws required that the early-onset requirement would only be applied to conditions that developed immediately after birth or in early childhood, such as Tay-Sachs and beta thalassemia. Although the term “early-onset” was not defined in the law,⁶⁰⁷ the biological fact that the vast majority of single-gene disorders develop in infancy acted as a natural constraint that restricted approved conditions

⁶⁰⁶ My argument about an expansive legal notion of genetic risk coincides with initial findings from the sociology literature about prospective parents’ growing sense of duty of to manage genetic risks by opting for susceptibility screening. See Anne Kerr, “Rights and Responsibilities in the New Genetics Era” (2003) 23:2 Critical Social Pol’y 208. See also Jessica Plozer, “Chapter 4 – Choice as Responsibility – Genetic Testing as Citizenship through Familial Obligation and the Management of Risk” in Bunton, R & A Petersen, eds, *Genetic Governance: Health, Risk and Ethics in a Biotech Era* (Oxford: Routledge, 2005). Also, see Paul Atkinson, Katie Featherstone & Maggie Gregory, “Kinscapes, Timescapes and Genescapes: Families Living with Genetic Risk” (2013) 35:8 Soc Health & Illness 1227.

⁶⁰⁷ For instance, the AGCT and HFEA 1999 consultation has recognized the term early onset is difficult to define. See AGCT and HFEA supra note 437 at 12.

to childhood-onset. Therefore prior to the change, the maximal age of onset remained rather stable, limited to the first decade of life.

However, after the change to permit susceptibility screenings, the biological contours of single-gene disorders could no longer continue to place limits on the maximum age of onset. Unlike single-gene disorders, susceptibility conditions are overwhelmingly adult-onset.⁶⁰⁸ Additionally, the unclear laws did not place any explicit limits on the maximal age of onset. With the approval of susceptibility conditions, the regulatory lines have effectively moved to a malleable distinction between late and non-late onset. However, the terms “late” and “non-late” onset were left unclear and undefined in the law.⁶⁰⁹ The distinction between late and non-late onset largely relies on subjective public perceptions of what is socially regarded as an early or late point in life to develop a disease.⁶¹⁰ Prospective parents’ perceptions of what constitutes late and non-late has proven to be a malleable distinction as regulators have approved conditions such as dementia susceptibility, which usually emerges in the seventh decade of life and beyond.⁶¹¹

The Change in the Assessment of Risk Rates

Prior to the approval of susceptibility screening, regulators have set clear limits on the minimal degree of risk of developing a serious condition. Regulators assessed the degree of risk based on penetrance rates.⁶¹² Penetrance is assessed in a rather objective matter based on studies and hereditary calculations.⁶¹³ Since penetrance rates are measurable, regulators were able to draw clear, bright-lines for appropriate risk

⁶⁰⁸ Benson and Haith *supra* note 576.

⁶⁰⁹ See Ray Noble, et al., “Pandora’s Box: Ethics of PGD for Inherited Risk of Late-Onset Disorders” (2008) 17 *Repro Biomed* online 57-59; See also Mohammed Taranissi, “Why Treat PGD for Late Onset Disorders Differently?” *Bionews*, (04 May 2005), online: http://www.bionews.org.uk/page_37798.asp

⁶¹⁰ See Knoppers et al. *infra* note 665.

⁶¹¹ I will further examine how unclear is the distinction between late and non-late onset by looking in the next section at a case study about familial Alzheimer’s susceptibility.

⁶¹² See HFEA and AGCT 1999 *supra* note 437 at 12, CCNE 2002 *supra* note 572 at 9.

⁶¹³ Tom Strachan & Andrew Read, *Human Molecular Genetics* (New-York: Taylor & Francis Group, 2010) at 79.

rates. The HFEA used to require about a 90 percent risk of transmission of the condition to the embryo to satisfy the high-penetrance requirement.⁶¹⁴ The French law often required a 90 percent bar as well.⁶¹⁵ The objective, measurable penetrance rate functioned, in effect, as a bright-line rule.⁶¹⁶ Conditions with 90 percent penetrance or higher were allowed, whereas conditions that were lower than 90 percent penetrance were disallowed. In that sense, the bright-line rule of 90 percent penetrance worked to set clear and effective limits, as well as to ensure the likelihood that a gene would have a strong link to the purportedly negative health outcomes.⁶¹⁷

After 2006, the HFEA and the ABM moved away from the more objective method using penetrance rates to the subjective legal construct of “perceived risk.” In May 2006, the HFEA decided to reduce the penetrance threshold from 90 percent to an unspecified point.⁶¹⁸ The HFEA suggested that the degree of risk to the child should not be measured based on technical penetrance rates, but rather from the standpoint of the parents’ subjective views. With this new policy, the HFEA deemed that because genetic diagnosis is an incredibly personal decision, prospective parents should have a far greater role in deciding the level of genetic risk.⁶¹⁹ Similarly to the HFEA, the ABM decided that the degree of acceptable risk would be undefined and would not have a measurable threshold but instead would be evaluated by

⁶¹⁴ HFEA, *Code of Practice*. 6th ed. (London: HFEA; 2003).

⁶¹⁵ CCNE 2002, *supra* 572 at 9.

⁶¹⁶ For more about bright-line rules role function in setting stable and predictable limits See Pierre Schlag, “Rules and Standards” (1985) 33 UCLA L. Rev 379. Ronald Dworkin, *Taking Rights Seriously* (Cambridge: Harvard University Press, 1978) 22-27. Frederick Schauer, *Playing by the Rules: A Philosophical Examination of Rule-based Decision-making in Law and in Life* (New-York: Oxford University Press, 1991) 104.

⁶¹⁷ From the standpoint of the initial normative considerations, selecting against embryos becomes less justified the weaker is the link between a gene to negative health outcomes. See Byk *supra* note 442.

⁶¹⁸ HFEA 2006 *supra* note 478.

⁶¹⁹ HFEA, Ethics and Law Advisory Committee, PGD Licensing Aide Memoire, 22.06.2010, (London: HFEA, 2010) For instance, the HFEA writes about the notion of “perceived risk” - The impact can differ both in terms of how an individual might perceive the risk as well as, more practically, the way that the condition will manifest in any particular family.

The decision to interpret risk probability as risk impact (seriousness) confuses the core tenants of risk assessment. Interpreting risk probability as risk impact (seriousness) simply replicates the serious requirement. See also Juliet Tizzard, “Sex Selection, Child Welfare and Risk: A Critique of the HFEA’s Recommendations on Sex Selection” (2004) 12 Healthcare Analysis 61-68.

the prospective parents. The ABM explicitly recognized that with the transition to susceptibility screening, the significant risk requirement remained unspecified and potentially unclear. However, the ABM contended that having prospective parent driven, unspecified degree of risk is justified given the margin of discretion the regulator is free to exercise.⁶²⁰ As Isasi et al. summarize, the UK and French laws have left the degree of risk requirement undefined.⁶²¹

Could the Blurry Lines Drawn by Regulators Get Crossed?

Both the HFEA and the ABM have suggested that although it remains a possibility, screening against embryos with low-risk susceptibility genes is highly unlikely to take place. The HFEA decided not to set explicit limits on penetrance based on the premise that prospective parents would not seek a genetic diagnosis for single-digit risks or very late-onset conditions. The HFEA consultation that anticipated susceptibility screening has suggested there is no evidence that prospective parents are presently interested in susceptibility screening in instances where penetrance is very low (i.e. below 30 percent) or that such interest would emerge in the future.⁶²² Similarly, the ABM has noted that there is no information to suggest that prospective parents will be interested in susceptibility screening for conditions with very low penetrance.⁶²³

On the surface, the HFEA's and ABM's suppositions seem logical. Prospective parents are seemingly rational agents and are overall expected to carefully consider the advantages and disadvantages of IVF and genetic diagnosis.⁶²⁴ In susceptibility screening, unlike in single-gene disorders, the statistically projected risk may never materialize. Furthermore, as penetrance decreases and the age of onset increases,

⁶²⁰ ABM *supra* note 440 at 28-30.

⁶²¹ Rosario Isasi et al. *supra* note 50 at 338-339.

⁶²² See HFEA 2004, *supra* note 555.

⁶²³ ABM *supra* note 440 at 25-27. However, in the very same report (at 29-30), the ABM suggested that even 20 percent risk rates (of a condition such as Retinoblastoma, which is also treatable and preventable) can be regarded as significant.

⁶²⁴ For more about the cognitive, emotional and ethical aspects in prospective parents' decisions making genetic diagnosis see Patricia E Hershberger, & Penny F Pierce, "Conceptualizing Couples' Decision Making in PGD: Emerging Cognitive, Emotional, and Moral Dimensions" (2010) 81:1 Patient Education and Counselling 53.

the risk to the future child becomes ever smaller and more remote. At the same time, prospective parents might also consider that undergoing IVF and genetic diagnosis may come at a great physical, financial, and emotional price.⁶²⁵ Those costs of IVF would seem to deter prospective parents from undergoing a genetic diagnosis where the relative health gains of the selection of a particular embryo are relatively marginal.⁶²⁶ According to this line of argument, although the regulatory requirements would not prevent screening where the risk rates are objectively very low or remote, the difficulties associated with genetic diagnoses' and diminishing returns as risk rates get lower would spontaneously create self-regulating behaviour.

V) When Unclear Regulations about Risks Meet Risk Averse Regulatees

The HFEA's and ABM's decisions not to place any explicit limits are premised on an implicit assumption of what rational behaviour looks like, without fully considering how rationality may be bounded. Additionally, such regulatory policy choices did not consider the chance that a group of parents might still have an interest in susceptibility screening for very low penetrance and disease onset in the last decades of life. As I will show, several factors can lead certain prospective parents to have an interest in such susceptibility screenings, including emotional pressures, cognitive biases, and more specifically, miscalculation or misunderstanding of the probabilistic risk rates tied to susceptibility genetics. Another distinct situation stems from a group of risk-averse prospective parents who are still interested in screening for low-penetrance rate or late-onset conditions and can put pressure on the unclear and malleable regulatory constructs.

⁶²⁵ Clare Williams & Steven Paul Wainwright, "Ethical and Social Aspects of PGD" in *Preimplantation Genetic Diagnosis in Clinical Practice* (Dordrecht, Springer, 2014) 165; Itziar Alkorta Idiakez, "Three Decades of Reproductive Rights: The Highs and Lows of Biomedical Innovations" (2010) 2 *Fem Challenges in the Social Sciences: Gender S in the Basque Country* 143 at 150.

⁶²⁶ Annelien L. Bredenoord et al., *supra* note 50. Bredenoord et al. further assert that the drawbacks of IVF will dissuade parents from engaging in susceptibility screening in instances that the risks are marginal, hence absolutely negating the logical version of the slippery slope to screening for lower penetrance conditions.

Risk-Averse Susceptibility Screening Driven by Feelings of Guilt and Duty

Aside from rational, calculated thinking, the reproductive decision-making of prospective parents undergoing genetic diagnosis is deeply affected by emotions.⁶²⁷ Although prospective parents are capable of understanding the ethical implications of their choices, they also feel guilt about the possibility of not sparing their future child from potential disease.⁶²⁸ Prospective parents who opt for susceptibility screening often have a familial history of the disease or trauma related to an unsuccessful pregnancy.⁶²⁹ Some prospective parents who are unaffected carriers themselves feel an obligation to spare the future child from a disease or disability.⁶³⁰ A systematic literature review about the attitudes of carriers of hereditary cancers suggests that they are more likely than non-carriers to be approving of genetic diagnosis for susceptibility conditions.⁶³¹

The increasing demand for susceptibility screening changes the thinking about birth in a matter that encourages risk-mitigation efforts. Genetic technology arguably transforms the once-natural process of childbirth (the “genetic lottery”) into a more controlled event that involves the management of risk

⁶²⁷ Jenny Cunningham et al., “The Evidence Base Regarding the Experiences and Attitudes to Preimplantation Genetic Diagnosis in Prospective Parents” (2015) 31:2 *Midwifery* 288; See also Stina Järholm, Malin Broberg & Ann Thurin-Kjellberg, “The Choice of Pre-Implantation Genetic Diagnosis (PGD), a Qualitative Study among Men and Women” (2014) 32:1 *J Repro & Infant Psychol* 57.

⁶²⁸ Celia Roberts & Sarah Franklin, “Experiencing New Forms of Genetic Choice: Findings from an Ethnographic Study of Preimplantation Genetic Diagnosis” (2004) 7:4 *Hum Fertility* 290-295.

⁶²⁹ Claire Basille et al., “Preimplantation Genetic Diagnosis: State of The Art” (2009) 145:1 *Eur J Obstetrics & Gynecology and Repro Biology* 9.

⁶³⁰ Kristin Zeiler, “Reproductive Autonomous Choice--a Cherished Illusion? Reproductive Autonomy Examined in the Context of Preimplantation Genetic Diagnosis” (2004) 7:1 *Med Health Care Philos* 275–283.

An interesting irony that came up in interviews with gene carriers prospective parents is that they realized if such reproductive decisions would have applied to them, they would have been screened out and never even been born. See Bredenoord et al. *supra* note 50 at 2398-2399.

⁶³¹ Q Lim et al., “Parents’ Attitudes Toward Genetic Testing of Children for Health Conditions: A Systematic Review: (2017) 92:6 *Clinical Genetics* 569-578.

A French study from 2017, which was not included in the systematic review further confirms the conclusions that gene carriers are more likely to support genetic diagnosis. See Christel Protière et al., “How Can Contingent Valuation Inform the Bioethics Debate? Evidence from a Survey on Hereditary Cancers in France” (2017) 68:3 *Rev économique* 379.

probabilities⁶³² Lemke Thomas argues that with the growing centrality of genetics in popular discourse and greater options for susceptibility screening, prospective parents feel a greater duty to mitigate potential genetic risks in the hope of producing healthier children.⁶³³

Novel methods to choose embryos based on their genes leads to a growing sense of duty among prospective parents to govern their procreation and genetic risks in the name of a reconceptualized notion of public health and duties to their descendants.⁶³⁴ Three studies suggest that women with positive views about genetic diagnosis also felt increased feelings of guilt for failing to use this technology.⁶³⁵ These studies demonstrate that prospective parents have a subjective feeling of parental duty to use reproductive technology to mitigate their future children's genetic risks.⁶³⁶ Interestingly, prospective parents' growing sense of duty to manage genetic risk factors resembles the "proactive beneficence" duty promoted by Julian Savulescu.⁶³⁷ Prospective parents, albeit being free to choose, are obliged by a newly created duty to produce children who (on the face of things) will be less likely to possess a deleterious gene or trait. The Ethics Committee of the American Society for Reproductive Medicine has raised concerns that new technological capabilities to screen embryos for susceptibility genes can increase parental expectations and "may foster inaccurate identification of genes with disease and thus inadvertently reinforce problematic views of genetic causation and responsibility."⁶³⁸

⁶³² Carlos Novas & Nikolas Rose, "Genetic Risk and the Birth of the Somatic Individual" (2000) 29:4 *Econ & Soc'y* 485.

⁶³³ Thomas Lemke, "Susceptible Individuals and Risky Rights" in Regula Valérie Burri & Joseph Dumit, eds, *Biomedicine as Culture: Instrumental Practices, Technoscientific Knowledge, and New Modes of Life* (Oxford: Routledge, 2007) 151. See also Nikolas Rose supra note 7 at 74. For a more specific analysis of prospective mother's testing with BRCA mutation see Nina Hallowell, "Doing the Right Thing: Genetic Risk and Responsibility" (1999) 21:5 *Soc Health & Illness* 597.

⁶³⁴ Judith Green & Ronald Labonté, *Critical Perspectives in Public Health* (New-York: Taylor & Francis, 2007) 221-226.

⁶³⁵ Lim et al supra note 631.

⁶³⁶ *Ibid.*

⁶³⁷ Compare with Julian Savulescu supra note 292.

⁶³⁸ Ethics Committee of the American Society for Reproductive Medicine, "Use of Preimplantation Genetic Diagnosis for Serious Adult Onset Conditions: A Committee Opinion" (2013) 100:1 *Fertility and Sterility* 54.

Challenges in Understanding Probabilistic Risks

Bernard Dickens warns of prospective parents developing unrealistic expectations of susceptibility screening and advises physicians and genetic counsellors to communicate in a manner that gives patients a more accurate perception of the risks and benefits of genetic diagnosis.⁶³⁹ However, although some physicians do perform their gatekeeping duty, other physicians are driven by an interest to push the envelope (and the boundaries of their practice) and test for new conditions in the name of medical innovation.⁶⁴⁰ Snelling et al. further add that embryologists are personally and professionally responsible for selecting the best available embryos, and that duty extends even to unaffected carriers.⁶⁴¹ As such, treating physicians are torn between their gatekeeping duty, their financial and personal interests, and the responsibility to produce the best available embryo.

Even when health-care professionals attempt to explain actual risk probabilities, “misinterpretation and selective listening can occur.”⁶⁴² Prospective parents are not always capable of accurately assessing the probabilistic risks presented to them by the medical team.⁶⁴³ Facing a myriad of options for a risk-mitigating genetic diagnosis, they may experience an “information overload.”⁶⁴⁴ Balancing the advantages

⁶³⁹ Bernard M Dickens, “Legal Developments in Assisted Reproduction” (2008) 101:2 Int’l J Gynecology & Obstetrics 213.

⁶⁴⁰ See Denis Berthiau, “Law, Bioethics and Practice in France: Forging a New Legislative Pact” (2013) 16:1 Law Health Care & Phil 108.

⁶⁴¹ Jeanne Snelling, Nicola Peart & Mark Henaghan, “Preimplantation Genetic Diagnosis: Testing the Legal Boundaries” (2011) 1:2 Genes, Society and the Future 95. Similar to Snelling et al., a French team of genetic diagnosis clinicians, Bouchghoul et al. describe their professional duty as extending to de-select unaffected carrier embryos. See Hanane Bouchghoul et al., “Prenatal Testing in Huntington Disease: After the Test, Choices Recommence” (2016) 24:11 Eur J Hum Genetics 1535.

⁶⁴² Patricia E Hershberger & Penny F Pierce *supra* note 624.

⁶⁴³ *Ibid.*

⁶⁴⁴ See Lidewij Henneman et al, “Responsible Implementation of Expanded Carrier Screening” (2016) 24:1 Eur J Hum Genetics 6. For more general psychological literature about consumer limitations in handling large amounts of information, including probabilistic information see Barry Schwartz, *The Paradox of Choice. Why More is Less* (New York: HarperCollins, 2004).

and disadvantages of genetic diagnosis can be a cognitively taxing task for prospective parents.⁶⁴⁵ Kalfoglou and Hudson's qualitative study reviewed the case of a woman who discussed her genetic diagnosis experience and openly acknowledged that the information about the actual degree of risk mitigation in susceptibility screening "didn't hit home."⁶⁴⁶ Prospective parents cannot be assumed to be self-regulating when their decision-making is influenced by cognitive deficits and biases, and when they have major gaps in understanding clinical genetics and attribute to genetic factors excessive predictive power.

Viewing Probabilistic Risks through Gene-Centric Lenses

A group of academics further suggest that the interest in susceptibility screening is driven by overly simplistic views about genes' predictive power.⁶⁴⁷ Epidemiologist Abby Lippmann pioneered research into the popular phenomenon of the public attributing to genes an excessive predictive power of health outcomes. She coined the term geneticization to refer to the phenomenon of looking at a myriad of human traits from the simplistic prism of genetics.⁶⁴⁸ Lippmann argues that not only is the consumer public increasingly learning to perceive complex susceptibility to diseases through the lens of geneticization but that medical professionals also reinforce these views when they interact with their patients.⁶⁴⁹ In the context

⁶⁴⁵ For more about the theoretical discussion about heuristics and cognitive challenges in probabilistic decision making see Daniel Kahneman & Amos Tversky, "Subjective Probability: A Judgment of Representativeness" (1972) 3:430 *Cogn Psychol* 430-454; Daniel Kahneman & Amos Tversky, "On the Psychology of Prediction" (1973) 80 *Psychol Rev.* 237; Amos Tversky & Daniel Kahneman, "Judgment under Uncertainty: Heuristics and Biases" (1974) 185 *Science* 1124.

⁶⁴⁶ Andrea L. Kalfoglou, Joan Scott, Kathy Hudson, "PGD Patients' and Providers' Attitudes to the Use and Regulation of Preimplantation Genetic Diagnosis" (2005) 11:1 *Repro Biomed Online* 486-496.

⁶⁴⁷ I would suggest that instead of fully explaining parental decision-making, geneticization and genetic reductionist arguments supplement accounts on prospective parents' bounded rationality, their biases, and their difficulties in making such cognitively taxing choices. For a syntactic re-appraisal of geneticization arguments see Kate Weiner et al., "Have we Seen the Geneticisation of Society? Expectations and Evidence" (2017) *Soc Health & Illness* 1-2.

⁶⁴⁸ Abby Lippman, "Prenatal Genetic Testing and Genetic Screening: Constructing Needs and Reinforcing Inequalities" (1992) 17 *Am J Land Med* 15-50.

⁶⁴⁹ Abby Lippman, "Geneticization and the Canadian Biotechnology Strategy" (2000) *the Gender of Genetic Futures: The Canadian Biotechnology Strategy* 32.

of genetic diagnosis, fertility clinics' marketing⁶⁵⁰ as well as media reports,⁶⁵¹ reinforce simplistic narratives that reduce the complex multifactorial nature of susceptibility to gene-centric risks.⁶⁵² Similarly, Pavone and Arias have uncovered in their interviews evidence of geneticization in genetic diagnoses for cancer and neurodegenerative disease susceptibility.⁶⁵³ Both prospective parents and the treating physicians are motivated to adopt susceptibility screening based on a view that gives disproportionate predictive power to genetic factors over other equally significant factors such as environmental, social, and economic determinants of health.⁶⁵⁴ Pavone and Arias suggest that the rise of geneticization in the context of genetic diagnosis fuels prospective parents' risk-mitigating behaviour, even when susceptibility screening can have poor predictive powers of actual health outcomes.⁶⁵⁵

Studies have shown that certain prospective parents maintain their interest in genetic diagnosis despite knowing that certain genes have very low or no penetrance and are highly unlikely to affect their child. The most illustrative examples are studies regarding attitudes towards genetic diagnoses to avoid the birth of an unaffected carrier, which has a 0 percent risk of developing the condition in question. Such studies are reflective of risk-averse behaviour because they demonstrate how a certain group of prospective parents are interested in deselecting even against embryos that carry genes deemed as deleterious but will be healthy. In an Australian study, 63 percent of prospective parents

⁶⁵⁰ Debra Swoboda, "Frames of Reference: Marketing the Practice and Ethics of PGD on Fertility Clinic Websites" in Brea L. Perry ed, *Advances in Medical Sociology* (New-York: Emerald Group Publishing Limited, 2015) 217-247.

⁶⁵¹ For example, see Dorothy Nelkin, "Molecular Metaphors: The Gene in Popular Discourse" (2001) 2 *Nature Rev Genetics* 555–59, at 557; See also Horace F. Judson, "Talking about the Genome: Biologists Must Take Responsibility for the Correct Use of Language in Genetics" (2001) 409 *Nature* 769; See also Tania Bubela, "Science Communication in Transition: Genomics Hype, Public Engagement, Education, and Commercialization Pressures" (2006) 70 *Clinical Genetics* 445–50, at 446. And see Sheldon Krinsky & Jeremy Gruber, *Genetic Explanations: Sense and Nonsense* (Cambridge Mass: Harvard University Press, 2013).

⁶⁵² Colleen M Berryessa & Mildred K. Cho, "Ethical, Legal, Social, and Policy Implications of Behavioral Genetics" (2013) 14:1 *Ann Rev Genomics & Hum Genetics* 519.

⁶⁵³ Vincenzo Pavone & Flor Arias, "Beyond the Geneticization Thesis: The Political Economy of PGD/PGS in Spain" (2012) 37:3 *Sci, Tech, & Hum Values* 235.

⁶⁵⁴ *Ibid.*

⁶⁵⁵ *Ibid* at 55.

that were at the time undergoing genetic diagnosis said they would not be willing to transfer an embryo that is identified as a healthy gene carrier.⁶⁵⁶ In comparison, in the control group of prospective parents that underwent IVF without genetic diagnosis, only 8 percent of participants supported not implanting healthy, unaffected gene carriers.⁶⁵⁷ Another study found that some parents went a step further by asking for the termination of pregnancies with fetuses who were unaffected carriers of X-linked recessive disorders such as hemophilia and fragile X syndrome. In the interviews, prospective parents explained that their motivation was not to simply mitigate health risks but to expunge these disease-causing genes from their descendants' bloodlines.⁶⁵⁸ Snelling et al. conclude that "clearly, there is evidence that some prospective parents have a strong desire to avoid the transmission of carrier status to their offspring."⁶⁵⁹ The evidence shows that contrary to regulatory claims, certain prospective parents still consider and undergo genetic diagnosis even if they are aware the gene in question poses a 0 percent risk to their child.

The potential interest of prospective parents in susceptibility screening when risks are minimal can even be seen in HFEA documents. The 2006 HFEA public consultation⁶⁶⁰ about participants' attitudes found that setting minimum targets for risk was not a popular option. The second-most popular position in the HFEA public consultation was that even risks as low as 1 percent are acceptable for screening and that "any risk is enough."⁶⁶¹ When the regulatory stance holds that any

⁶⁵⁶ Mandy G Katz, et al., "Issues and Concerns of Couples Presenting for Preimplantation Genetic Diagnosis (PGD)" (2002) 22:12 *Prenatal Diagnosis* 1119-1120.

⁶⁵⁷ *Ibid.*

⁶⁵⁸ See Robert Boyle & Julian Savulescu *supra* note 81.

⁶⁵⁹ Snelling et al. *supra* note 641 at 95.

⁶⁶⁰ Rev. Dr. Stephan Bellamy, who sat on the HFEA public consultation to extend genetic diagnosis for susceptibility screening, argues that the HFEA used directive questions and presented skewed information during the public discussion portion to obtain the desired outcome. He writes: "I agree with this extension of PGD and I am a supporter of the HFEA... Despite all this, the consultation leaves me uneasy because one thing is clear – what determined the final decision of the HFEA about the questions raised in 'Choices and Boundaries' was not public opinion."

In Stephan Bellamy, "Two Cheers for Public Consultations: but..." at Elford, R J & D G Jones, eds, *A Tangled Web: Medicine and Theology in Dialogue* (Bern: Peter Lang, 2009) at 222-229.

⁶⁶¹ HFEA, Annex: An Analysis of the Responses to Choices and Boundaries, (London: HFEA, 2006)

risk is enough, a group of prospective parents can put pressure on these very amorphous boundaries to include their own subjective and expansive views on what constitutes a risk.

VI) Review of Case Studies that Illustrate Screening against Low Risk Conditions

I will examine three case studies: screening for a very mild cystic fibrosis mutation that is only 3 percent penetrant, familial Alzheimer's disease susceptibility and unaffected carrier screening. These three cases best illustrate the extent to which the boundaries have been extended. Additionally, these cases demonstrate some of the concerns underlying the previous regulatory stance of disallowing susceptibility screening on the grounds that such practices would lead to intervening on genes with little to no effect on health outcomes. I will also demonstrate how under the revised rules the vague notions of "perceived risk" and "later-onset" function as malleable constructs that accommodate a group of prospective parents' expansive notions of genetic risk.

Familial Alzheimer's Susceptibility – How Late Could "Non-Late" Onset Be?

The familial Alzheimer's susceptibility screening case demonstrates a change in the age of onset requirement.⁶⁶² To better understand the case study, let us first examine some of the clinical characteristics and the age of onset of familial Alzheimer's. The genes linked to familial Alzheimer's, APP and PSEN2, are very rare. As noted above, the APP gene mutation's average age of onset is 51.3 years, and the PSEN2 gene mutation's age of onset is 57.1 years.⁶⁶³ More specifically, to illustrate how late PSEN2 can manifest, the typical age of onset range is between 40 to 75 years, and at times, the age of onset can be later than 80 years.⁶⁶⁴

The case of genetic diagnosis for Alzheimer's susceptibility illustrates the significant weakness of the

⁶⁶² The significance of the age of onset requirement is that the later the age of onset, the greater is the number of years of unaffected health and the chance that medical progress will lead to the development of better avenues to manage, treat and cure the disease. See Merle Spriggs, "Genetically Selected Baby Free of Inherited Predisposition to Early-Onset Alzheimer's Disease" (2002) 28 J. Med. Ethics 290.

⁶⁶³ See Cruts & Van Broeckhoven *supra* note 592.

⁶⁶⁴ Thomas D. Bird, "Early-Onset Familial Alzheimer Disease" in Pagon RA, Adam MP, Ardinger HH et al., ed, *GeneReviews* (Seattle, University of Washington, 2012).

restriction of genetic diagnosis to non-late onset cases. I have shown that the bar for the maximal age of onset steeply climbed shortly after the introduction of susceptibility screening from the first to the sixth and seventh decades of life. How did the regulatory lines shift so rapidly and extensively? A key answer lies in the language that regulators have used to demarcate the boundaries between the late and non-late onset conditions and the manner in which they have been interpreted.

Has the regulatory distinction between what is regarded as late and non-late onset remained stable or not? In practice, what constitutes late and not late in life depends on rising societal expectations of good health and longevity. Knoppers et al. explain that under the revised UK and French rules, the age of onset is defined based on societal expectations. Societal expectations of good health tend to fluctuate and, with them, so will the age of onset.⁶⁶⁵ Knoppers et al. suggest that as life expectancy rises, so does people's perception of being "young" or "old" change. In certain societies where life expectancy nears eighty, a disease that manifests in a person's forties seems like one that strikes at a relatively young age.⁶⁶⁶ Likewise, Allan Thornhill, the first UK clinician to perform genetic diagnosis for familial Alzheimer's, defended his practice by suggesting that an onset at the age of fifty is not late-onset, but rather early because future life expectancy is expected to continue to increase.⁶⁶⁷ William Saletan observes that the age of onset bar will keep on being raised to later and later ages as society's expectations of a long life expectancy increase.⁶⁶⁸

The Implications of Drawing Malleable Lines regarding Late-Onset age

Academics have warned that failing to set a minimal bar might effectively mean the abolishment of the thresholds because each and every person is genetically susceptible to developing diseases later in life.

⁶⁶⁵ See Bertha Knoppers et al., "Preimplantation Genetic Diagnosis: An Overview of Socio-Ethical and Legal Considerations" (2006) 7 *Annu Rev Genomics Hum Genet* 201. See also Wertz & Knoppers supra note 79 at 34.

⁶⁶⁶ *Ibid.*

⁶⁶⁷ Dr. Alan Thornhill, "PGD for Early Onset Alzheimer Disease: Preventing Disease. Not the Cure", *Bionews.com* (17 April 2007) online: http://www.bionews.org.uk/page_37928.asp

⁶⁶⁸ William Saletan, "Cut-off genes: Our Gentle Descent toward Eugenics" *Slate* (May 19 2006) online <http://www.slate.com/id/2141968/>.

Without a restriction of susceptibility screening for non-late onset conditions, the concept of genetic risk could be potentially applied to every single embryo.⁶⁶⁹ Genetic studies confirm that susceptibility genes are even more common as susceptibility is associated with a later age of onset.⁶⁷⁰ For example, highly common disease susceptibilities with onset at post-reproductive ages include a variety of cancers, neurodegenerative diseases, and coronary heart disease.⁶⁷¹ Soini et al. point out that “the relative risk for common multifactorial diseases (such as diabetes and some cardiovascular diseases) are so common that it is hard to imagine that they could be an indication for PGD because it would mean that an indication for such a test would exist in most families.”⁶⁷² A UNESCO report further asks “in the long run [once susceptibility genetics is better understood] every embryo and person will appear to be genetically at increased risk for some medical condition, so where is the limit?”⁶⁷³

In a system that regards an age of onset in the seventh decade as non-late, it is not clear which age of onset remains excluded by the regulators as being late. As these expectations increase, the age of onset bar is pushed later and later into older and older ages. Even today, regulators approve susceptibility screening for conditions with an age of onset between the sixth and eighth decades of life such as Parkinson’s, dementia, and Alzheimer’s. If susceptibility to conditions such as Parkinson’s, dementia, and Alzheimer’s

⁶⁶⁹ It could be said the best remedy against eugenic applications is to simply understand and accept that everyone is at risk to develop a condition later in life. However, as biomedical technologies elevate expectations, more consumers are likely to see a shift in their thinking from viewing universal risks tied to the human genome as normal and acceptable to something that has to be managed and minimized through novel reproductive technologies.

⁶⁷⁰ See Ju-Hyun Park et al., “Distribution of Allele Frequencies and Effect Sizes and their Interrelationships for Common Genetic Susceptibility Variants” (2011) 108:44 *Proceedings of the National Academy of Sciences* 18026. See also Ivan P Gorlov et al., “Evolutionary Evidence of the Effect of Rare Variants on Disease Etiology” (2011) 79:3 *Clinical Genetics* 199. See also Zuobin Zhu et al., “Enrichment of Minor Alleles of Common SNPs and Improved Risk Prediction for Parkinson’s Disease” (2015) 10:7 *PLOS ONE* e0133421.

⁶⁷¹ *Ibid.* Gorlov et al. further explain that from an evolutionary biology perspective, a key reason why late onset susceptibility genes are common is since these genes do not come under the same evolutionary selective pressures as early onset disease.

⁶⁷² Sipra Soini, et al., “The Interface between Assisted Reproductive Technologies and Genetics: Technical, Social, Ethical and Legal Issues” (2006) 14:1 *Eur J Hum Genet.* 602-605.

⁶⁷³ Hans Galjaard *supra* note 555 at 13.

qualify as being non-late, which age of onset would regulators regard as late? This curious case illustrates the much diminished boundary-setting function of the age of onset requirement.

Class IV CF – 3 Percent Risk Rate and the Considerable Risk Requirement

Formally, the UK and French laws required the risk level of developing a serious disease to be “significant.”⁶⁷⁴ However, in practice, this is interpreted via the proxy of prospective parents’ “perceived risk.” Would the requirement of significant risk enable screening for a single-digit risk⁶⁷⁵ of developing a very mild form of cystic fibrosis (CF)? The answer is yes. Unlike other, more common CF mutations that are highly penetrant (often around 80 to 90 percent),⁶⁷⁶ the R117H mutation is only 3 percent penetrant.⁶⁷⁷ When put in perspective, a 3 percent penetrance rate means that, statistically, in a cohort of 100 children with the R117H mutation, only 3 percent of those children would develop this mild form of cystic fibrosis and 97 percent would not be affected by the condition at all.

Could a very low-risk probability still be justified under a law that formally requires significant risk rates? The HFEA argued that in cases of a particularly serious condition, even a low-risk probability should be allowed.⁶⁷⁸ Bredenoord et al. further contend that even though balancing between the degree and probability of “harm” is a rather vague and malleable formula, it would nevertheless prevent a “slippery slope” in which prospective parents would screen for ever-lower risk rates. When performing the balancing of harms and benefits, prospective parents would naturally not

⁶⁷⁴ See Section 9A, HFEA, 8TH Code of Practice (London: HFEA, 2016).

⁶⁷⁵ Susceptibility screening for conditions with single digit risk rates may result in a “false negative” diagnoses, since the selected embryo could have susceptibilities to other conditions with overall worse health outcomes. The frequent “false negatives” diagnoses cast doubts on the purported health benefits of susceptibility screening in instances of very low or single digit risk rates. For example, see Ernest Beutler, “Carrier Screening for Gaucher Disease: More Harm than Good?” (2007) 298:11 JAMA 1329.

⁶⁷⁶ See Rusian Dorfman & Julian Zielenski, “Genotype-Phenotype Correlations in Cystic Fibrosis” in Bush, A et al., eds, *Cystic Fibrosis in the 21st Century* (Basel: Karger, 2006) at 61.

⁶⁷⁷ See Rabah M. Shawky, “Reduced Penetrance in Human Inherited Disease” (2014) 15:2 Egy J Med Hum Genetics 103.

⁶⁷⁸ HFEA, Ethics and Law Committee, “Case by Case Decision Making in PGD”, ELAC (12-09) 3 15/12/2009, 4. (London: HFEA, 2009).

choose to undergo susceptibility screening when conditions are less serious and the risk rates are very low.⁶⁷⁹

In the case of the R117H mutation, not only is it only 3 percent penetrant, but in cases when the mutation affects the person, it produces one of CF's mildest forms.⁶⁸⁰ Like most conditions with genetic origins,⁶⁸¹ different CF mutations affect patients in different ways, ranging from mild to severe.⁶⁸² Unlike the more common forms of CF,⁶⁸³ Class IV (associated with the R117H mutation) is regarded as one of the mildest forms of the condition, and it is highly unlikely ever to materialize. The key symptom is mild pulmonary dysfunction; however, this symptom often does not develop in childhood.⁶⁸⁴ In extremely rare cases (less than 1 percent), adult patients might develop disseminated bronchiectasis (an obstruction of the respiratory tract by mucus).⁶⁸⁵ Individuals with Class IV CF genes have overall life expectancies that are in line with national averages.⁶⁸⁶ Moreover, in light of the progress in precision medicine,⁶⁸⁷ trials for the recently approved drug Ivacaftor, which is the first to

⁶⁷⁹ Bredenoord, *supra* note 50 at 2397-2399.

⁶⁸⁰ See A. Lording et al., "Pulmonary Infection in Mild Variant Cystic Fibrosis: Implications for Care" (2006) 5:2 J of Cystic Fibrosis 101; See also David Hughes et al., "Mutation and Haplotype Analysis of the CFTR Gene in Atypically Mild Cystic Fibrosis Patients from Northern Ireland" (2001) 38:2 J Med Genetics 136.

⁶⁸¹ In genetics, conditions are often categorized into different types and classes based on the gene mutation and this particular mutation causes a more severe or milder form of the disease. See Lynn B Jorde, John C Carey & Michael J Bamshad, *Medical Genetics*, 5TH ed. (Philadelphia: Elsevier, 2015) 72.

⁶⁸² See Gerald L. Feldman and Kristen G Monaghan, "Prenatal Diagnosis of Cystic Fibrosis" in A Milunsky, ed, *Genetic Disorders and the Fetus: Diagnosis, Prevention, and Treatment* (Baltimore: Johns Hopkins University Press, 2004) 596-600.

⁶⁸³ Cystic Fibrosis is the most common indication for genetic diagnosis. The R117H mutation is frequently tested as well. For more about CF being the most common indication for genetic diagnosis in Europe see the report Europe Society of Reproduction and Embryology - Joyce C Harper et al., "The ESHRE PGD Consortium: 10 Years of Data Collection" (2012) 18:3 Hum Repro update 239-242. For more information about CF as a popular indication in France see Carazo Fernandez et al., "Preimplantation Genetic Diagnosis for Cystic Fibrosis: The Montpellier Center's 10-Year Experience" (2015) 87:2 Clinical Genetics 124.

⁶⁸⁴ Christel Thauvin-Robinet et al., "The Very Low Penetrance of Cystic Fibrosis for the R117H Mutation: A Reappraisal for Genetic Counselling and Newborn Screening" (2009) 46:11 J Med Genetics 754-758.

⁶⁸⁵ *Ibid.*

⁶⁸⁶ See Carrie A. Schram, "Atypical Cystic Fibrosis: Identification in the Primary Care Setting" (2012) 58:12 Can Fam Physician 1341.

⁶⁸⁷ The NIH defines precision medicine as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person." The NIH further adds that precision

treat the underlying causes of CF, significantly improved lung function in adult patients with the R117H mutation.⁶⁸⁸

There are practical reasons to question the legal policy of allowing genetic diagnosis when the penetrance of the gene is only 3 percent and the condition is arguably not as serious as its name implies. Analogous circumstances might be able to give some answers as to the preferable legal policy. Scotet et al. have recommended removing the R117H mutation from neonatal screening programs because when considering the degree of risk versus the expected benefits of the genetic screening, the 3 percent risk is too low to justify the difficulties and risks relating to IVF.⁶⁸⁹ Likewise, a group of French clinicians recommended removing the screening for the R117H mutation from the national neonatal screening program given the procedure's negligible health benefits.⁶⁹⁰ Such evidence from the same case in a similar context cast doubts on whether the regulatory policy for genetic diagnosis has appropriately grappled with the risks⁶⁹¹ and benefits of screening for a mild form of CF that is highly unlikely to develop. What are some of the implications of this lax regulatory policy that approves susceptibility screening even when the likelihood that a gene would affect health outcomes is extremely low?

medicine" will allow doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work in which groups of people. It is in contrast to a one-size-fits-all approach, in which disease treatment and prevention strategies are developed for the average person, with less consideration for the differences between individuals." See US National Institutes of Health, "What is Precision Medicine?" National Institutes of Health (November 26, 2019) Online: <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition>

⁶⁸⁸ See Richard B Moss et al., "Effects of Ivacaftor in CF Patients with R117H-CFTR" (2014) North American Cystic Fibrosis Conference. Atlanta: *Pediatr Pulmonol.* 221. Richard B Moss et al., "Efficacy and Safety of Ivacaftor in Patients with Cystic Fibrosis who have an Arg117His-CFTR Mutation: A Double-Blind, Randomised Controlled Trial" (2015) 3:7 *The Lancet Respiratory Medicine* 524; See also S Carter et al., "Ivacaftor as Salvage Therapy in a Patient with Cystic Fibrosis Genotype F508del/R117H/IVS8-5T" (2015) 14:4 *J Cystic Fibrosis* 4.

⁶⁸⁹ Virginie Scotet et al., "Immunoreactive Trypsin/DNA Newborn Screening for Cystic Fibrosis: Should the R117H Variant Be Included in CFTR Mutation Panels?" (2006) 118:5 *Pediatrics* 1523.

⁶⁹⁰ Christel Thauvin-Robinet et al. *supra* note 684 at 752.

⁶⁹¹ Studies found that IVF is linked to an increased risk of mothers and their children developing certain diseases. For instance, a large meta-analysis found that compared to women in the spontaneous conception group, women in the assisted reproductive technology group had a 53% chance of developing gestational diabetes. EMJ, Review of the 55th Annual Meeting of the European Association for the Study of Diabetes (EASD), *Eur Med J* (05 November 2019) online: <https://www.emjreviews.com/diabetes/congress-review/review-of-the-55th-annual-meeting-of-the-european-association-for-the-study-of-diabetes-easd/>

The Implications of Setting the “Significant Risk” Bar at a Low Point

Interviews with health-care professionals help to shed light on the rarely discussed topic of susceptibility screening for very low penetrance rates. A nurse in a UK fertility clinic observed,

What’s the point of doing PGD where the misdiagnosis risk is 2%, and where the risk of having a child born with the condition is 1% that logically doesn’t work for me. Yet couples will turn it around, and see that 2% risk as small, and the 1% risk as massive for some of the single gene disorders, there’s a 5–7% misdiagnosis risk per embryo some of my colleagues would say they’re reducing that couple’s 25% risk of having a child affected down to a 5–7% chance, and people are happy with that. I don’t know whether we should be offering PGD in those circumstances.⁶⁹²

Geneticist Shirley Hodgson stresses the importance of setting a minimal rate of penetrance at a probability rate that is not overly low. Hodgson provides practical reasons, explaining that not setting minimum rates for penetrance would essentially mean that all embryos will be found to be at risk. She says, “I think it would be a big mistake to start testing embryos for mutations that only alter susceptibility a little, by a factor of 2 or 3, for example.”⁶⁹³ Hodgson points out that because low-penetrant mutations exist in virtually every person (and embryo), all could be diagnosed with a genetic abnormality. She adds: “[t]here are lots of such gene mutations with low penetrance for cancer and that would certainly imply a big slippery slope.”⁶⁹⁴

The case of Class IV CF demonstrates the problem of subjective “perceived risk” in setting meaningful limits to exclude very low penetrance rates. The shift of the regulatory risk threshold all the way from 90 percent to 3 percent demonstrates the extent of change in the interpretation and

⁶⁹² Clare Williams et al., “Facilitating Choice, Framing Choice: Staff Views on Widening the Scope of Preimplantation Genetic Diagnosis in the UK” (2007) 65:6 *Social Science & Medicine* 1000.

⁶⁹³ Rice *supra* note 555.

⁶⁹⁴ *Ibid.*

application of the rule. This change reflects a tension with both the spirit and the letter of the law. In terms of the spirit of the law, regulators, at least initially, stressed the significance of restricting genetic diagnosis to high-risk rates because it is warranted in cases where there is a strong link between the gene and serious health outcomes. In terms of the letter of the law, this reduction of penetrance rate to 3 percent shows a potential tension with the language of the UK and French acts, which require a significant risk of developing a serious disease. If a 3:100 risk rate could still be regarded as significant, then it begs the question: what would be legally regarded as an insignificant rate? If even risks at the very bottom of the scale are regarded as significant, it implies that very few risks (if any) would fall below the bar.

“The Risk of Transmitting a Risk” – Genetic Diagnosis for Unaffected Gene Carriers

When the regulatory requirements of significant risk and age of onset are pushed to their utmost extremes, even unaffected carrier embryos could be considered undesirable, despite the fact that such children would be unaffected by the disease. To fathom the extent of the legal change to the notion of “genetic risk,” let us examine the important case of unaffected carrier screening. First, unaffected carrier screening is at odds with the significant risk requirement because the putative child is at no known genetic risk of developing the purported disease or disability. In unaffected carrier screening, the gene is 0 percent penetrant.⁶⁹⁵ To illustrate, consider an example of carrier screening for genes of sickle cell anemia,⁶⁹⁶ a condition with a higher prevalence amongst people of sub-Saharan African descent.⁶⁹⁷ If a child has one

⁶⁹⁵ Alan R. Thornhill et al., ‘ESHRE Consortium “Best Practice Guidelines for Clinical Preimplantation Genetic Diagnosis (PGD) and Preimplantation Genetic Screening (PGS)”’ (2005) 20 Hum Repro 35, 45.

⁶⁹⁶ It is worthy to mention that the sickle cell anemia gene also confers resistance to certain communicable disease such as Malaria. Evolutionary geneticists hypnotize the sickle cell genes were naturally selected because of the resistance to pandemics they confer See David C Rees, Thomas N Williams & Mark T Gladwin, “Sickle-Cell Disease” (2010) 376:9757 The Lancet 2018.

⁶⁹⁷ Bernadette Modell & Matthew Darlison, “Global Epidemiology of Haemoglobin Disorders and Derived Service Indicators” (2008) 86:6 Bull World Health Organization 480.

copy of the HBB gene, he or she will be an unaffected carrier of sickle cell anemia.⁶⁹⁸ The unaffected carrier child will not develop the condition at any point. As such, the unaffected carrier child is not at risk of developing a disease or disability based on his or her genetic inheritance.

For Whom is it Serious that a Child is Born as an Unaffected Gene Carrier?

What would enable regulators to approve genetic diagnosis even when the condition poses no risk to the child? The answer is found in the regulatory requirements' ambiguous language. Although initially, the implicit assumption in the text is that the condition is serious for the child alone, this interpretation was not made a part of a binding definition in either the UK or in France.⁶⁹⁹ With the lack of a binding definition or an agreed upon interpretation, an ambiguity later arose: for whom is the condition serious—the child, the parents, or third parties? This ambiguity in the law enabled regulators and the national ethical advisory bodies (the CCNE and HGC) to expand the seriousness standard to apply to third parties.⁷⁰⁰ The CCNE has explicitly noted that “the extension of PGD is no longer purely in the interests of the child to be born but also in the interests of a third party.”⁷⁰¹ The French law is ambiguous on the question of for whom is the condition serious, the child, parents, or other third parties.⁷⁰² Likewise, the UK law is

⁶⁹⁸ Michael A. Bender & Gabrielle Douthitt Seibel, “Sickle Cell Disease” (2014) GeneReviews, NCBI Bookshelf online: <https://www.ncbi.nlm.nih.gov/books/NBK1377/>.

⁶⁹⁹ For more about the legal theory of how without an anchor in the legal text, an ambiguous concept can be changed in transformed through application and adjudication See Ross Charnock, “Clear Ambiguity” in Anne Wagner & Sophie Cacciaguidi-Fahy eds, *Legal Language and the Search for Clarity: Practice and Tools* (Berlin: Peter Lang, 2006) 70-75.

⁷⁰⁰ The very same question serious for whom, was used to justify genetic diagnosis licensing to create “savior sibling” embryos. In the case of a genetic diagnosis to detect a savior sibling, the future child will not suffer from any serious disease. However, “savior sibling” creation is premised on the assumption that such genetic diagnosis is done in the interest of a third party. For a defense of genetic diagnosis in the interest of third parties (such as “savior sibling” and unaffected carrier screening) see Guido De Wert, “Preimplantation Genetic Diagnosis: The Ethics of Intermediate Cases” (2005) 20:12 Hum Repro 3261. For a critical viewpoint see Andorno supra note 61 at 96-101.

⁷⁰¹ CCNE, 2002 supra note 572 at 1.

⁷⁰² See Michelle Plachot & Jean Cohen, “Regulations for Preimplantation Genetic Diagnosis in France” (2004) 21:1 J of Assisted Repro & Genetics 5; See also Peter R. Brinsden, *A Textbook of in Vitro Fertilization and Assisted Reproduction: The Bourn Hall Guide to Clinical and Laboratory Practice* (New-York: Taylor & Francis, 2005) at 668.

ambiguous about the question for whom the condition should be serious.⁷⁰³ The ambiguity concerning for whom this condition is serious has enabled regulators to recognize genetic diagnosis for medical purposes in the interest of third parties.

Regulators and other authorities have recognized that third parties who might be affected by the deleterious gene are the putative future child's potential offspring. For instance, the UK House of Commons Report explicitly recognized that unaffected carrier screening is performed in the interest of avoiding risks to the potential grandchildren.⁷⁰⁴ The regulatory approval of unaffected carrier screenings has created, de facto, an entirely new category of risks—transgenerational risks to the putative child's own potential future offspring. If a transgenerational risk would ever materialize, it would be for only the child's potential grandchildren or their descendants.⁷⁰⁵ In essence, the underlying assumption of such a view of genetic risks is that the embryo could potentially be deselected on the premise that if born, he or she would cause a risk by transmitting a deleterious gene to their future lineages.⁷⁰⁶

Transgenerational Risk's Remoteness and Hypothetical Status

In some cases, the risks associated with unaffected carriers might only develop at a very distant point in the future, far removed from the present day by several generations. Clinical geneticist Pierre Ray explains that unlike unaffected carriers of dominant genes, for unaffected carriers of recessive genes, the

⁷⁰³ Ilja Richard Pavone, "The Legal Implications of Preimplantation Genetic Diagnosis" in *Biotech innovations and fundamental rights*, Roberto Bin, Sara Lorenzon & Nicola Lucchi eds, (Milan: Springer, 2012) 155.

⁷⁰⁴ See United Kingdom, House of Common Science and Technology Committee Human Reproductive Technologies and the Law Fifth Report of Session 2004–05 Volume I 64–64. (London: HSMO, 2005).

⁷⁰⁵ Annelien L Bredenoord, et al., "Avoiding Transgenerational Risks of Mitochondrial DNA Disorders: A Morally Acceptable Reason for Sex Selection?" (2010), 25:6 Hum Repro at 1356–1358.

⁷⁰⁶ The UK House of Commons report rejected claims by academics of screening for unaffected carriers of deleterious genes is a eugenic practice. Instead, the House of Commons report argued the motivation behind this practice is simply to spare future descendants of the emotional and financial costs involved in undertaking themselves the same genetic interventions for genetic predispositions. See House of Commons supra note 704.

The UK House of Commons' analysis focuses on prospective parents' motivations instead of the outcomes of their choices. Yet, as I have shown in chapter 2 and elsewhere, prospective parents are not likely to adopt the eugenic ideology, yet this does not change the fact that choices to deselect against putative healthy children that simply because they carry a gene deemed deleterious can produce over time eugenic outcomes.

chance that their future descendants will develop the condition substantially decreases. Ray exemplifies this point with the case of CF, a recessive disease whose inheritance is not linked to a sex chromosome. For unaffected carriers of CF, the chance of transgenerational penetrance is 1:100. This extremely low transgenerational penetrance rate means that not only are the grandchildren unlikely to develop CF but also the grandchildren's descendants are unlikely to develop the condition.⁷⁰⁷ Ray further asserts that, given the low transgenerational penetrance, the risks are not only remote but could be considered outright hypothetical.⁷⁰⁸

Ray asserts that these remote and hypothetical risks to future descendants do not comfortably fit with the requirements set by the French Bioethics Law. He argues that the unaffected carrier screening is at odds with the notion of "genetic risk," because the future child is at no such risk. Moreover, he points out that the risk's remoteness is also in conflict with the notion of onset, as the onset may only pose a risk for the grandchildren or even later generations, many decades from now.⁷⁰⁹ Ray concludes that there will be a great difficulty in reconciling unaffected carriers' remoteness and low-risk profile with the law's requirement of significant risk and early onset.⁷¹⁰

Unaffected carrier screening demonstrates how the risk, which was initially, under the law, supposed to materialize immediately after birth, may now take place so late it may only affect future generations. For unaffected carriers of recessive genes, the associated risks would only materialize long after the unborn child is dead. The purported benefits of unaffected carrier screening are to future offspring, who will

⁷⁰⁷ Pierre F. Ray, "Ethics and Genetics of Carrier Embryos" (2006) 21:10 Hum Repro 2723.

⁷⁰⁸ *Ibid.* Moreover, the implicit premise that the unborn child would be a source of risk to its children cannot always be substantiated. Regulators would do best to avoid making hypothetical assumptions about unborn children's future reproductive choices. What if the unaffected carrier child decides not to have children, adopt or to conceive via sperm or ova donation? The yet unknown reproductive choices of future children illustrate that the risk attributed to unaffected carriers can be outright unfounded.

⁷⁰⁹ Ray further mentions that by the time a susceptibility gene may manifest as a disease in the grandchildren or their descendants, the condition may be treatable (and hence should not be screenable). This begs the question what is the urgency to expand resources now for a low probability risk that may or may not materialize even as late as many decades from now?

⁷¹⁰ Ray *supra* note 707.

hopefully have the deleterious gene expunged from their bloodlines.⁷¹¹ In examining the operative logic of carrier screening, one uncovers an implicit assumption that being an unaffected carrier inadvertently creates risks for one's future lineages. However, every person (and embryo) is estimated to be an unaffected carrier of several genes linked to diseases.⁷¹² The acceptance of transgenerational risks shows how wide-ranging the redefinition of the legal notion of "genetic risk" has become—that everyone procreating naturally might hypothetically be a source of genetic risks to their future lineages.

VII) Universalizing Risk: Reflections on the Potential Outcomes of the Legal Change

How would one reflect on the change to the rule regarding susceptibility screening? Several commentators would view the legal change as a positive development, as a removal of technical, arbitrary and unneeded barriers. Scott argues that as long as a condition is serious, the risk rates are rather insignificant boundary markers, even if the risk rates are minimal.⁷¹³ Amor and Cameron suggest that there should not be limitations on the minimal degree of risk that may arise from genetic inheritance. They support their assertion with what they regard as a particularly serious condition—the autism spectrum disorder (which I will cover in detail in the next chapter). In cases of such serious conditions, a genetic diagnosis is advisable, especially when the risk rate of developing the condition is higher than 1 percent.⁷¹⁴

One can easily be sympathetic to prospective parents' wishes to spare their child from disease, but should the regulatory system, which is entrusted a public role as well, entirely forgo setting reasonable limits

⁷¹¹ A fertility doctor commented on the eugenic potential of unaffected carrier screening, saying: "If we do it once, we'll do it every time, and then we can erase hemophilia from the earth and I think that we are not allowed to push evolution in this way. We are not gods." A quote from Melisa Soto-Lafontaine et al., "Dealing with Treatment and Transfer Requests: How PGD-Professionals Discuss Ethical Challenges Arising in Everyday Practice" (2018) 21:3 Med, Health Care & Phil 380.

⁷¹² See Roxanne Mykitiuk, & Isabel Karpin, "Fit or Fitting in: Deciding Against Normal When Reproducing the Future" (2017) Continuum 1. See also Snelling supra note 641 at 96-97. See also Inmaculada de Melo-Martin & Zev Rosenwaks, "Searching for the Perfect Child" (2015) 103:2 Fertility and Sterility 342-343.

⁷¹³ Robert Scott, "Choosing between Possible Lives: Legal and Ethical Issues in Preimplantation Genetic Diagnosis" (2006) 26:1 Oxford J Leg S 176.

⁷¹⁴ David J Amor & Carolyn Cameron, "PGD Gender Selection for Non-Mendelian Disorders with Unequal Sex Incidence" (2008) 23:4 Hum Repro 729.

to the risks' probability and remoteness? What those who advocate for the removal of these regulatory restrictions fail to understand is that by ignoring the age of onset and significant risk requirements, they advocate for a legal notion of genetic risk that is so pervasive that it could potentially apply to every single embryo. The HFEA itself has explicitly warned that without restrictions regarding the minimal penetrance rate and the age of onset, emerging technologies (such as whole-genome sequencing) will show that every single embryo is at risk, with a number of gene based susceptibilities.⁷¹⁵ This newly expanded notion of risk opens the door for industry practices that exploit parental risk-averse behaviour in order to grow the genetic diagnosis market, even if the risks are highly uncertain, are low probability, or are contingent upon unknown environmental factors. The CCNE and Baroness Deech, the former HFEA chair, warned that unrestricted access to susceptibility screening could create a "prediction mania". Under such conditions, the consumer public would press regulators and clinics to access susceptibility screening for genes linked to very low-risk rates, even when the benefits of the procedures could be relatively marginal or even negligible. These early concerns do not seem unjustified given the expansive notions of "genetic risk" that the regulatory system has inadvertently created in a relatively short period.

From a broader perspective, what could be some of the long-term ramifications of an expansive legal notion of "genetic risk" that could potentially apply to every embryo? How realistic is the expectation that an embryo will be found free of susceptibilities genes where those would naturally be found in every single genome? Is the newly emerging standard that children will not be susceptible to disease as they age in life even feasible or attainable? What happens once whole-genome sequencing becomes commonplace, and prospective parents, who wish for the healthiest child, find that all of their embryos have genes linked

⁷¹⁵ The HFEA itself has explicitly warned that without limits on penetrance and onset, once technology further develops (such as with whole-genome sequencing), virtually all prospective parents will find out that every single embryo is at risk with some susceptibility. See HFEA 2004 *supra* note 555.

to disease susceptibility?⁷¹⁶ As a partial solution, Jennifer Doudna, a co-developer of the CRISPR-Cas 9 gene editing technique,⁷¹⁷ suggests using genetic modification to possibly “edit out” genes linked to susceptibility to diseases and disabilities out of the human genome.⁷¹⁸ This novel biotechnological quest to prevent the unborn from developing a disease later in life brings us ever closer to a perfectionist notion of human health.⁷¹⁹

Conclusion

The regulatory requirements governing the notion of genetic risk have departed from a rather restrictive policy to a highly permissive one. In the past, regulators have restricted genetic diagnoses to the

⁷¹⁶ For instance, geneticist and honorary president of INSERM, Jacques Testart explains that in the long term, susceptibility screening leads to “universalizing” genetic risk and creating unattainable perfectionist bars. See Jacques Testart, “DPI : Vers un Nouvel Eugénisme ?” Bioethique.com, (20 March 2014) online : <http://bioethique.com/index.php/handicap/eugenisme/64-dpi-vers-un-nouvel-eugenisme>

Disability scholars Heath, Rapp and Taussig further argue that since everyone is genetically susceptible to develop disease, and the logic of risk mitigation is inflationary and pervasive, current susceptibility screening is a canary in the coalmine for more extensive endeavours to target and mitigate genetic risks, See Deborah Heath, Rayna Rapp & Karen-Sue Taussig, “10 Genetic Citizenship” in David Nugent & Joan Vincent eds. *A Companion to the Anthropology of Politics* (Cornwall: Blackwell, 2007) 159.

⁷¹⁷ Gene editing is a collective term for a number of new genetic modification techniques. The CCNE defines gene editing as:

” These new techniques use endonucleases to cut a gene very precisely, either to inactivate it or to replace it with a functional gene. This extreme precision is made possible by the use of a guide RNA prepared by the experimenter to aim the endonuclease at the chosen DNA sequence ... Several methods are used, including the technique called CRISPR-Cas9, which is currently the most developed.”

See CCNE, Opinion No. 133 “Ethical Challenges of Gene Editing: Between Hope and Caution” (Paris: CCNE 2019) online: https://www.ccne-ethique.fr/sites/default/files/publications/avis_133_-_def_1702.pdf

⁷¹⁸ Jennifer Kahn, “The CRISPR Quandary”, *New York Times*, (11 November, 2015) online: http://www.nytimes.com/2015/11/15/magazine/the-crispr-quandary.html?_r=0

James Watson, a Noble Laureate for his role in describing the DNA double helix, warns of the attempt to eliminate susceptibility genes. Watson gives the example of genetic modification of genes correlated to an increased susceptibility to develop schizophrenia, in which the removal of these genes can also harm creativity. Watson warns of this kind of tampering with the human genome, which can lead to negative, unforeseen outcomes. See Michael Le Page, “Barriers to Embryo Testing go Down”, *Newscientist* (1 June, 2005) online <https://www.newscientist.com/article/mg18625023-900-barriers-to-embryo-testing-go-down/>

⁷¹⁹ In its report on human genetic modification, the French National Medical Academy points out that countless edits would be needed to be made on the human genome because of the numerous genes involved in susceptibility to cardiovascular diseases, cancer, neurodegenerative diseases and infectious diseases. Such multiple edits to the human genome can itself significantly increase the risk of disease. See Académie Nationale De Médecine infra note 969.

Andy Greenfield, the Chair of the HFEA Licensing Committee further responded to Julian Savulescu’s suggestion to eradicate disease susceptibility from the human genome. Greenfield opined that an attempt to eradicate susceptibilities would require a large-scale project to extensively reengineer the human genome. Such a colossal project could eventually boldly redefine human health standards. See Oxford Martin School, “Gene Editing, should there be Any Limits?” Youtube (Jan 25, 2017) online: <https://www.youtube.com/watch?v=DSEEsOaVHFY>

detection of a gene that almost certainly causes the child to develop a disease in infancy. The normative considerations behind the rules did not favour genetic diagnoses for susceptibility conditions because the link between genes and serious conditions is uncertain, and the risk is often remote. However, since 2006, regulators have decided to allow screening against late-onset, lower-penetrance conditions. In a matter of a few short years, the age of onset bar, which was supposed to exclude remote risks, steeply climbed from infant onset to onset of disease only potentially in the seventh decade of life, such as familial Alzheimer's, dementia and Parkinson's. The penetrance bar, which was intended to maintain a strong link between embryo screening and health outcomes, has been progressively reduced from 90 to 0 percent risk of developing an illness. The approval of unaffected carrier screening on the premise that unborn children might create risks for their potential grandchildren and future lineages demonstrates how expansive the legal notion of "genetic risk" has become. As genetic science and technology continue to show that virtually all are susceptible and are unaffected carriers, can human reproduction realistically meet these newly elevated standards of people being free of susceptibility to disease as they age?

Chapter Six

“Seriously Serious?” Legal Change Concerning Mild Conditions

The legal system has stepped into a new, ethically complicated territory in considering which potential lives should be prevented even before pregnancy. Significant decisions regarding future births and lives hang on one primary consideration – is the putative child likely to develop a condition that is “serious”.⁷²⁰ One must ask: how do regulators determine which conditions and disabilities are “serious” and which are not? For whom is a certain condition serious, for the child, the prospective parents or to society? Can a steady and consistent distinction between serious and non-serious conditions be made in an era in which rapid technological advances redefine societal standards and raise expectations?

In this chapter, I will examine the changes to the rule that prohibits screening against mild, non-serious conditions. Originally, lawmakers and regulators intended to restrict genetic diagnosis to cases in which the putative child’s health would be profoundly impacted. They further cautioned against the deselection of embryos with disfavoured cosmetic or behavioural traits, practices that are primarily motivated by socio-cultural and personal preferences. I will review the changes in the rule’s application and trace them back to the very notion of “seriousness”, which is conceptually unclear, subjective, and lacks limits to its expansive scope. The laws in France and the UK do not define the term, but rather give treating physicians and prospective parents a very significant role in interpreting the unclear notion of a serious condition. This lax approach to determining conditions’ seriousness eventually resulted in approving screening against a multitude of body variations such as dwarfism, mild albinism, webbed hands, intersex and crossed eyes. In all of these conditions, lifespan is normal and the degree of comorbidity and impairments are minor. Yet, all of these mild conditions

⁷²⁰ For instance, legal theorist Ronald Dworkin drew parallels between the use of the term serious genetic disorders to criteria governing decision making in physician assisted suicide. See Ronald M Dworkin, *Life’s Domain: An Argument about Abortion, Euthanasia and Individual Freedom* (New-York: Knopf, 1993).

are commonly medicalized and stigmatized for deviating from the socially constructed notion of bodily normalcy.

D) The Normative Considerations behind Restricting Genetic Diagnosis to Serious Conditions

Lawmakers and regulators provided three key arguments for why genetic diagnosis should be restricted to serious conditions (and disallowed for non-serious conditions). First, unlike serious conditions, non-serious conditions fail to evoke the same degree of profound risks to the potential child's life and health that justify on balance using genetic diagnosis to pre-empt such potential births. Second, the milder the condition is, the less it has medical justification and the more it is likely to be motivated by social motivations of having a child with more desirable traits. Third, screening against non-serious, mild conditions and the motivation of having a child with more desirable traits are a significant step down the slippery slope to eugenic practices.

A determination that a condition is serious suggests that there are significant enough reasons to warrant genetic diagnosis.⁷²¹ Serious conditions pose significant impacts for a future child's health that warrant not allowing an embryo to develop further.⁷²² Some conditions evoke a sense of seriousness more so than others. For instance, the 1993 Mattei-Chérioux Joint Committee mentions rare congenital malformations and inborn diseases that are characterized by an infant suffering and that can end in an early childhood death.⁷²³ The child's short life would be marked by illness and pain. In these circumstances, the medical harms to the putative child outweigh the ethical harms related to performing such genetic diagnosis. In stark contrast, non-serious conditions⁷²⁴ would only have minor effects on the putative child's health.

⁷²¹ HGC, *Choosing the Future: Genetics and Reproductive Decision Making* (London: HGC, 2001) at 19.

⁷²² HFEA, "ELC 12/3 Ethical Values and the HFEA" (London: HFEA, 2003) at 7-8.

⁷²³ Mattei, Chérioux J. *supra* note 423.

⁷²⁴ For example, see Jeffery Botkin, "Prenatal Diagnosis and The Selection of Children" (2002) 30 Fla. St. UL Rev 265.

Non-serious conditions are also known in the literature as mild, trivial or socially motivated interventions.

Hence, such mild, non-serious conditions on balance do not outweigh the ethical harms of such potential life prevention.⁷²⁵

Medical vs. Social Motivations to Trait Deselection

The restriction of genetic diagnosis to serious conditions is closely tied to a second, broader conceptual distinction regulators have made between medical and social motivations.⁷²⁶ Unlike with genetic diagnosis to prevent medically harmful conditions, socially motivated trait selection is impermissible because it seeks to satisfy parental interests of producing a child with characteristics deemed more desirable. The distinction between medically and socially motivated genetic diagnoses is commonly featured in documents that discuss the normative considerations underlying the regulatory restrictions. The 1984 Warnock Report distinguishes between screening for medical and social reasons.⁷²⁷ Unlike in medical selection that intends to prevent a life-threatening or profoundly debilitating congenital malformation, social selection seeks to satisfy prospective parents' whims and desires.⁷²⁸ The HFEA and the AGCT's consultation specifically mentions that it would not be acceptable to test for any social or psychological normal variants that are not tied to

⁷²⁵ The HFEA has stated that a key concern with trivial conditions is that they would also trivialize and devalue the lives of people with disabilities. See HFEA *supra* note 447.

The Council of Europe report further explains that genetic diagnosis for non-serious conditions "is objectionable because it involves a morally impermissible selection amongst those with an equal right to life." See Council of Europe *infra* note 735 at 30.

⁷²⁶ The distinction between medically and socially motivated trait selection is central to understanding the normative underpinnings of the seriousness standard. However, much like the seriousness standard itself, this distinction is not very useful in making clear determinations which interventions belong in each group (either social or medically motivated). Various interventions can be classified as either medically or socially motivated, depending on the normative and clinical perspectives applied when examining the intervention in question. See Ruth Deech & Anna Smajdor, *from IVF to Immortality: Controversy in The Era of Reproductive Technology* (Oxford: Oxford University Press 2007) at 65.

⁷²⁷ The distinction between social and medical selection directly underlies the distinction between permissible medical sex selection (such as avoiding a sex-chromosome linked genetic disease) and the impermissible social sex selection (for choosing a desired gender of the child).

⁷²⁸ Similar conceptions exist in the French law, See Pierre F. Ray *supra* note 707.

The UK Court of Appeals in *Quintavalle* discussed the great difficulty in making a clear distinction between legitimate medical interest and illegitimate screening based on parental preferences. Lord Mance opined that there is arguably a large grey area between medically and socially motivated interventions. See *R (on the application of Quintavalle) v Secretary of State for Health* [2003] EWCA Civ 667 at para 134.

serious health outcomes. Socially motivated diagnosis for desirable traits underlies the restriction of genetic diagnosis to serious conditions alone.⁷²⁹ The HGC report similarly states that the restriction of genetic diagnosis only to serious conditions intends to prevent the selection of embryos based on “trivial or for social reasons.”⁷³⁰

As the French judge, Christian Byk writes: “[w]hen the medical indication disappears, the justification that PGD is in the interest of the child (preventing that he/she would be affected with a major disease) is also disappearing. Then cultural and individual choices become prevalent.”⁷³¹ The Mattei-Chérioux joint committee warned that social, cultural and individual choices should not come to bear on such decisions. Otherwise, there is a real risk that the regulatory system would no longer be centred on the prevention of medical harms, but rather on parental desires and convenience.⁷³² Jean-François Mattei further commented that choices based on parental preferences “open the door for the selection of embryos that will be either preserved or eliminated based on arbitrary criteria, which is essentially a eugenic approach.”⁷³³

Slippery Slope Concerns regarding Screening against Non-Serious Traits

The restriction of genetic diagnosis to serious conditions has been repeatedly tied to the acts’ key goal of preventing a slippery slope to eugenic practices. The HFEA 1992 2nd Annual report and the foundational Lenoir report have discussed the significance of restricting genetic diagnosis solely to serious, life-endangering conditions. The two reports explain that the restriction is intended to avoid practices associated with the “slippery slope” of selection against trivial traits that have very little to do with preventing

⁷²⁹ HFEA & AGCT, *supra* note 437 para 2.

⁷³⁰ HGC, *supra* note 721 at 19.

⁷³¹ Byk *supra* note 442 at 100.

⁷³² Mattei & Chérioux *supra* note 423.

⁷³³ Jean-François Mattei *supra* note 431.

medical harms, and more with producing a desirable child.⁷³⁴ Selecting against children with trivial traits encourages a parental mindset that lacks appreciation for children as they come. Instead, such trait selection could encourage objectifying views of future children.⁷³⁵ The HGC summarized the underlying considerations of limiting genetic diagnosis to serious conditions, writing that “perhaps the most important is that this technique should not be used for the purposes of trait selection or in a manner in which could give rise to eugenic outcomes.”⁷³⁶ The HFEA further explained the rationale, maintaining that the slippery slope to eugenics entails the selection of children with more desirable characteristics, a practice in which parents “impose their expectations on these children in a way which fails to respect the autonomy and individuality of a child.”⁷³⁷ The CCNE opinion no. 107 maintains that certain prospective parents aim to have a baby as close to “perfect” in their eyes by screening against mild and minor abnormalities, an impermissible practice.⁷³⁸ To better evaluate such concerns flagged about the future use and misuse of the technology, let us examine the process of legal change to the rule restricting genetic diagnosis to serious conditions.

II) The Early Application of the Seriousness Standard

Between 1998 and 2001, regulators restricted genetic diagnosis primarily to rare, inborn genetic conditions that are characteristically life-threatening. As I will later explain, this earlier restriction to life-threatening conditions was tied to a stricter interpretation of the seriousness standard at the time. Studies and

⁷³⁴ HFEA, 2ND Annual Report (London: HFEA, 1992) 26. See also Noëlle Lenoir *supra* note 409, 57-60 and 201-204.

⁷³⁵ Legislation and Reports by Derek Morgan Human Fertilisation & Embryology Authority, “Sex Selection; Public Consultation Document” (London: HFEA, 1993); The Mattei-Chérioux joint committee report *supra* note 418.

The Mattei-Chérioux joint committee report further states that society must stay on guard to prevent consumer-driven eugenics that could emerge with genetic technologies to select traits, by restricting genetic diagnosis to serious conditions. The argument was echoed by the Council of Europe, see Council of Europe Steering Committee On Bioethics (CDBI), the Protection of the Human Embryo *in Vitro* - Report by the Working Party on the Protection of the Human Embryo and Fetus (CDBI-CO-GT3) Strasbourg, 19 June 2003, online: <https://rm.coe.int/16803113e6>

⁷³⁶ HGC, *supra* note 721, para 6.

⁷³⁷ HFEA, 2003 *supra* note 722 at 7.

⁷³⁸ CCNE, Opinion no. 107 *supra* note 48.

official reports show that genetic diagnosis at the turn of the century was primarily restricted in France and the UK to a handful of life-threatening conditions. The ESHRE, the embryology industry association, has published in 2000 a report based on official data from clinics and national registries that showed that genetic diagnosis is limited to a few, life-threatening conditions.⁷³⁹ A 2001 study shows that fertility centers in the UK and France only diagnosed about 10 conditions such as Tay-Sachs, Lesch-Nyhan syndrome, Myotonic dystrophy and Spinal muscular atrophy.⁷⁴⁰ A study by one of the only three clinics in France at the time using data from the national registry shows genetic diagnosis was restricted to a small number of monogenetic conditions that substantially shorten lifespans such as Tay-Sachs and Muscular dystrophy.⁷⁴¹ The HFEA and AGCT identify a number of conditions that are regarded as serious such as Cystic fibrosis, Duchenne muscular dystrophy, the thalassemias and a number of hereditary, infant-onset cancers (such as Li-Fraumeni syndrome).⁷⁴² A follow-up 2001 report by the HFEA and HGC states that the HFEA restricted its licenses to fatal or seriously debilitating childhood conditions with a few prospects for treatment.”⁷⁴³

During the period of 2002-2006, the HFEA and ABM approved a few conditions that are potentially life-threatening. However, the probability of death is substantially lower than in previously approved conditions as reflected by the higher life expectancy with these conditions. Such conditions include the metabolic disorder Medium-Chain Acyl-CoA Dehydrogenase deficiency, a benign tumour condition, Tuberous Sclerosis and the blood disorder Haemophilia. The average life expectancy of patients with

⁷³⁹ ESHRE PGD Consortium Steering Committee, “ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium: Data Collection II” (2000) 15:12 Hum Repro 2673.

⁷⁴⁰ Joep PM Geraedts et al., “Preimplantation Genetic Diagnosis (PGD), A Collaborative Activity of Clinical Genetic Departments and IVF Centres” (2001) 21:12 Prenatal Diagnosis 1086.

⁷⁴¹ Rene Frydman et al supra note 464.

⁷⁴² HFEA and AGCT, supra note 437 para 5.

⁷⁴³ HFEA and HGC, “Outcome of the Public Consultation on Preimplantation Genetic Diagnosis” (London, HFEA, 2001).

Hemophilia is about ten years shorter than the general population.⁷⁴⁴ Conditions approved during the period of 2002-2006 and onward,⁷⁴⁵ such as Haemophilia, reflect a notable change from earlier genetic diagnosis against congenital malformations such as Trisomy 13 and Muscular dystrophy.⁷⁴⁶ Yet the greatest changes in regulatory policy were those that came later. In 2006, Suzy Leather, the then Chair of the HFEA said the regulator will not approve non-serious, mild conditions.⁷⁴⁷ But the test of time has proven otherwise.

III) An Overview of the Legal Change of the Seriousness Standard

The approval of genetic diagnosis for crossed-eyes (Strabismus) by the HFEA in 2006 was a major turning point in the licensing of non-serious conditions. The licensing of screening of crossed-eyes has attracted a few predictions that the bar of seriousness is about to be set much lower. Geneticist David King described the emerging shift in the notion of seriousness standard as a move “from preventing children who will die young to those who might become ill in middle age.” He noted: “[n]ow we discard those who will live as long as the rest of us but are cosmetically imperfect.”⁷⁴⁸ Similarly, Professor Geddis Grudzinkas, the head of the London clinic that performed the first genetic diagnosis for crossed eyes predicted that “we will increasingly see the use of embryo screening for severe cosmetic conditions.”⁷⁴⁹ Professor Grudzinkas and

⁷⁴⁴ C Mejia-Carvajal, E Czapek & L A Valentino. “Life Expectancy in Hemophilia Outcome” (2006) 4:3 J Thrombosis & Haemostasis 507.

⁷⁴⁵ In 2009, the CCNE published an opinion on genetic diagnosis for Down syndrome. The CCNE opinion and the very topic itself stirred some controversy at the time in France. The CCNE opined that Down syndrome could be classified as a serious condition since certain prospective parents may view it as potentially associated with financial and emotional difficulties. However, the CCNE did recognize that classifying Down syndrome as a “serious” condition is neither simple nor clear from both the clinical and ethical standpoints. CCNE avis 107 supra note 48 at 13-17

⁷⁴⁶ I will not suggest that regulatory decisions to approve the above-mentioned impairment and disease are free from scrutiny. However, this chapter will place particular emphasis on the conditions that are arguably non-serious.

⁷⁴⁷ HFEA, Authority Decision on PGD Policy - Statement on the use of Preimplantation Genetic Diagnosis (PGD) for Inherited Cancer Susceptibility, (10 May 2006), online: <http://hfeaarchive.uksouth.cloudapp.azure.com/www.hfea.gov.uk/622.html>

⁷⁴⁸ Father John Flynn, “The Search for Perfection”, *Zenit* (June 25, 2007) online: <https://zenit.org/articles/the-search-for-perfection/>

⁷⁴⁹ Ronald Hancock, “Clinic to Weed out Embryos with a Squint”, *The Telegraph*, (07 May, 2007) online: <http://www.telegraph.co.uk/news/uknews/1550785/Clinic-to-weed-out-embryos-with-a-squint.html>

Dr. King's predictions have arguably come true, as regulators approved screening for a number of "serious cosmetic" conditions.

Primarily after 2006, the HFEA and ABM began approving conditions that are arguably non-serious. Such non-serious, mild conditions do not affect lifespan and overall health. The degree of impairment associated with such conditions is often moderate to minor.⁷⁵⁰ In addition, many mild conditions such as cleft palate, webbed hands and crossed eyes-can all be well treated. The regulatory approval of screening against treatable, mild conditions is seemingly at odds with the formal legal restriction of genetic diagnosis solely to serious and untreatable conditions. The HFEA and ABM have overall approved about a dozen non-serious, mild conditions. Such conditions include intersex, albinism (mild, type 2), and Pseudoachondroplasia (a form of dwarfism).⁷⁵¹ Furthermore, the HFEA and the ABM have approved genetic diagnosis for non-symptomatic hearing loss, which can impair the child's audio-sensory abilities. For instance, the HFEA has approved screening against Usher syndrome type 2, in which a child will develop in early adulthood a mild to moderate hearing and visual impairments.⁷⁵² In the UK, the list includes night

⁷⁵⁰ In this review, I will partially rely on the definition of mild conditions developed by Benjamin Wilfond. Wilfond, who is a physician and a bioethicist, developed one of the first known definitions of mild conditions. He describes mild conditions in the context of genetic intervention as having:

Signs and symptoms of the condition are typically not life-threatening, although in rare instances they might be life-threatening. Patients with the condition typically experience only mild or moderate disruption to normal activities and functions (e.g., poor vision vs. blindness). If there is treatment available, the treatment itself is not considered highly burdensome in terms of the medical interventions or lifestyle modifications that are required. With treatment, patients may experience few or no symptoms of the condition. Most children will have medical problems that require occasional extra medical visits, occasional medications, a slightly modified diet, or surgery; or will have mild problems with learning, vision, hearing, or mobility.

See Benjamin S Wilfond, "Breaking the Sounds of Silence: Respecting People with Disabilities and Reproductive Decision Making" (2017) 17:1 Am J Bioethics 37.

⁷⁵¹ Tom Shakespeare, a British scholar with pseudoachondroplasia argued before the UK House of Commons Science and Technology Committee that restricted growth has only minor and trivial effects and does not merit deselection. See Committee, Great Britain Parliament House of Commons Science and Technology, *Human Reproductive Technologies and the Law: Fifth Report of Session 2004-05, Vol. 1: Report, Together with Formal Minutes* (London: HMSO, 2005), 66.

⁷⁵² ABM, *supra* note 465.

blindness (X-linked congenital stationary night blindness), cleft palate, extra fingers and webbed hands.⁷⁵³ In France, the list also includes short fingers (Brachydactyly) and Cherubism, a condition that results in an excessive build-up of jawbone tissue and creates an appearance of an enlarged jawline but otherwise has only minimal effects on the child's health.⁷⁵⁴

The change pattern reveals how the seriousness standard has shifted from life-threatening congenital malformation to screening even against mild conditions that barely affect the child's health. The above-listed conditions often do not affect the child's health in a profound way but are often stigmatized as cosmetically, bodily or neurologically abnormal. The seriousness standard that was once set a considerably higher bar was gradually lowered to accommodate screening against mild conditions – the opposite of the goal that this standard was originally intended to serve.

IV) The Role of the Seriousness Standard's Lack of Clarity in the Legal Change

The legal construct of seriousness has been transformed due to changes in its interpretation and application over the years. The self-restraint in the interpretation helped contain the application of the otherwise overbroad seriousness standard to a rather specific group of lethal congenital malformations. Regulators initially only licensed screening against lethal congenital malformations such as Spinal Atrophy, Tay-Sachs and Muscular dystrophy. The interpretation of serious conditions as requiring they would be life-threatening created an informal and yet effective criterion to distinguish between conditions eligible and ineligible for screening. While the term life-threatening is not free from unclear interpretations,⁷⁵⁵ the bar it

⁷⁵³ HFEA, *supra* note 465; See also HFEA, "Regulation Activity Report", 3 December 2008, online: http://www.hfea.gov.uk/docs/AM_Item9a_Dec08.pdf

⁷⁵⁴ People with Cherubism can opt for surgery to remove the fibrous tissue from their jawline. However, in many instances, the condition remises after puberty and surgery is not needed. See Brad W. Neville et al., *Oral and Maxillofacial Pathology* (St. Louis: Elsevier Health Sciences, 2008) 630-631.

⁷⁵⁵ See for instance, Tracy K Koogler, Benjamin S Wilfond & Lainie Friedman Ross, "Lethal Language, Lethal Decisions" (2003) 33:2 Hastings Ctr Rep 37.

has set meant that many milder conditions (such as intersex, crossed eyes and autism) would not be approved. As such, the initial interpretation of the seriousness standard as implying licensed conditions should be life-threatening thus created at the time a somewhat clear and stable distinction between permissible and impermissible conditions for screening.⁷⁵⁶

In its early days, the HFEA's 1993 consultation on genetic diagnosis specifically named the more stringent standard of “life-threatening” as a criterion to license genetic diagnosis.⁷⁵⁷ Further, the now defunct HFEA Ethics Committee wrote in 1995 that: “Members felt that it was important to distinguish between diseases that were life-threatening and disease that affects the quality of life. ... Members felt that defining criteria that could be enforced would be difficult. Even if only medical categories were agreed this cause problems as even this definition is not clear.”⁷⁵⁸ Members of the HFEA Ethics Committee agreed that setting criteria was important, but was nonetheless a difficult task. Likewise, Baroness Deech, the then Chair of the HFEA in her 1998 article specifically stated that the seriousness standard refers to life-threatening conditions.⁷⁵⁹ However, Baroness Deech also mentioned the great difficulty in creating a uniform definition of the notion of serious conditions. Baroness Deech explained that the seriousness standard currently involves subjective judgment and that regulators should exercise caution to avoid stigmatizing children with certain traits, by making decisions that imply they should not have come into existence.⁷⁶⁰

Jacques Testart, the then Director of Research in INSERM, recommended that the undefined seriousness standard in the French legislation should be interpreted in a restricted manner to avoid misuse. Testart suggested that the regulator is presently only approving life-threatening conditions such as muscular

⁷⁵⁶ For more about how restriction to a rather particular group (such as life-threatening conditions) helps reduce vagueness, see for instance Jeremy Waldron, “Vagueness in Law and Language: Some Philosophical Issues” (1994) 82 Cal L Rev 522-526.

⁷⁵⁷ See HFEA, Sex Selection Public Consultation Document (London: HMSO, 1993), para 28.

⁷⁵⁸ HFEA *supra* note 7.

⁷⁵⁹ Ruth Deech *supra* note 568 at 703.

⁷⁶⁰ *Ibid.*

dystrophy and Cystic Fibrosis.⁷⁶¹ However, as genomics advances open the door for new choices in child genetics, the seriousness standard may not be able to set effective limits.⁷⁶² Without an obvious manner to distinguish serious from non-serious conditions, this standard runs the risk of enabling the regulators to gradually approve conditions that are less and less serious, thus exacerbating the risk that the slippery slope would become a reality.⁷⁶³

Indeed, as time went by, regulators moved from the stricter construction of the seriousness standard as meaning life-threatening to a far more permissive approach that with time has culminated in the approval of milder conditions. As I will soon discuss, this transition to a more expansive interpretation of the notion of serious conditions was made possible since the early interpretations of the standard as implying the life-threatening criterion were never binding. The lack of an agreed interpretation or a binding definition of serious conditions enabled regulators to eventually move away from the life-threatening criterion and transition to a more expansive interpretation of this otherwise highly broad and conceptually unclear notion of a serious condition.

A Serious Condition – A Construct without a Definition

The French and UK laws and regulations are not alone in failing to define “serious condition”: similar laws in Europe and Oceania that use the standard to regulate genetic diagnosis also fail to do so. It is therefore

⁷⁶¹ As noted in the previous chapters, the life expectancy of people with cystic fibrosis was significantly lower in the 1990s than it presently is, and was around 30 years. Medical advancements in the treatment of people with cystic fibrosis have made the condition arguably somewhat less serious.

⁷⁶² Jacques Testart, “Diagnostic Génétique Pré-Implantatoire (DPI) : Réponse À un Editorial” (1997) 13 *Médecine/Sciences* 134.

⁷⁶³ *Ibid.*

An official report by the German Bundestag examined data from the 2003 French official registry and found that indication for genetic diagnosis were restricted to lethal congenital malformation. However, similar to Testart predications, the CNMBRDP (the ABM’S predecessor) has approved one screening against a non-lethal condition – Fragile X syndrome. See Germany, Büro für Technikfolgen-Abschätzung beim Deutschen Bundestag, “Präimplantationsdiagnostik Praxis und Rechtliche Regulierung in Sieben Ausgewählten Ländern Sachstandsbericht” (2004) at 66-68, online: <https://www.tab-beim-bundestag.de/de/pdf/publikationen/berichte/TAB-Arbeitsbericht-ab094.pdf>

difficult to find inspiration in foreign laws. Karpin and Savell conducted a survey of the general regulatory requirements in 13 jurisdictions and found that laws and regulations neither define the term “serious” nor specify who should be responsible for providing such a definition.⁷⁶⁴ The HFEA and the HGC made attempts to advance towards a definition of the term serious condition for over 5 years but were unsuccessful.⁷⁶⁵ The HGC report summarized its efforts to find a definition, concluding that “the concept of serious in the context of PGD has been proven impossible to define.”⁷⁶⁶

The academic literature also failed to provide a definition of what the term serious conditions means in the context of genetic diagnosis. The Institute of Medicine's Committee on Serious and Complex Medical Conditions examined various factors such as diagnostic manuals, management guidelines and physiological measurements, but was unable to find an agreed definition of what serious conditions are. The committee stated that “the state of current clinical and research literature does not yet support the selection of specific categories of patients or service needs to define serious or complex medical conditions.”⁷⁶⁷ Further, a Hastings Center team with over 30 bioethicists and clinicians was unable to find any definition of the notion of a serious condition. The only agreement reached by the Hastings Center researchers was that it is impossible to find an agreed definition of what serious conditions are.⁷⁶⁸ In 2017, Vcy et al.'s review of the clinical literature did not find any agreement on how to distinguish between conditions that are serious and which are not.⁷⁶⁹

⁷⁶⁴ Isabel Karpin & Kristin Savell, *Perfecting Pregnancy: Law, Disability, and the Future of Reproduction* (New York: Cambridge University Press, 2012) 160-161.

⁷⁶⁵ HGC *supra* note 743 at 20.

⁷⁶⁶ *Ibid.*

⁷⁶⁷ Institute of Medicine Committee on Serious and Complex Medical Conditions, Chrvala CA, Sharfstein S, eds, *Definition of Serious and Complex Medical Conditions* (Washington (DC): National Academies Press, 1999) 3.

⁷⁶⁸ Erik Parens & Adrienne Asch, “The Disability Rights Critique of Prenatal Genetic Testing: Reflections and Recommendations” (1999) 29:5 *Hastings Ctr Rep* 30.

⁷⁶⁹ See Lee Vcy et al., “Preimplantation Genetic Diagnosis for Monogenic Diseases” (2017) 44 *Best Practice & Research Clinical Obstetrics and Gynecology* 68.

V) Relying on Parental Perceptions of Seriousness – A Way Forward or Backward?

On what kind of conceptions can laws rely when the terms they use cannot be defined? Owing to the inability to define this unclear legal construct,⁷⁷⁰ the law has moved to increasingly rely on prospective parents and treating physicians' viewpoints on the seriousness of the conditions. The 6th version of the HFEA Code of Practice introduced a major change to the manner in which seriousness is determined. In 2003, it revised its guidance to abandon the dependence on the Royal College of Gynaecologists' recommendations, which placed greater attention on the health impacts for the child when assessing the seriousness of the condition.⁷⁷¹ Instead, Section 10.6 of the 6th version of the HFEA Code of Practice has given a greater role to the 'perception of the level of risk by those seeking treatment'. The seriousness of the condition, therefore, is negotiated between the prospective parents seeking treatment and their medical team.⁷⁷² A similar shift in the interpretation of serious conditions has taken place in France. In France, prospective parents and clinics are responsible for considering what counts as serious in their particular case.⁷⁷³ The HFEA and ABM's revised positions on interpreting the seriousness standard fit well with Wertz and Knoppers's observation that in the absence of a definition, law and policymakers are presumably relying upon a "common [consumer]

⁷⁷⁰ From a legal theory standpoint, the seriousness standard is complex to define because it contains not one, but at least three types of indeterminacies: a) a textual indeterminacy, b) a methodological indeterminacy and c) an adjudicative indeterminacy. First, the seriousness standard suffers from textual indeterminacy, since the text does not provide a concrete definition of the term. The text is also ambiguous about the question for whom is the condition serious, for the child, the parents or the society? Second, the notion of seriousness suffers from methodological indeterminacy, owing to different methods in which an assessor can assign the seriousness label to conditions. Assessors can draw on medical literature regarding the condition's clinical symptoms, conduct interviews with people with the condition or assign the status based on personal impressions. Third, the seriousness standard suffers from adjudicative indeterminacy, in which different adjudicators would apply the requirement in an extremely divergent and inconsistent manner.

For more about the topic of linguistic indeterminacy see Pierluigi Chiassoni, *Defeasibility and Legal Indeterminacy*, in Jordi Ferrer Beltrán & Giovanni Battista Ratti eds, *The Logic of Legal Requirements: Essays on Defeasibility* (Oxford: Oxford University Press, 2012) 159-188.

⁷⁷¹ HFEA 2004 *supra* note 555.

⁷⁷² HFEA, Code of Practice, Ed. 6, (London: HFEA, 2003) Sections 10.6-10.7.

⁷⁷³ CCNE *supra* note 48.

public understanding of what constitutes a serious disorder."⁷⁷⁴ This begs a follow-up question: what does this elusively articulated notion of consumer public understanding of serious conditions entail?

Consumer Public Views on Serious Conditions

Can the consumer public views of serious disorders provide concrete and consistent guidance to regulatory policy? Studies on prospective parents' viewpoints and the public's understanding of the notion found an inability amongst members of the public to agree on which conditions are serious and what does this concept really entails. A study by Kerr et al. demonstrates a disagreement amongst laypeople about distinguishing between serious and non-serious conditions. The study also found that participants were unable to define what these concepts even encompass.⁷⁷⁵ A 2006 study by Hudson shows that the majority of the public cannot agree on how to distinguish between a serious and mild condition. Moreover, the study has found great difficulty amongst participants about which traits should even count as a pathology.⁷⁷⁶ The findings of those studies fit well with Van Wagner and Mykitiuk's observation that the seriousness standard is inherently subjective.⁷⁷⁷ The inability to find an overall agreement on the notion of serious condition indicates how subjective this notion is. The great challenges in providing even a basic definition of this legal term and its high degree of subjectivity could indicate the notion of a serious condition itself is based on changing social constructs.

⁷⁷⁴ Dorothy C Wertz & Bartha Maria Knoppers *supra* note 79 at 30.

⁷⁷⁵ Anne Kerr, Sarah Cunningham-Burley & Amanda Amos, "Drawing the Line: An Analysis of Lay People's Discussions about the New Genetics" (1998) 7:1 Public Underst Sci 131–133.

⁷⁷⁶ Kathy L. Hudson, "Preimplantation Genetic Diagnosis: Public Policy and Public Attitudes" (2006) 85:6 Fertility and Sterility 1639.

⁷⁷⁷ Estair Van Wagner & Roxanne Mykitiuk, "Constructing 'Health', Defining 'Choice': Legal and Policy Perspectives on the Post-PGD Embryo in Four Jurisdictions" (2008) 9:1 Med L Int'l 53.

The Social Construction of a Condition's Seriousness

Critical scholars and sociologists have linked the notion of a serious condition to the social construction of bodily normalcy.⁷⁷⁸ Philosopher of science Georges Canguilhem has defined the concept of bodily normalcy as: “a living person is normal in a given environment when she/he is the morphological and functional solution found by the life to meet all the requirements of this environment”.⁷⁷⁹ Canguilhem’s definition indicates that bodily normalcy (which arguably underlies the notion of seriousness) is dependent on values, social context and expectations of bodily performance. Resnik further explains that that bodily normalcy defies definitions because it is a social construct that is contingent on changing public attitudes, state of medicine and technology.⁷⁸⁰ Similarly, de Falco suggests that, much like bodily normalcy, the notion of a serious condition could potentially evolve over time as attitudes change.⁷⁸¹

Health sociologists tend to view bodily normalcy as a dynamic concept that could evolve as technology advances and expectations rise. Biomedical innovations elevate treatment standards and society’s expectations. The health sociology perspective⁷⁸² sheds light on how conditions previously regarded as near “normal”, such as milder physical or intellectual disabilities can be turned into a “serious” pathology as

⁷⁷⁸ Supra note 128; See also Erik Parens & Adrienne Asch, “The Disability Rights Critique of Prenatal Genetic Testing” (1999) 9:2 Hastings Ctr Rep Suppl: 1-22.

⁷⁷⁹ Georges Canguilhem, *Essai sur Quelques Problèmes Concernant le Normal et le Pathologique* (Paris : La Montagne, 1943) 3.

⁷⁸⁰ David B Resnik, “The Moral Significance of the Therapy- Enhancement Distinction in Human Genetics” (2000) 9 Cambridge Q Healthcare Ethics 366.

⁷⁸¹ Andrea arz de Falco, “Que Faire Face À Un Très Grand Nombre De Choix Possibles ? ” in C. Kind, et al, eds *Sélectionner ou Accepter ? La Vie en Devenir Face aux Diagnostics Prénataux et Préimplantatoire*, (Chênebourg : Éditions Médecine et Hygiène, 2009) at 96 – 97.

⁷⁸² Although physical conditions bring to mind a body of objective medical knowledge, it is also important to recognize that illness and health also entail an additional layer, that of social construction. The sociology of medicine often distinguishes between the biological condition (the disease) and the social dimensions of the condition (the illness). Illness refers to the cultural context that surrounds the social perspectives on the biological condition, which also entails the prevalent social costumes, folkways and mores. A person with an illness will be defined as one who deviates from the socially acceptable notion of health, whereas a healthy person is one who stays within such normative boundaries. See Peter Conrad, “The Shifting Engines of Medicalization” (2005) 46 J Health and Soc’ Behav at 3; David Tuckett, *An Introduction to Medical Sociology* (Oxford: Routledge, 2003) 334; Deborah Lupton, *Medicine as Culture: Illness, Disease and the Body* (London: Sage, 2012).

technology advances.⁷⁸³ The interplay of reproductive technology and societal norms reframes conditions (such as having short limbs, lack of skin pigmentation or enlarged genitalia) as preventable traits using reproductive technologies. Müller explains that prospective parents' rising expectations encourage screening for a growing list of conditions labelled as "abnormal". He notes "the boundary between 'normal' and 'pathological' is a fluid one and the evaluation of health and disease is influenced by technical progress." He opines that technical progress and rising expectations turn more near normal or mild conditions into a preventable pathology using genetic interventions.⁷⁸⁴

Other social science accounts further explain how biotechnological innovations raise standards and increase societal expectations. Health anthropologist Linda Hogle describes the manner in which prospective parents' increasing ability to make choices about their future child genetics gradually redefines deeper norms relating to expectations about bodily and mental normalcy in the biotech era.⁷⁸⁵ Gail Landsman brings accounts of prospective mothers who feel pressure and a duty to keep up with rising standards of bodily normalcy that new reproductive technologies promote. The expectation to utilize new reproductive technologies is often socially framed as a part of their maternal role.⁷⁸⁶ In an age of greater genetic choices, prospective parents play a role in redefining evolving standards of bodily normalcy. With the evolution of the notion of bodily normalcy and elevated expectations, more conditions could come to be viewed as abnormal.⁷⁸⁷ This view of the notion of seriousness as an evolving concept has been shared even by medical

⁷⁸³ See Lennart Nordenfelt & Per-Erik Liss, *Dimensions of Health and Health Promotion* (Linköping: Rodopi, 2003).

⁷⁸⁴ Hansjakob Müller, "Should There Be a Uniform List of Genetic Diseases Allowing Access to PID?" in Elisabeth Hildt & Graumann, S. eds, *Genetics in Human Reproduction* (Aldershot: Ashgate: 1999) 47-54.

⁷⁸⁵ Linda F. Hogle, "Enhancement Technologies and the Body" (2005) 34 *Annu. Rev. Anthropol.* 698.

⁷⁸⁶ Gail Landsman, *Reconstructing Motherhood and Disability in the Age of Perfect Babies* (New-York: Routledge, 2009).

⁷⁸⁷ See for instance Gregor Wolbring, "Science and Technology and the Triple D (Disease, Disability, Defect)" in William Sims Bainbridge, ed, *Converging Technologies for Improving Human Performance: Nanotechnology, Biotechnology, Information Technology and Cognitive Science* (Berlin: Springer Science & Business Media, 2013) 232-238.

professionals, who explained in interviews with Scott et al. that as genetic technology advances, more conditions will eventually become regarded as serious.⁷⁸⁸

The Subjective Views and Interests of Medical Professionals

Medical professionals could act as gatekeepers and advise prospective parents to forgo genetic diagnosis for milder conditions.⁷⁸⁹ Armed with the corpus of medical knowledge, clinicians might only consider genetic interventions where a condition has demonstrable and considerable health impacts on the future child. In this ideal situation, clinicians would provide advice and educate prospective parents that certain conditions do not affect the child's health in a significant manner, and hence are not quite serious. Clinicians could also attempt to dissuade prospective parents from screening conditions that in their medical opinion are not sufficiently serious.

Yet, the question of which conditions are serious and which are not shows to be subjective even in the eyes of medical professionals themselves. A cross-national survey of 1,481 clinicians found major discrepancies in what serious conditions mean in the clinical context of genetic diagnosis. This quantitative study has found a significant overlap between the categories of serious and non-serious conditions. 46% of the 400 conditions that were listed as "serious" by some physicians were listed as "not serious" by others. Furthermore, a relatively small, but still notable percentage of physicians ranked conditions such as intersex, webbed hands, cleft lip, and clubfoot as serious.⁷⁹⁰

⁷⁸⁸ Scott et al. supra note 543.

⁷⁸⁹ For more about the gatekeeping in France and the UK see Jeanne Snelling & Collin Gavaghan, "PGD Past, Present and Future: is the HFE Act 1990 now 'Fit for Purpose'?" in Horsey, K ed. *Revisiting the Regulation of Human Fertilisation and Embryology* (Oxford: Taylor & Francis, 2015) 89-90; See also Marie Gaille & Géraldine Viot supra note 308.

⁷⁹⁰ Wertz and Knoppers Supra note 79 at 29.

A qualitative study by Scott et al. indicates that not only genetic diagnosis clinicians deeply disagree about which conditions should be regarded as serious, but also about the very basic method of how they assess whether a particular condition is serious or not.⁷⁹¹ One account from a fertility physician is particularly revelatory on how he grapples in practice with the regulatory notion of seriousness. He says ‘what I feel is serious, minor, is a very subjective issue especially to parents’. He further adds: “Maybe for a parent having a child with six fingers is minor. That’s the only thing I can think of myself. Anything beyond that, any handicap in a child, I would not consider not serious. So, we have to – it’s a very personal opinion as to – I mean I can’t off hand think of any condition which should not be tested because it’s not serious.”⁷⁹²

The obstetricians-gynecologists, Azria and Grangé opine that despite the ABM’s seeming regulatory control, the judgment of what is regarded as serious is primarily left to the subjective discretion of clinicians. Many clinicians hold the view that a child with nearly any disability should be avoided.⁷⁹³ Former clinical geneticist Jacques Testart comments that the French law’s requirement of seriousness is so eminently vague and subjective that a case could be made for virtually every disability, major or very minor to be classified as a serious condition.⁷⁹⁴

Physicians’ financial interest in satisfying market demands may pull them in the opposite direction of offering such services.⁷⁹⁵ Treating clinicians stand to financially gain by having more permissive views on which conditions should be screenable. Clinical geneticists and fertility physicians who view the legal notion

⁷⁹¹ Supra note 543 at 352-355.

⁷⁹² Scott supra note 79 at 330.

⁷⁹³ Azria, E & G Grangé, supra note 53.

⁷⁹⁴ Jacques Testart, “Bioéthique et Embryons in Vitro : Diagnostic Pré-Implantatoire, La Face Cachée D’un L’eugénisme démocratique?” Genethique (05 Mars 2018) online : <http://www.genethique.org/fr/bioethique-et-embryons-vitro-diagnostic-pre-implantatoire-la-face-cachee-dun-leugenisme-democratique#.W1OF7LCheUk>

⁷⁹⁵ For more about the financial interest of physicians in adopting a more permissive stance to genetic diagnosis, see Michelle Bayefsky & Bruce Jennings, *Regulating Preimplantation Genetic Diagnosis in the United States: The Limits of Unlimited Selection* (New York: Palgrave Macmillan, 2015) 78-81.

of serious in a restrictive manner stand to lose potential revenues to other clinics who would be willing to take an approach that is more permissive. Physicians, therefore, have a strong incentive to adopt a permissive attitude that considers parental preferences with a view to accommodate it.⁷⁹⁶ Legal academic Denis Barthiau argues that despite the fact the French law imposes on physicians a gatekeeping duty to prevent eugenic practices,⁷⁹⁷ physicians are not truly concerned by such considerations in their practice. Instead, physicians prefer not to act as gatekeepers, but as facilitators, working together with the prospective parents to accommodate their views on which conditions they view as serious.⁷⁹⁸ The combination of lax legal limits and the regulatees' expansive views of the vague seriousness standard enables extending screening into milder conditions.

VI) Review of Illustrative Case Studies that Demonstrate Screening against Mild Conditions

I will examine three illustrative cases that demonstrate the great extent to which the elusive notion of seriousness has been extended to include conditions that are arguably not serious. These three illustrative cases are genetic diagnosis for webbed hands, intersex and the autism spectrum. For all of these cases, the effects of these conditions on the people's overall health are rather minor and can be well managed. Despite certain medical and socially created challenges, people with these bodily and neurological variations live healthy, long lives. I will show that even in cases when there is a weak medical justification to perform genetic diagnosis against these conditions, regulators have nonetheless approved it. These case studies further highlight how the complex interplay between technological advances, rising expectations and

⁷⁹⁶ Wertz notes that the physicians did however mostly agree that prospective parents should make the decision which conditions they view as "serious" entirely by themselves. These findings that physicians believe they should defer decisions about the seriousness of conditions to prospective parents' cast some doubts that physicians in fact act as gatekeepers. See Dorothy C Wertz, "Ethics Watch: Did Eugenics Ever Die?" (2002) 3 :6 *Nature Reviews Genetics* 408.

⁷⁹⁷ See Article L.2131-4 and Article 2131-10 du Code de la Santé Publique.

⁷⁹⁸ Denis Berthiau *supra* note 640.

medicalization⁷⁹⁹ puts pressure on the fluid notion of seriousness to encompass conditions that would previously be regarded as non-serious.

Intersex – The Medicalization of Non-Binary Bodies

The case of genetic diagnosis against intersex illustrates screening against a condition that is regarded as an abnormality of sexual characteristics, despite lacking any significant impacts on the child's health. As explained earlier, to be classified as serious, a condition needs to meet a bar of substantial impacts on the child's life and health. Such a case about substantial medical impacts could barely be made for intersex. Intersex is an umbrella term,⁸⁰⁰ which refers to a number of indications including Congenital Adrenal Hypoplasia, 5-Alpha Reductase Deficiency and Klinefelter syndrome. These intersex indications were approved by the HFEA and ABM.⁸⁰¹ The lifespan of people with intersex is not shortened and is the same as the general population.⁸⁰² However, neither lifespan is affected by such conditions, nor there are no significant health impacts or comorbidities.⁸⁰³ In certain intersex indications, individuals with testosterone imbalance can opt for hormone replacement therapy so their elevated risk to develop osteoporosis is reduced.⁸⁰⁴ The key "medical deficiency" with intersex and the hormonal imbalance is reduced fertility rates. The reduced fertility rates in certain intersex indications can widely vary from complete infertility to mild,

⁷⁹⁹ Sociologist Pierre Bourdieu has predicted that a medicalized discourse about genetic interventions would be a guise for the emergence of market eugenics. The façade of medical choice would essentially give proto-eugenic practices the legitimacy that medical institutions enjoy with the public. Pierre Bourdieu *supra* note 309.

⁸⁰⁰ Vernon A. Rosario, "'Is It a Boy or a Girl?' Introduction to Special Issue on Intersex" (2006) 10:2 J of Gay & Lesbian Psychotherapy 1.

⁸⁰¹ See ABM, HFEA *supra* note 465.

⁸⁰² Ieuan A Hughes & Asma Deeb, "Androgen Resistance" (2006) 20:4 Best Pract. Res. Clin. Endocrinol. Metab. 577–98.

⁸⁰³ See Garry L Warne et al., "A Long-Term Outcome Study of Intersex Conditions" (2005) 18:6 J Pediatric Endocrinology & Metabolism 555; Amy B Wisniewski, et al., "Complete Androgen Insensitivity Syndrome: Long-Term Medical, Surgical, and Psychosexual Outcome" (2000) 85:8 J Clinical Endocrinology & Metabolism 2664.

One particular exception to the general good health of people with intersex is the salt-wasting type of Congenital Adrenal Hypoplasia, which increases the risk of dehydration. I will not be discussing this variant in this short review.

⁸⁰⁴ Garry L Warne, Sonia Grover & Jeffrey D Zajac, "Hormonal Therapies for Individuals with Intersex Conditions" (2005) 4:1 Mol Diag Ther 19.

treatable fertility.⁸⁰⁵ In addition, advancements in microsurgical techniques and artificial reproductive technologies have greatly improved fertility rates amongst patients. These techniques may enable patients with intersex to conceive.⁸⁰⁶ The fact that intersex individuals' live healthy lives with a lifespan and a health profile comparable to the general population cast profound doubt on the viewpoint that intersex should be classified as "serious".

Medicalizing "Deviant" and "Abnormal" Non-Binary Sexual Characteristics

When concrete medical justification cannot be mustered, regulatory decisions to screen against intersex could be based on medicalizing views on bodies that are not deemed as sufficiently masculine or feminine. The HFEA 2014 decision to screen against intersex named seemingly medical symptoms such as enlarged female genitalia (Clitoromegaly), enlarged breast in men (Gynecomastia) or small male genitalia. (Microphallus)⁸⁰⁷ On the face of things, medical professionals could see symptoms such as Microphallus and Gynecomastia through the prism of medicine as abnormalities in the development of sexual characteristics. However, geneticist Jeff Nisker argues the seemingly medical prism conceals deep value judgments about intersex as deviating from stereotypical sex binary norms.⁸⁰⁸ Nisker argues that the view that intersex is a serious medical abnormality has much to do with an intolerant social climate and very little to do with medicine. Once one goes beyond the medicalized viewpoint, one can see a rather poor medical argumentation and a much stronger social motivation to avert children with traits deemed undesirable.⁸⁰⁹

⁸⁰⁵ Yvonne Lundberg Giwerzman et al., "An Androgen Receptor Gene Mutation (E653K) in a Family with Congenital Adrenal Hyperplasia due to Steroid 21-Hydroxylase Deficiency as well as in Partial Androgen Insensitivity" (2002) 87:6 J. Clin. Endocrinol. Metab. 2623–8. Zuccarello et al., "Detailed Functional Studies on Androgen Receptor Mild Mutations Demonstrate Their Association with Male Infertility" (2008) 68:4 Clin. Endocrinol. 580–8.

⁸⁰⁶ Ranjith Ramasamy et al. supra note 107. See also Aksglaede, L. & A Juul, "Therapy of Endocrine Disease: Testicular Function and Fertility in Men with Klinefelter Syndrome: A Review" (2013) 168:4 Eur J Endocrinology 67.

⁸⁰⁷ HFEA Licensing Committee, "Application for Androgene Insensitivity Syndrome" (London: HFEA, 2014).

⁸⁰⁸ Jeff Nisker, "Informed Choice and PGD to Prevent 'Intersex Conditions'" (2013) 13:10 Am J Bioethics 47.

⁸⁰⁹ *Ibid.*

Choosing to frame intersex as a medical disorder stems from a viewpoint that sexual characteristics variations are abnormalities.⁸¹⁰ Davis argues that discriminatory views drive turning body variations such as intersex into a mere medical disorder. In turn, the medicalizing of sexual development further promotes a view that intersex is a body abnormality to be eradicated with genetic and biomedical techniques. The medicalizing views ignore the gender identity and cultural affiliation of intersex people and the attempt to extinguish a culture that is frequently ignored and marginalized.⁸¹¹ According to Behrmann and Ravitsky, screening against intersex runs contrary to attempts of LGBTQI advocacy and civil rights groups to combat discriminatory attitudes and promote the inclusion of diverse gender identities.⁸¹² Similarly, a Council of Europe report on Intersex and Human Rights contends that screening against intersex reinforces discriminatory views against people who are non-gender binary.⁸¹³ The Council of Europe report regards genetic diagnosis against intersex as both a form of genetic discrimination (prohibited by Article 12 of the Oviedo Convention) and as a selection against non-serious disease, akin to social sex selection (prohibited by Article 14).⁸¹⁴

⁸¹⁰ For more about the intersexed body as being deviant from the acceptable notion of bodily normalcy see Sharon E. Preves, “Sexing the intersexed: An Analysis of Sociocultural Responses to Intersexuality” (2002) 27:2 Signs: J Women in Culture & Soc’y 523. See also Georgiann Davis, *Contesting Intersex: The Dubious Diagnosis* (New- York: NYU Press, 2015).

⁸¹¹ Georgiann Davis, “The Social Costs of Preempting Intersex Traits” (2013) 13:10 Am J Bioethics, 51.

⁸¹² Jason Behrmann & Vardit Ravitsky, “Queer Liberation, Not Elimination: Why Selecting against Intersex is Not ‘Straight’ Forward” (2013) 13:10 Am J Bioethics 39.

⁸¹³ The report on Intersex and Human Rights is grounded in a perspective repeatedly voiced by the Council of Europe and UNESCO that explicitly stipulates that people with a disability have an equal right to life. Following from that premise, the Council of Europe and UNESCO documents have opined that the systematic application of selective reproductive practices could amount to discriminatory practices against people with disabilities and body variations.

See UNESCO, Declaration on the Responsibilities of the Present Generations towards Future Generations (1997), Article 6 (preservation of the human genome in its diversity). See also International Bioethics of UNESCO. “Third Session”. Volume 1 DRG.96/WS/8 (1996), 33-35. See also Council of Europe Steering Committee on Bioethics supra note 735 at 29-30.

⁸¹⁴ The Council of Europe warns that the attempt to genetically prevent from existence the birth of children with intersex runs contrary to their equal right to life. See Council of Europe, “Human Rights and Intersex People”, 2015, at 30 online: <https://wcd.coe.int/com.instranet.InstraServlet?command=com.instranet.CmdBlobGet&InstranetImage=2933521&SecM ode=1&DocId=2367288&Usage=2>

The case of intersex illustrates how viewing sexually diverse characteristics as medical abnormalities are translated in the regulatory context into determinations that these conditions are serious. The seriousness standard allows incorporating the medicalized views on variations in sexual characteristics while concealing the social motivation of avoiding the birth of a child with less distinct gender characteristics.⁸¹⁵ The broad and malleable seriousness standard is particularly prone to medicalization, owing to the combination of being implicitly based on social views on normalcy while lacking formal limits that would weed out attempts to medicalize body variations.⁸¹⁶ The regulators' inability to set a minimum bar of seriousness has enabled licensing screening of intersex and the medicalization of non sexually binary bodies. Ironically, the seriousness standard that was meant to prevent the approval of conditions with weak medical rationale and strong social motivation has come to do exactly that with intersex. The case of genetic diagnosis against intersex illustrates how behind the veil, one can find persistent social stigmas, which label non-binary sexual characteristics as deviant and abnormal.

Webbed Fingers - Screening Against the Impairment or the Disability?

Genetic diagnosis against webbed fingers (syndactyly), presents an interesting case because the condition does not significantly impact the child's health and it is fully treatable. In 2009, the HFEA approved

⁸¹⁵ It is interesting to note the CCNE has written an opinion solely dedicated to the medicalization of sexuality in the context of Viagra, and yet these same insights of the medicalization of sexuality are not equally applied by French authorities to genetic diagnosis for intersex. See CCNE, Opinion no. 62, The Medicalization of Sexuality: The Case of Viagra. Reply to the Secretary of State for Health (Paris: CCNE 1999). online: <http://www.ccne-ethique.fr/sites/default/files/publications/avis062en.pdf>

⁸¹⁶ A report by the European Parliament Science and Technology Committee specifically addressed the inability of the seriousness standard to set an effective limit that would curbs medicalization, stating that:

A remarkable feature of current regulative dynamics is the persistent pressure on widening the indications for PGD, leading to a further medicalization of society. Current laws even seem to trigger this tendency; for every formulation of a limit remains arbitrary to some extent, challenging groups to debate it. ... So whereas the law intends to strictly limit the use of PGD to the prevention of severe diseases, the unintended effect seems to be a shift towards a further enhancement that is hardly indistinguishable from a process of medicalisation.

European Union, European Parliament, Directorate for Internal Policies Policy Department: "Human Enhancement" (Brussels: European Parliament, 2009) 80.

genetic diagnosis for webbed hands.⁸¹⁷ In webbed hands, the child's fingers are wrapped together in extra skin. In cases where the bones are not fused, the fingers themselves are intact, but the child cannot move them independently because of the extra skin.⁸¹⁸ Hand surgeon Carl Wagerich writes that there is a wide agreement in the clinical literature that webbed fingers is a condition that is purely cosmetic.⁸¹⁹ Webbed hands can be treated with a straightforward surgery to remove the webbed skin that confines the fingers (and separate the fused bones if needed). The result of the surgery is fully functioning fingers with the restoration of the cosmetic appearance of the hands.⁸²⁰ The procedure to remove the extra skin is routinely performed at a very young age, when the child is about 2 to 4 years, before they begin school.⁸²¹ Webbed hands satisfy neither the requirement that the condition is serious nor that it is untreatable. Arguments that webbed hands clearly satisfy the regulatory requirements are at best weak because of the condition's minor impacts and because it is so well treated.

⁸¹⁷ HFEA Licensing Committee, "Clubbed Hands and Feet Application" (London: HFEA, 2009).

The ABM did not approve genetic diagnosis for webbed fingers. The ABM did however approve genetic diagnosis for cleft hands and feet, which could manifest in missing or malformed of the fingers or toes. Notable people with cleft hands are world chess champion Michal Tal and Pianist Lee-Hee Ha.

⁸¹⁸ David B. Lumenta et al., "Long-term Outcomes of Web Creep, Scar Quality, and Function after Simple Syndactyly Surgical Treatment" (2010) 35:8 J Hand Surgery 1323.

⁸¹⁹ Carl R. Wagerich, "Congenital Deformities" in Banks, A S. *McGlamry's Comprehensive Textbook of Foot and Ankle Surgery* (Philadelphia: Lippincott Williams & Wilkins, 2001) 1438.

⁸²⁰ Khiem D Dao et al., "Surgical Treatment of Congenital Syndactyly of the Hand" (2004) 12:1 JAAOS-J the Am Academy of Orthopaedic Surgeons 39.

⁸²¹ Mininder Kocher & Michael B. Millis, *Operative Techniques: Pediatric Orthopaedic Surgery* (E-BOOK: Elsevier Health Sciences, 2011) 108.

Image: The Results of the Corrective Surgery for Webbed Hands (Syndactyly)⁸²²



Wertz and Knoppers et al. examine the normative question of whether regulators should allow screening not based on the actual degree of physical impairment, but based on society's disabling views that regard certain bodily variations are undesirable. The authors examine the case of hand abnormalities, which in their view can be regarded as serious if one considers the ostracism that extra fingers or webbed hands may cause in social interactions.⁸²³ The HFEA decision to license this type of screening similarly argues that webbed hands should be regarded as a serious condition because of the social ostracism caused by living with

⁸²² The picture shows complete, complex syndactyly, before (left) and after (middle and right) surgery

The picture is taken from the Children's Hospital of Pennsylvania's online: <https://www.chop.edu/conditions-diseases/syndactyly>

⁸²³ Wertz and Knoppers further argue that: "social ostracism could make a hand abnormality serious, and difficulty finding a mate could make it a genetic lethal disorder." Wertz and Knoppers's comment begs three questions. First, why do the authors contend that not finding a mate should be regarded as lethal? Is it the case a person is effectively regarded as if they were dead if she does not find a mate or procreate? Second, how supportable is the authors' assumption that people with webbed hands would not find a mate? Third, is it a truly accurate, supportable and sensible position – to base decisions regarding a condition's seriousness on subjective perceptions of the future child's degree of attractiveness?

See Wertz and Knoppers *supra* note 79 at 34.

this “deformity”.⁸²⁴ In the license, the HFEA’s key argument was that the psychological implications of being born with “lobster claws” are profound and cannot be overlooked. The HFEA Licensing Committee argued that the deformity has a number of serious effects on psychological and social functioning. The HFEA Licensing Committee further argued that it has been well demonstrated that persons with physical deformities are at a greater risk for anxiety, depression, low self-esteem and social withdrawal.⁸²⁵

According to this new line of reasoning, a condition is no longer serious because of the physical impairment,⁸²⁶ but because society’s disablement and intolerance are supposedly so devastating that lives with such body variations warrant their prevention. The HFEA does not argue that the gene encoding finger formation disrupts the brain’s chemical balance and leads to anxiety and depression. The anxiety and depression, if they do occur, are not the result of a psychiatric disorder that people with webbed hands are born with. Depression and anxiety experienced by people with disabilities are rather a symptom of an unaccepting society.⁸²⁷ Instead of focusing on the cause of this malaise - society’s intolerance, the regulators choose to focus on offering birth prevention of people whose skin, complexion, sexual organs, height and other cosmetic traits are deemed unusual, abnormal or an overall failure to meet society’s expectations. By determining that “serious” cosmetic traits warrant life prevention because it would cause social ostracism, regulators inadvertently reward disabling views. A seeming solution to society’s intolerance towards “abnormal” cosmetic traits is using genetic technologies to avert the birth of such children. The case of

⁸²⁴ HFEA Licensing Committee, “Clubbed Hands and Feet Application” (London: HFEA, 2009).

⁸²⁵ *Ibid.*

⁸²⁶ For more about the distinction between the impairment and social disablement see Mike Oliver, “Defining Impairment and Disability: Issues at Stake” in Colin Barnes and Geof Mercer eds. *Exploring the Divide: Illness and Disability* (Leeds: The Disability Press, 1996) 39.

⁸²⁷ Tom Shakespeare, “The Social Model of Disability” in Davis, L. J. *The Disability Studies Reader* (Oxford: Routledge, 2013), 215-217. See more broadly, Patrick Fougeyrollas, Line Beauregard, “Disability an Interactive Person-Environment Social Creation” in Gary L. Albrecht, Kathrine. D. Seelman & Michael Bury, *Handbook of Disability Studies* (Thousand Oakes: SAGE Publications, 2001) 171-194.

genetic diagnosis for webbed hands reveals that behind a weak medical rationale one can find a strong societal motivation of preventing seemingly “unsightly” serious cosmetic conditions.

The Autism Spectrum Disorder - The Regulation of “Serious” Behavioural Patterns

One of the most illustrative cases of screening for behavioural traits⁸²⁸ is that of genetic diagnosis against the autism spectrum disorder.⁸²⁹ Regulators already approved screening against PKU (treatable with low protein diet) and Fragile X, a condition in which a considerable amount of children present symptoms on the autistic spectrum, but otherwise have health and a lifespan comparable to the average population. In addition, there is at least one recorded case of the HFEA licensing sex selection against male embryos to avoid autism.⁸³⁰ In 2014, the HFEA licensing committee formally rejected a blanket license for sex selection for autism⁸³¹ because selection against male embryos is neither determinative nor effective enough method to genetically avert the birth of children on the autism spectrum.⁸³² Nevertheless, the HFEA licensing

⁸²⁸ The license application for the autism spectrum disorder is a major turn in policy for the HFEA. Only in 2006, the HFEA has reiterated it would not allow for genetic diagnosis for behavioural traits due to concerns such interventions can seek to normalize human behaviour. See HFEA, “Authority Decision on PGD Policy”, 10 May 2006 (London: HFEA, 2006).

⁸²⁹ Note that the regulators’ use of the word disorder together with the autistic spectrum denotes both negative attitudes and a medicalized viewpoint. For more about the negative connotations terminology of disorder together with the autistic spectrum see Baglieri, S. *Disability Studies and the Inclusive Classroom: Critical Practices for Embracing Diversity in Education* (New-York: Taylor & Francis, 2017) 19.

⁸³⁰ David J Amor & Carolyn Cameron supra note 714.

Note that the HFEA has not retained the license for sex selection for autism on its website.

⁸³¹ The HFEA’s authority to license sex selection to avoid autism spectrum disorder owes to another legal change to the restriction of sex selection to medical purposes. The 2008 HFE Act Section 14 (4) 11 (b) has reduced the threshold related to the sex selection provisions from the point of permitting screening only sex-linked chromosomal disease (such as the X-linked Haemophilia for boys) to a variety of genetic conditions that has a different distribution amongst the sexes. See HFEA Statutory Approvals Committee, “Centre 004 (Centre for Reproductive and Genetic Health (CRGJ)) – PGD Application for Autism Spectrum Disorder” (London: HFEA, 2014).

Baroness Deech, the former chair of the HFEA points out that the boundaries between medical and social sex selection will not always be clear-cut. See Deech and Smajdor supra note 726 at 65.

⁸³² The HFEA decision cited studies that the autism spectrum disorder is not intrinsically linked to the male Y chromosome. While the ratio between males and females with the autistic spectrum is 4:1, this still does not mean that selection of a female embryo would guarantee that girls would be free from autism. In addition, genes have not yet conclusively been linked to the autistic spectrum in a manner that makes targeted genetic diagnosis available at the moment.

committee determined that in principle, the autism spectrum disorder is a cluster of serious conditions.⁸³³ The HFEA decision paves the way for screening against the autism spectrum once genes are identified.⁸³⁴

Without directly ruling on its status as serious, the ABM decided to fund research specifically intended to pave the way for genetic diagnosis of the autism spectrum disorder by finding the presently unknown genetic markers.⁸³⁵ The ABM's 2014 funded research project document asserts that genes linked to autism, regardless if they lead to an intellectual disability or not, are a cause of a “major public health problem”.⁸³⁶ The regulatory decision to allocate public money to find the potential genetic causes of this “major public health problem”⁸³⁷ strongly implies that the prevention of the potential births of individuals on the autism spectrum could be a desirable route.

Genomic discoveries of genes linked to the autism spectrum could pave the way for a regulatory classification of this group of conditions as serious. Israël Nisand, a gynecologist and a former member of the CCNE, predicts that once genomic discoveries pave the way for genetic diagnosis for the autism spectrum, many parents will want to access the technology to ensure their child is autism free. Many

⁸³³ HFEA Licensing Committee Meeting, Centre 0078– PGD for Autism Spectrum Disorder, 07/03/2013, (London: HFEA, 2013) point 3.

⁸³⁴ Since the HFEA decision in 2014, studies have found low penetrance genes correlated with autism. See Consortium, Autism Spectrum Disorders Working Group of the Psychiatric Genomics et al., “Meta-analysis of GWAS of over 16,000 Individuals with Autism Spectrum Disorder Highlights a Novel Locus at 10q24. 32 and A Significant Overlap with Schizophrenia” (2017) 8 *Molecular Autism* 1.

⁸³⁵ Interestingly, the HFEA explicitly (and the ABM implicitly) argued that Autism Spectrum Disorder is a serious set of conditions. The reason for not formally classifying the Autism Spectrum Disorder as serious is more to do at this point with the lack of technical feasibility of such genetic diagnosis (due to lack of associated genes) rather than substantive reasons that the autism spectrum is not serious.

Note the interplay between increasing identification of new genetic markers and regulatory approval of genetic interventions. I have shown in chapter 2 that genomic sciences are increasingly moving beyond the study of congenital disorders to genes linked to disease susceptibility, behavioural traits and even cosmetic traits. Will this relation between the advances in genomic sciences and eventually regulatory approval of newly available genetic intervention continue?

⁸³⁶ ABM, Résumés des Projets de Recherche Financés dans le Cadre de l'appel d'offres 2014 “ AMP, Diagnostic Préimplantatoire et Diagnostic Génétique ” (2014) Agence de la Biomédecine, online : https://www.agencebiomedecine.fr/IMG/pdf/resume_projets_finances_aor_amp2014.pdf

⁸³⁷ For a more critical perspective on the idea that the autism spectrum disorder is a public health problem, transmitted through genetic means see Maja Holmer Nadesan, “Autism and Genetics: Profit, Risk, and Bare Life” in Joyce Davidson and Michael Orsini eds, *Worlds of Autism: Across the Spectrum of Neurological Difference* (University of Minnesota Press, 2013) 117.

prospective parents view the autism spectrum disorder as a “life not worth of living”. Regulators will have a hard time ignoring prospective parents who wish to avert the birth of such children and are eventually likely to regard the autistic spectrum as a serious condition.⁸³⁸ Nisand’s commentary illustrates how new discoveries linking bodily and behavioural variations to biology can promote a new viewpoint that the lives of children with such variations are better off prevented.

The Autism Spectrum: Is it really a Set of Serious Medical Conditions?

The regulatory viewpoint is not that the autism spectrum is linked to profound medical symptoms, but that autistic behaviour patterns themselves warrant classification as “serious”. The HFEA decision regarded the autism spectrum as serious, regardless of the existence of an intellectual disability or the child’s level of functioning. The HFEA’s decision specifically regarded the high functioning Asperger⁸³⁹ syndrome as serious because of difficulty in understanding the rules governing social interactions.⁸⁴⁰ With the autism spectrum, regulators are crossing into a new territory of conditions that have no impact on lifespan or physical health. Rather, behavioural patterns like autism, which may affect future children’s social functioning warrant their classification as “serious”.⁸⁴¹

Even based on the regulatory logic, it is very questionable if the broad set of behaviours that fall on the autism spectrum could be all classified as serious conditions.⁸⁴² The HFEA decision classified the entire

⁸³⁸ Israël Nisand *supra* note 50.

⁸³⁹ Recent and extensive evidence reveals that Hans Asperger, the Austrian physician after whom the syndrome is named after was involved in the euthanasia of patients with intellectual disabilities. Asperger collaborated with Nazi authorities to diagnose and administer lethal injections to 800 children who were deemed by the law to be genetically incapable of social conformity or to have genetically determined psychological “defects.” See Simon Baron-Cohen et al., “Did Hans Asperger Actively Assist the Nazi Euthanasia Program?” (2018) 9 *Molecular Autism* 28.

⁸⁴⁰ HFEA *supra* note 833.

⁸⁴¹ *Ibid.*

⁸⁴² Walsh et al, discuss the ethical issues arising from screening against the autistic spectrum, which is very heterogeneous and has variability in its phenotypic expression. The authors raise questions regarding whether the autism spectrum is a disability or difference and is screening against embryos with the autism spectrum biomarkers is warranted. See Pat Walsh et al., “In Search of Biomarkers for Autism: Scientific, Social and Ethical Challenges” (2011) 12:10 *Nature Reviews Neurosci* 603-612.

spectrum as serious, with no regard that even on this broad spectrum, the alleged serious deficits in social communication greatly varies.⁸⁴³ Individuals on the autism spectrum may benefit from therapeutic approaches such as Early and Intensive Behavioural Intervention. Studies on Early and Intensive Behavioural Intervention show children on the autism spectrum reach developmental milestones and can develop better social communication skills.⁸⁴⁴ Accommodations, modifications and the creation of an inclusive environment in schools help people on the autism spectrum realize their potential.⁸⁴⁵ The very existence of treatment options and accommodations cast further doubts on the regulatory classification of the wide range of behavioural variations on the autism spectrum as being serious. With the right conditions, many people on the autistic spectrum can flourish and even excel. The decision to classify the broad autism spectrum as serious overly emphasizes the diagnosis and neglects how people on the spectrum can cope, adapt and learn to form meaningful, satisfying relations.

The regulatory stance ignores the viewpoint that the autism spectrum is not a disorder but a part of the diverse range of human behaviours. The neurodiversity movement views the autism spectrum, not as a disease, disability, or disorder, but rather a natural variation of human behaviour.⁸⁴⁶ The neurodiversity does not accept the view that autism is a disease to be treated.⁸⁴⁷ As one teenager with autism explained, “We don’t have a disease ... So we can’t be ‘cured.’ This is just the way we are.”⁸⁴⁸

⁸⁴³ Jamie L Anderson & Simon Cushing, *The Philosophy of Autism* (Plymouth: Rowman & Littlefield Publishers, 2012) 214-215.

⁸⁴⁴ Lars Klintwall, Sigmund Eldevik & Svein Eikeseth, “Narrowing the Gap: Effects of Intervention on Developmental Trajectories in Autism” (2015) 19:1 *Autism* 53; Sigmund Eldevik et al., “Meta-analysis of Early Intensive Behavioral Intervention for Children with Autism” (2009) 38:3 *J Clinical Child & Adolescent Psychol* 43; Brian Reicho, et al., “Early Intensive Behavioral Intervention (EIBI) For Young Children with Autism Spectrum Disorders (ASD)” (2012) 5 *Cochrane Database of Systematic Reviews* 10.

⁸⁴⁵ See for instance, Kimberly Maich & Carmen Hall, *Autism Spectrum Disorder in the Ontario Context: An Introduction*. (Toronto: Canadian Scholars’ Press, 2016) 248-251.

⁸⁴⁶ See Katherine Runswick-Cole, “‘Us’ and ‘them’: The Limits and Possibilities of A ‘Politics of Neurodiversity’ in Neoliberal Times” (2014) 29:7 *Disability & Soc’y* 1117.

⁸⁴⁷ Thomas Armstrong, *Neurodiversity: Discovering the Extraordinary Gifts of Autism, ADHD, Dyslexia, and Other Brain Differences* (Boston: Da Capo Press, 2013).

⁸⁴⁸ Simon Baron-Cohen, “Does Autism Need a Cure?” (2009) 373: 9675 *the Lancet* 1595.

People on the autism spectrum can be successful if provided with the right opportunities. Further, people with autism can be gifted and creative. Simon Baron-Cohen, a Cambridge psychiatrist and a leading authority on autism suggests that Isaac Newton, Henry Cavendish and Albert Einstein exhibited behaviours that fall on the autism spectrum.⁸⁴⁹ People on the autism spectrum self-report happiness and satisfaction with life.⁸⁵⁰ Arguments about diminished human flourishing fail to appreciate the diversity of human thinking and eventually may be employed to eliminate this intellectual diversity.

The Medicalization of Intellectual Diversity

A decision to permit genetic diagnosis for the autism spectrum would go against the view it is a neurological diversity and instead treats it as a medical disorder. The classification of the autism spectrum as a medical disorder suggests that a solution to this medical “problem” is enabling prospective parents to prevent the birth of children with this disorder.⁸⁵¹ However, such medical categorization ought to be questioned. Karpin and O'Connell criticize the regulatory decision in Australia to permit screening sex selection to prevent the autism spectrum as stigmatizing autistic behavioural diversity as a neurological disorder.⁸⁵² An editorial published at Harvard Law Review writes that such medicalization: “not only do such labels reflect regulators’ social attitudes, they also ossify such social attitudes under the guise of medicine, ethics, and law, often in the midst of social movements denying the very applicability of these labels.”⁸⁵³ Instead of giving due respect to the diversity of human traits, regulators frame those they view deviating from the elusive notion of the normal as serious.

⁸⁴⁹ Simon Baron-Cohen et al., 'The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Males and Females, Scientists and Mathematicians' (2001) 31:1 J Autism & Developmental Disorders 5-17.

⁸⁵⁰ See Eva Billstedt, Carina Gillberg, & Christopher Gillberg, “Aspects of Quality of Life in Adults Diagnosed with Autism in Childhood: A Population-Based Study” (2011) 15:1 Autism 7.

⁸⁵¹ See for instance Kristin Bumiller, “The Geneticization of Autism: From New Reproductive Technologies to the Conception of Genetic Normalcy” (2009) 34:4 Signs: J Women in Culture & Soc’y 875.

⁸⁵² Isabel Karpin & Karen O'Connell, “Stigmatising the 'Normal': The Legal Regulation of Behaviour as a Disability” (2015) 38 UNSWLJ 1467.

⁸⁵³ Editorial, “Regulating Preimplantation Genetic Diagnosis: The Pathologization Problem” (2005) 118:8 Harv L Rev, 2770.

Arbitrariness in Deciding Which Human Behaviours are “Serious”

With decisions concerning the autism spectrum, regulators are stepping into an uncharted, ethically contentious territory of determining which human behaviours are normal, which deviate from the norm they and which warrant prevention through novel biotechnological means. Attempts to determine which human behaviours belong in the “serious conditions” group would inescapably invite some prevalent social stigmas, prejudices and discriminatory viewpoints into the decision-making process. Regulators’ decisions already inadvertently reflect negative value judgment of non-behavioural, physical conditions, despite having centuries-old science and concrete medical evaluation methods to rely upon. Yet, the task of assessing a conditions’ seriousness becomes even more challenging when attempting to determine which human behaviours should be regarded as “serious”. Not only that behavioural sciences are relatively newer fields of study with many key questions still open, but classifications of human behaviours as either normal or abnormal largely depend on social context and subjective value judgments.⁸⁵⁴ Labelling behavioural traits as serious could continue the pattern of screening against traits deemed undesirable in a potentially more problematic way. For example, a child with allegedly serious behavioural traits (such as the autism spectrum) would have a long, healthy life. The question, therefore, is for whom serious behavioural traits (such as the autism spectrum) are serious: for the child, for the parents or for society? The legal change pattern already shows increasing deselection of traits deemed by some as socially undesirable and economically burdensome. This pattern could be exacerbated by legally labelling behavioural traits as serious, further ossifying stigmas against marginalized, vulnerable groups. The practice of labelling human behaviours as deviant has a long history of abuse.⁸⁵⁵ For instance, early 20th-century eugenics sterilizations attempted to prevent passing on to progeny addictive tendencies, disobedience

⁸⁵⁴ Paige L Sweet & Claire Laurier Decoteau, “Contesting Normal: The DSM-5 and Psychiatric Subjectivation” (2018) 13:1 *BioSocieties* 103; Jaime Murphy, “Chapter 27 - The Flexible Psychological Concept of Normality” in Michel Tibayrenc & Francisco J Ayala, eds, *On Human Nature* (San Diego: Academic Press, 2017) 451.

⁸⁵⁵ See Michel Foucault, *Madness and Civilization: A History of Insanity in the Age of Reason* (New-York: Knopf Doubleday Publishing Group, 2013).

and sexual promiscuity.⁸⁵⁶ In the biotechnology era, the social construction of normalcy is likely to be influenced by the manner in which technology elevates the parental and societal expectations of the unborn.⁸⁵⁷ Genomic discoveries are not only increasingly identify new genes that have a role in human behaviour,⁸⁵⁸ but they open the door to pre-empt the birth of children with behavioural traits deemed undesirable.⁸⁵⁹ The seriousness standard is inapt to set limits precisely because it increasingly draws on the consumer public's perceptions of which traits are normal and which are abnormal. Existing regulatory tools are inadequate in handling this looming revolution of influencing newborn's behaviour before birth.

VII) Perfectionism and Its Price: Reflections on the Potential Outcomes of the Legal Change

The shift in the notion of seriousness from life-threatening to conditions viewed as sensory, behavioural and cosmetic abnormalities is likely to be welcomed by those who seek to give prospective parents greater choices in child genetics. Boyle and Savulescu argue that the HFEA's seriousness standard places unfair regulatory hurdles for prospective parents who have an interest in sparing their child from developing mild conditions. According to Boyle and Savulescu, the prevention of birth of children with mild conditions is surely not a step down the slope to eugenic practices.⁸⁶⁰ English clinician Alan Handyside advocates for the HFEA to take a more permissive approach and allow selecting even against mild conditions because the prospective parents know best which genetic traits would be a disservice to their future child.⁸⁶¹

⁸⁵⁶ Kevles supra note 2.

⁸⁵⁷ See for instance, Rob Deiches & Adil Ahmed, "Redefining Disease" (2007) *Colum U J Bioethics* 70-72.

⁸⁵⁸ See Wiebke Bleidorn, Christian Kandler & Avshalom Caspi, "The Behavioural Genetics of Personality Development in Adulthood—Classic, Contemporary, and Future Trends" (2014) 28:3 *Eur J Personality* 244; Tena Vukasović & Denis Bratko, "Heritability of Personality: A Meta-Analysis of Behavior Genetic Studies" (2015) 141:4 *Psychol Bull*, 769; Robert Plomin et al., "Top 10 Replicated Findings from Behavioral Genetics" (2016) 11:1 *Perspectives on Psychol Science* 3.

⁸⁵⁹ See Erik Parens, Audrey R. Chapman, & Nancy Press eds., *Wrestling with Behavioral Genetics: Science, Ethics, And Public Conversation* (Baltimore: John Hopkins University Press, 2006); Julian Savulescu et al., "Behavioural Genetics: Why Eugenic Selection Is Preferable to Enhancement" (2006) 23:2 *J Applied Phil* 157-171.

⁸⁶⁰ Robert J Boyle & Julian Savulescu supra note 81.

⁸⁶¹ Alan Handyside, "Let Parents Decide" (2010) 464:7291 *Nature* 980.

De Wert et al. similarly advocate for screening against serious cosmetic conditions because they can nevertheless profoundly affect the child's self-esteem, body image and cause them to feel sexually unattractive. Hence, the authors assert that prospective parents should be able to screen even in cases where the condition is clinically not serious, but rather cosmetically serious.⁸⁶²

Yet, behind the discourse of liberalization lies also the threat that determining "seriousness" based on the viewpoints of physicians and prospective parents' invites perfectionist and ableist attitudes to shape the law and practice. Studies already show that fertility physicians and prospective parents hold negative attitudes against the idea their child might develop a certain impairment.⁸⁶³ Scholars⁸⁶⁴ and international organizations such as the Council of Europe,⁸⁶⁵ WHO⁸⁶⁶ and UNESCO⁸⁶⁷ warned that genetic diagnosis against conditions deemed serious could be reinforcing the already prevalent negative attitudes against people with disabilities. Deselection against certain traits sends a message to society (and to other prospective parents) that children with certain impairments or characteristics are better off not born.⁸⁶⁸ A Council of

⁸⁶² Guido De Wert et al, "ESHRE Task Force on Ethics and Law: Preimplantation Genetic Diagnosis" (2014) 29:8 Hum Reprod, 1612.

The authors mention specific conditions they view as serious cosmetic disorders, which include Achondroplasia and Vitiligo.

⁸⁶³ See the review in Ian Basnett, "Health Care Professionals and Their Attitudes toward Decisions Affecting Disabled People" in Gary L Albrecht, Kathrine. D Seelman & Michael Bury, *Handbook of Disability Studies* (Thousand Oaks: SAGE Publications, 2001) 450.

⁸⁶⁴ Tim Stainton, "Missing the Forest for the Trees? A Disability Rights Take on Genetics Commentary on Stowe et al," (2007) 13:2 J Developmental Disabilities 91-92; Mary Crossley & Lois Shepherd, "Genes and Disability: Questions at the Crossroads" (2002) 30 Fla. St. UL Rev. XII; Alexandra Plows, *Debating Human Genetics: Contemporary Issues in Public Policy and Ethics* (New-York: Routledge, 2010) 152.

⁸⁶⁵ Council of Europe, Committee of Ministers Recommendation No. R (90) 13 of the Committee of Ministers to Member States on Prenatal Genetic Screening, Prenatal Genetic Diagnosis and Associated Genetic Counselling (Adopted by the Committee of Ministers on 21 June 1990 at the 442nd meeting of the Ministers' Deputies).

⁸⁶⁶ WHO, "Review of Ethical Issues in Medical Genetics" (Geneva: World Health Organisation, 2003) 10.

⁸⁶⁷ UNESCO, "Rapport du CIB sur le Diagnostic Génétique Préimplantatoire et Les Interventions Sur La Lign Ée Germinale" (2003), SHS/EST/02/CIB-9/2, online : [http : //www.unesco.org/](http://www.unesco.org/), 9,

⁸⁶⁸ The above argument is based on sociological observations of sociologists such as Margaret Mead and Erving Goffman. According to symbolic interactionism theory, prominent institutions (such as legal institutions) send an expressive message to the public on how to direct their lives and make fundamental choices. The public can redirect their behaviour according to these expressive messages because of their normative content and the perceived legitimacy of legal institutions. See Erving Goffman, *Stigma; Notes on the Management of Spoiled Identity* (Ann Arbor: University of Michigan, 1963).

Europe report further warned that if laws come to allow screening against milder conditions, the stigma that children with such traits are better not born would follow.⁸⁶⁹ A climate of genetic perfectionism could gradually emerge, leading some prospective parents to be less tolerant to even of some of the mildest conditions and body variations.⁸⁷⁰ A social climate of genetic perfectionism could weaken the liberal foundations of free choice in reproductive decisions, driving more prospective parents towards greater utilization of genetic interventions.⁸⁷¹ Prospective parents are shown to be influenced by social climates, prevalent attitudes and institutional norms that suggest certain children are better off not born.⁸⁷² With a growing list of ever milder bodily variations stigmatized and perceived as better off prevented, a new form of genetic perfectionism might be emerging. Genetic intervention laws were set to prevent it, but seem rather unable to prevent this looming genetic perfectionism.

Conclusion

This chapter examined the extensive changes to the rule prohibiting screening against non-serious conditions. The key legal objectives were to restrict genetic diagnosis only to conditions with profound medical impacts and avoid screening against traits deemed socially undesirable. The regulatory practice moved further away from these legislative goals over time. This legal change analysis shows a pattern of screening against increasingly milder conditions, including crossed-eyes, webbed fingers, mild albinism, partial hearing impairment and night blindness. In all of these conditions, lifespan is comparable to that of the general public and the degree of health impairment is minor. This review explained that a key reason for this legal change to the standard of seriousness is this construct's conceptual unclarity, subjectivity and overbroad scope. Over

⁸⁶⁹ See also Council of Europe 735 at 29-32.

⁸⁷⁰ Baroness Deech has written that: "Principally, there is a fear that modern genetics will create a society in which people are intolerant of anything less than perfection and in which the family becomes the focus of ensuring that that perfection is created in a new generation." See Ruth Deech, "Family Law and Genetics" (1998) 61:5 Modern L Rev 714.

⁸⁷¹ Council of Europe *supra* note 735.

⁸⁷² See Sonia M. Suter, "A Brave New World of Designer Babies?" (2007) 22:2 Berkeley Tech L J 936.

time, regulators moved away from interpreting the seriousness standard as meaning that the condition will be life-threatening to increasingly rely on prospective parents' subjective viewpoints. Yet, the elusive notion of a serious condition changes across social contexts and time. As technology opens new options for traits selection and elevates expectations, the legal notion of "serious" conditions is being transformed. Regulators' assessments of seriousness have shifted from solely focusing on medical considerations to consider social considerations such as the alleged harms in being born with traits labelled as cosmetically, sensory or anatomically deviating from the socially constructed notion of normalcy. As reproductive biotechnology leaps forward, are we moving towards a society that increasingly accepts and celebrates genetic differences, or eliminates them before birth?

Chapter Seven

Defying Natural Limits: Legal Change Concerning Inheritable Genetic Modification

A merit of good lawmaking is knowing where effective limits can be set and where it cannot. Heritable genetic modification governance raises a critical question about knowing and acknowledging the laws' limitations in setting effective boundaries to a technology that defies conventional ethical and medical distinctions between treating and enhancing human performance. As market applications are seen on the horizon, the French and UK governments are considering replacing their long-standing bans with regulations that would allow inheritable genetic modification for therapeutic purposes. Regulators and government entities have recently argued that the new regulations will ensure the novel ability to tinker with the code of life will not result in misuse, such as the creation of genetically enhanced children.⁸⁷³ It is, however, critically important to inquire if such purported legal lines between therapy and enhancement can actually be drawn using language that is imprecise and unclear.

This chapter argues that the regulation of inheritable genetic modification suffers from a number of problems that make it particularly prone to overextensive legal change. This chapter identifies and describes three particular ways in which the use of overbroad, unclear legal standards such as “serious conditions” and “therapeutic” purposes are likely to enable the very same legal change and eugenic risks legislatures seek to prevent. First, the use of genetic diagnosis’s unclear and overbroad regulatory requirements will import a number of line-drawing weaknesses to the more ethically contentious context of heritable genetic modification. In particular, such line-drawing weaknesses would enable the potential approval of hereditary genome editing of genes linked to mild and treatable conditions. Second, the seriousness standard’s unclear

⁸⁷³ Supra note 49 see als notes 72-75.

wording supports regulatory interpretations that allow editing in “protective genes”, which might lower disease susceptibility but also simultaneously enhance the future person’s immune, physiological or cognitive performance.⁸⁷⁴ Third, a legal gap about which genes would be inserted in the place of the deleted genes linked to serious conditions would effectively create a new loophole. This new loophole would enable prospective parents to opt for intervening on their future child’s genome in a way that is simultaneously therapeutic and enhancing. Moreover, even if lawmakers were to become aware of these two previously unflagged loopholes, they would encounter profound difficulties in closing them. Closing these two loopholes would essentially require devising a legal test to effectively distinguish between therapy and enhancement, a nearly insurmountable task. These two difficult to close loopholes would make it particularly difficult for regulators to accomplish the key legislative goal of preventing the misuse of germline engineering to create genetically enhanced humans and the associated medical, human rights and societal risks.

I) The Normative Considerations Behind the Ban on Inheritable Genetic Modification

For over two decades, French and UK laws have banned heritable genetic modification primarily on two main grounds.⁸⁷⁵ First, the modification of the germline genome raises profound health risks to the line of descendants as a result of the manipulation of the inheritable genetic material. The purported benefits of inheritable genetic modification are outweighed by the direct and unforeseeable risks to the offspring’s

⁸⁷⁴ Consider Harvard geneticist George Church’s examples of preventing osteoporosis by endowing children with an extra-strong bones gene, preventing muscle degeneration with the “Schwarzenegger gene” and preventing potential neurodegenerative disease by cognitively enhancing children. See The Niche, Knoepfler Lab Stem Cell Blog, “A Conversation with George Church on Genomics & Germline Human Genetic Modification”, (March 9, 2015) *IPSCell*, online: <https://www.ipscell.com/2015/03/georgechurchinterview/>

⁸⁷⁵ As early as 1982, the Council of Europe has made a distinction between two types of risks arising from human genetic modification. First, “those arising from uncertainty as to the health, safety and environmental implications of experimental research”, and second “those arising from the longer-term legal, social and ethical issues raised by the prospect of knowing and interfering with a person’s inheritable genetic pattern”. See Council of Europe Parliamentary Assembly Recommendations 934- Genetic Engineering. S. 2.

lineage.⁸⁷⁶ Second, genetic modification and genetic enhancement, in particular, raise a number of considerable ethical and human rights risks to the child's autonomy, human dignity and freedom from discrimination.

I will discuss the human rights and ethical issues raised by the UK and French commissions, national ethics committees and regulators.⁸⁷⁷ Additionally, I will briefly highlight the relevant international human rights law considerations, including concerns identified by the Council of Europe's⁸⁷⁸ Oviedo Convention,⁸⁷⁹ and UNESCO's Declaration for the Protection of Human Rights and Dignity.⁸⁸⁰ Despite their rather opaque stipulations and lack of supranational enforcement mechanisms,⁸⁸¹ these two international human rights

⁸⁷⁶ See CCNE, Opinion No. 8 supra note 36; See also CCNE, Avis no. 36 sur l'application des Procédés de Thérapie Génique Somatique, Paris, 22 Juin 1993, CM Clothier & Great Britain, "Report of the Committee on the Ethics of Gene Therapy" (1992) London: HMSO, par. 2.26-2.27.

⁸⁷⁷ The UK and France were key players in negotiating relevant human rights instruments in parallel to developing their national laws and regulations on genetic intervention technologies.

⁸⁷⁸ Despite the UK not being formally bound by it, the European Court of Human Rights has used the Oviedo Convention as an interpretative tool regarding the UK's obligations in the field of medical law. See *Evans v. United Kingdom* [GC] [2008] App. No. 6339/05, Judgment of 10 April 2007; *Glass v. United-Kingdom* [GC] [2004] App No. 61827/00, Judgment of 9 March 2004; *MAK and RK v. United Kingdom* [2010] App No. 45901/05, Judgment of 23 March 2010. See also Francesco Seatzu, 'The Experience of the European Court of Human Rights with the European Convention on Human Rights and Biomedicine' (2015) 31 UJIEL 5, 14.

In addition, the UK influenced the convention's development and was itself normatively influenced by the Oviedo Convention. See Herman Nys, "Towards an International Treaty on Human Rights and Biomedicine-Some Reflections Inspired by UNESCO's Universal Declaration on Bioethics and Human Rights" (2005) 13:1 Eur J of Health L 7. See also F William Dommel & Duane Alexander, "The Convention on Human Rights and Biomedicine of the Council of Europe" (1997) 7:3 Kennedy Institute of Ethics J 259-260.

⁸⁷⁹ The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, Articles 13, 14.

See also a commentary by a member of the Oviedo Convention's drafting committee about the underlying human rights considerations, Johanna K Nieuwenkamp, "The Convention on Human Rights and Biomedicine" in J D Rentdorff & P. Kemp eds, *Basic Ethical Principles in European Bioethics and Biolan*, vol. II (Barcelona: Centre for Ethics and Law, 2000) 329.

⁸⁸⁰ UNESCO, Universal Declaration on Bioethics and Human Rights (2005) SHS/ EST/05/CONF.204/3REV.

⁸⁸¹ The Universal Declaration on the Human Genome and Human Rights is declaratory law and non-enforceable. The Oviedo Convention is legally binding, but its application and enforcement is up to the member states. The discretionary enforcement of these supranational instruments by member states makes its implementation more difficult. See Alta R Charo, "The Legal and Regulatory Context for Human Gene Editing, Issues in Science and Technology" (2016) 32:3 Issues in Sci & Tech 41.

Challenges with interpreting and enforcing international law instruments are not unique to these two conventions. This critique could be levelled against a large number of international human rights law instruments. Nonetheless, these challenges do not diminish the significance of international human rights laws in setting norms. International human rights instruments of this nature are not akin to a physical barrier that prevents traversing a perilous path but rather act more like signposts that provide indications for the appropriate rules of conduct.

instruments played a central role in shaping and framing the national legal limits on genetic interventions.⁸⁸²

In particular, the Oviedo Convention is a legally binding international law instrument that has been ratified by 29 European countries, including France.⁸⁸³

Health and Safety Risks Arising from Inheritable Genetic Modification

Heritable genetic modification primarily presents two types of risks to human health, unforeseeable adverse effects, which often manifest in later generations and direct safety risks. In terms of direct safety risks, on a clinical level, the process of modifying the germline genome could cause off-target mutations in the embryo.⁸⁸⁴ Off-target mutations often manifest in the failure of the embryo to further develop, as lethal congenital malformations in infancy, or manifest later, typically as cancer.⁸⁸⁵ French and British foundational documents (the White Paper, the Warnock Report, the Clothier Commission, the Lenoir report and the

⁸⁸² Supra note 89.

⁸⁸³ Supra note 380.

⁸⁸⁴ See for instance recent evidence that even advanced gene editing methods currently cause off-target mutations and deletions that could result in pathologies. Michael Kosicki, Kärt Tomberg & Allan Bradley, "Repair of Double-Strand Breaks Induced by CRISPR-Cas9 Leads to Large Deletions and Complex Rearrangements." (2018) *Nature Biotech*, 1; Beeke Wienert et al., "Unbiased Detection of CRISPR off-targets in Vivo Using DISCOVER-Seq" (2019) 364:6437 *Science* 286-289; Kellie A. Schaefer, et al., "Unexpected Mutations after CRISPR-Cas9 Editing in Vivo" (2017) 14:6 *Nature Methods* 547-548; Emily Mullin, "Scientists Edited Human Embryos in the Lab, and It Was a Disaster", *OneZero* (June 16, 2020) online: <https://onezero.medium.com/scientists-edited-human-embryos-in-the-lab-and-it-was-a-disaster-9473918d769d> See also a statement by official bodies that germline genetic modification is presently unsafe. National Academy of Medicine et al. (2020) supra note 72.

Council of Europe, Parliamentary Assembly, "PACE – Report No. 14328 (2017) - The Use of New Genetic Technologies in Human Beings", online: <http://assembly.coe.int.proxy.bib.uottawa.ca/nw/xml/XRef/Xref-DocDetails-en.asp?FileID=23730&lang=en>; European Commission - European Group On Ethics in Science and New Technologies, Statement on Gene Editing, (Luxembourg: Publications Office of the European Union 2017).

⁸⁸⁵ Geneticist Jacques Testart critiqued the use of the popular metaphoric reference to CRISPR-CAS 9 gene editing as precise molecular scissors and explained that:

'Editing techniques entail collateral damage. The targeted parts of the genome are not the only ones that are modified, without us always understanding why or being able to predict their occurrence... the vectors used, whether bacteria, particles or even micro-injection, are as destructive as a bulldozer... the stress induced leaves uncontrolled traces in the form of mutations or epimutations'.

Jacques Testart, "Engineered Humans Could Change our Species", *La Monde Diplomatique*, (13/08/2017), online: <https://mondediplo.com/2017/08/13genome>

Even MIT geneticist, George Church, a pioneer of the gene editing technique, himself has indicated that "most of what we call genome editing is really genome vandalism." Quoted in Marina Cavazzana, "Thérapie Génique : Beaucoup Plus De Questions Que De Réponses" (2017) 33 :5 *Med Sci* 461-462.

CCNE opinions) all directly recognize the risk of germline genetic modification to human health and hence recommended a ban. Furthermore, the damage that could arise from modifying the germline genome is inheritable, thus risking not only the first but subsequent generations. The above normative sources further regard genetic modification as posing a profound and irreversible risk to future generations. Given the present state of genetic science and technology, modification of the germline genome is irreversible.⁸⁸⁶ The potential to reverse the modification is not only presently theoretical, but also itself risks further harm to the DNA and the person's health.⁸⁸⁷ British and French foundational documents have asserted that purported health benefits (while also considering the safer alternative of genetic diagnosis)⁸⁸⁸ are outweighed by the multi-generational health risks.⁸⁸⁹

Even if the direct safety risks could be eventually overcome, inheritable genetic modification still presents a second type of risks - unforeseen adverse effects. Synthetic biologist Eric Lander explains that even a "successful" insertion of genetic material without off-target mutations can still cause unexpected harmful adverse effects. The complex interaction between genetic, other biological and environmental factors can cause unforeseen outcomes. Lander provides the example of the tp53 gene knockout mouse that was developed to help fight against cancer but also unexpectedly caused the mouse to prematurely age.⁸⁹⁰ To

⁸⁸⁶ According to the Canadian Tri-Council Policy Statement: "Gene alteration is irreversible – the cell and its descendants are forever altered and introduced changes cannot be removed" Canadian Tri-Council, TCPS2- 13.7G (2014) Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans Government of Canada, Interagency Advisory Panel on Research Ethics. "Interagency Advisory Panel on Research Ethics", (5 February 2016), online: <http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/>.

⁸⁸⁷ See commentary by a UCLA geneticist, Paul Knoepfler, "Designer Baby Dilemma: Germline DNA Modifications Not Reversible", *Genetic Literacy Project* (22.02.2016) online: <https://geneticliteracyproject.org/2016/03/22/designer-baby-dilemma-germline-dna-modifications-not-reversible/>

⁸⁸⁸ The CCNE asserted in three different opinions that inheritable genetic modification not only raises profound ethical and clinical risks but is also essentially redundant. It would be unethical to modify the human germline genome when genetic diagnosis is already employed for the very same conditions and does not pose the same risks of irreversible harms to the health of future generations. The UNESCO International Bioethics Commission (IBC) invoked the precautionary principle to encourage the use the safer alternative to genetic modification - genetic diagnosis. See UNESCO IBC infra note 907 at para 88.

⁸⁸⁹ See CCNE supra note 876; See also CCNE, Avis no. 36 supra note 876, Clothier supra note 876.

⁸⁹⁰ Eric S. Lander supra note 206.

further illustrate the unforeseen adverse effects, consider examples reviewed in chapter 2 of how the athletically enhanced “mighty mouse” exhibited an unexplained surge of physical and sexual aggression, and that the cognitively enhanced “Doogie Howser” mouse suffered from an unexplained sensitivity to pain.⁸⁹¹ Furthermore, recent experiments using newer gene editing methods resulted in a number of unforeseen adverse effects. Pigs that were modified to be leaner grew extra vertebrae. In another experiment, goats modified to have longer cashmere wool grew too large in the womb and put the mothers’ lives at risk.⁸⁹² Such outcomes might first manifest only in the second and third generations, making it harder to predict and mitigate the unforeseen adverse effects of heritable genetic modification. French and British reports have acknowledged the unforeseeable adverse effects of genetic modification in addition to the direct harms of off-target mutations.⁸⁹³ Given the present state of genetic science, French and British plans to permit genetic modification of the nuclear DNA could be hasty and potentially clash with earlier normative guidance that asserts that such purported benefits are outweighed by the risks to future individuals’ health and lives.

Ethical and Human Rights Risks from Inheritable Genetic Modification

On top of the health risks, the looming regulatory licensing of inheritable genetic modification raises a number of human rights and broader societal risks stemming from the techniques’ potential to produce eugenic outcomes. In general, relevant national and international law associate germline genetic modification with eugenics due to the fact that this technique introduces inheritable changes to future generations’ genome. Eugenic practices⁸⁹⁴ that seek to breed out “bad traits and breed in “good traits” are tied to infringements of

⁸⁹¹ William J. Cromie *supra* note 175.

⁸⁹² Preetika Rana & Lucy Craymer, “Big Tongues and Extra Vertebrae: The Unintended Consequences of Animal Gene Editing”, *Wall St. J.* (Dec. 14, 2018) online: <https://www.wsj.com/articles/deformities-alarm-scientists-racing-to-rewrite-animal-dna-11544808779>

⁸⁹³ Mary Warnock, the chair of the seminal commission that recommended the establishment of the HFEA, has explained some of the concerns that underlined the legislation of the ban on human genetic modification. See Mary Warnock “Ethical Challenges in Embryo Manipulation” (1992) 304:18 *Brit Med J* 4. See also Clothier *supra* note 876 at para 5.1; CCNE, 1990 *supra* note 561, CCNE 1993 *supra* note 876.

⁸⁹⁴ For greater detail about the potential interpretation of the term eugenic practices and its application, see discussion in the paragraphs below.

the future child's autonomy, human dignity (through instrumentalization, commodification and life devaluation) and could be regarded as a discriminatory practice. In the UK, the Warnock Report, the White Paper, and the Clithier Report, the three most authoritative sources regard inheritable genetic modification as a technique that has eugenics consequences and raises significant ethical concerns. In France, three CCNE opinions, as well as the Braibant and Lenoir reports tie inheritable genetic modification to neo-eugenic human rights risks. Article 24 of the UNESCO Universal Declaration on the Human Genome and Human Rights stipulates that "germ-line interventions" could be considered as practices which are 'contrary to human dignity'.⁸⁹⁵ The UN Declaration of Human Rights and Biomedicine Article 1 regards inheritable genetic modification potentially as a human right infringement.⁸⁹⁶ Roberto Andorno, a drafter of the UNESCO Universal Declaration, explains that one of the two rationales behind its ban on inheritable genetic modification (the other being the irreversible health risk to future generations) is "the serious concern about the possible use of this technique for eugenic purposes."⁸⁹⁷ Francioni and Scovazzi further link the eugenic rationale to the UNESCO Universal Declaration's dignitarian values. Eugenic practices promote discriminatory values and infringe upon future children's fundamental freedoms such as their autonomy and human dignity.⁸⁹⁸ Article 13 of the Council of Europe Oviedo Convention prohibits inheritable genetic modification on the grounds of being contrary to human dignity. Section 89 of the Explanatory Report to the Oviedo Convention explains the rationales behind Article 13's prohibition that genetic modification could be used to "produce individuals or entire groups endowed with particular characteristics and required

⁸⁹⁵ UNESCO, Universal Draft Declaration on Bioethics and Human Rights (2005), Article 24.

⁸⁹⁶ The Universal Declaration on the Human Genome and Human Rights, in Article 2 concerning its implementation, underscores the need to identify practices such as germ-line interventions that might be contrary to human dignity and assigns responsibility for this to the International Bioethics Committee of UNESCO (IBC).

⁸⁹⁷ Roberto Andorno, "Chapitre 8. Towards an International Bioethics Law" (2004) 15:2 J Int'l Bioéthique 137.

⁸⁹⁸ Francesco Francioni & Tullio Scovazzi, *Biotechnology and International Law* (London: Bloomsbury Publishing, 2006) 319.

qualities.”⁸⁹⁹ This rationale underlying Article 13 condemns the use of germline genetic modification as a eugenic practice as children should be brought into the world free of biological pre-conditioning and of “good” and “bad” behaviours according to social presumptions and prejudices.⁹⁰⁰

Depending on the interpretation taken, the eugenic rationale may apply to inheritable genetic modification to prevent diseases, disorders and abnormalities. National normative sources such as the Warnock Report,⁹⁰¹ the Clothier Report,⁹⁰² and Article 16-4 of the Code Civil⁹⁰³ contain a degree of ambiguity whether the eugenic rationale applies to therapeutic genetic modification.⁹⁰⁴ One notable exception is a definition of eugenics provided by the Conseil d’État in its review of the 2008 revision of the Bioethics Law, which could potentially apply to diseases.⁹⁰⁵ However, indications from relevant international law sources suggest that attempts to eradicate genes linked to diseases or disabilities from future descendants’ genome

⁸⁹⁹ Explanatory Report to The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, Section 89.

⁹⁰⁰ Ibid. See also Gilbert Hottois, “A Philosophical and Critical Analysis of the European Convention of Bioethics” (2000) 25:2 J Med & Phil at 141.

⁹⁰¹ Warnock Report supra note 24.

⁹⁰² Clothier supra note 876 at para. 2.26-2.27.

⁹⁰³ *Code Civil, Art. 16-4* (Inséré par la Loi No 94-653 du 29 juillet 1994 art. 1 1, II, art. 3 J Officiel du 30 juillet 1994 ; Loi nO 2004-800 du 6 août 2004 art. 21 Journal Officiel du 7 août 2004) ; Loi nO 2004-800 du 6 août 2004 relative à la bioéthique, J.O. 6 août 2004 online : <http://www.legifrance.gouv.fr/WAspad/Visu?cid=26590&indice=l&table=CONSOLIDE&ligneDeb=1>

⁹⁰⁴ The terms eugenics and eugenic practices have not been formally defined in legal and policy documents. Different documents take somewhat different approaches to regarding certain genetic interventions as eugenic. However, a common interpretation of the national and international instruments is that the inheritable genetic modification for human enhancement purposes is likely to be considered a eugenic practice. See for instance a discussion of the interpretation of the term eugenic practices in the context of the European Charter of Human Rights and Freedoms - Steve Peers et al., *The EU Charter of Fundamental Rights: A Commentary* (Oxford: Hart Publishing, 2014) at 50.

⁹⁰⁵ The Conseil d’état opined that:

“eugenics can be defined as all methods and practices aimed at improving the genetic makeup of the human species. It may be the fruit of a policy deliberately implemented by a state and contrary to human dignity. It may also be the collective result of the sum of individual convergent decisions taken by future parents, in a society that promotes the search for the child who is “perfect”, or at least free of numerous serious illnesses.”

Conseil D’État supra note 35 at 40.

could constitute a eugenic practice.⁹⁰⁶ The 2003 UNESCO IBC report contends that therapeutic genetic modification can nonetheless end up producing eugenic outcomes due to the deeming of certain genes linked with physical and mental disabilities as “deleterious” genes to be eliminated from the genomes of future descendants.⁹⁰⁷ The Council of Europe Committee on Bioethics has expressed the opinion that “It could also be argued that the selection of offspring for health purposes triggers the risk of ‘eugenics’ with respect to persons with disabilities, incited by the ideal to create a ‘perfect society’”.⁹⁰⁸ The Council of Europe’s Parliamentary Assembly declared that the 2015 HFEA move to approve genetic modification of the human mitochondria is in contravention of the international law norms of Article 13 of the Oviedo Convention and section 24 of the UNESCO Universal Declaration. Their statement reads “The undersigned members of the Parliamentary Assembly affirm that the creation of children with genetic material from more than two progenitor persons, as is being proposed by the United Kingdom Human Fertilisation and Embryology Authority, is incompatible with human dignity and international law.”⁹⁰⁹

Ethical and Human Rights Risks Arising from the Potential Approval of Genetic Enhancements

The potential approval of genetic enhancements poses the risk of infringing on future generations’ rights to autonomy, dignity, and freedom from discrimination. The UNESCO IBC report on genetic

⁹⁰⁶ As Ishii reminds us, eugenics is not restricted to positive eugenics (which largely relates to the human genetic enhancement spectrum) but also attempts to eradicate disease and disability from offspring genome using genetic modification (negative eugenics). See Tetsuya Ishii, “Germ Line Genome Editing in Clinics: The Approaches, Objectives and Global Society” (2017) 16:1 *Brief Funct Genomics* 51.

⁹⁰⁷ See UNESCO International Bioethics Committee (IBC), “Report on Pre-Implantation Genetic Diagnosis and Germ-line Intervention”, 24 April 2003, Paragraphs 91-99.

⁹⁰⁸ See Council of Europe - Committee on Bioethics, *International Case-Law in Bioethics: Insights and Foresight* (Strasbourg: European Court of Human Rights Press, 2016).

⁹⁰⁹ Council of Europe, Parliamentary Assembly, “Creation of Embryos with Genetic Material from More than Two Progenitor Persons” Written Declaration No. 557, Doc. 13325. (03 October 2013) online: <http://assembly.coe.int/nw/xml/XRef/Xref-XML2HTML-en.asp?fileid=20204&lang=en>.

The literature has discussed whether inheritable human genetic modification is compatible with international human rights law, see Roberto Andorno, “International Policy and A Universal Conception of Human Dignity” in *Human Dignity in Bioethics* (Oxford: Routledge, 2013) 141-155; also see Stephen P. Marks, “Tying Prometheus Down: The International Law of Human Genetic Manipulation” (2002) 3 *Chi. J. Int’l L.* 115. For a somewhat different viewpoint see R. Alta. Charo, “Germline Engineering and Human Rights” (2018) 112 *AJIL Unbound* 344-349.

modification condemns eugenic practices as attempts to biologically condition “good” and bad” human traits. The attempt of previous generations to impose their preferences, biases and views regarding their preferred physical and mental traits for future generations to possess constitutes a form of “intergenerational tyranny”.⁹¹⁰ Choices imposed by past generations on future generations are done systematically without their assent. The UNESCO IBC report, as well as the 2003 HFEA ethics report further cautions that such pre-selection of a future child’s biological traits could negatively affect her self-perception as an autonomous agent.⁹¹¹ Furthermore, the imposition of parental and societal preferences of desirable appearance, behavioural characteristics and cognitive abilities not only instrumentalize the child to the interests and desires of third parties⁹¹² but also objectifies and commodifies the child. Such an instrumental, commodifying treatment infringes on the rights to dignity of vulnerable future generations.⁹¹³ The novel ability to select future generations’ genetic characteristics before they are even born gives unprecedented power to those with influence over such decisions.

⁹¹⁰ See UNESCO IBC supra note 907.

⁹¹¹ UNESCO IBC supra note 907; HFEA supra note 69.

⁹¹² Rt. Justice Noëlle Lenoir, the author of the foundational Lenoir report and a drafter of the UNESCO Universal Declaration explains links genetic modification to violations of human dignity. The attempt to select children based on parental and societal preferences is a eugenic practice that instrumentalizes children. See Noëlle Lenoir, “Europe Confronts the Embryonic Stem Cell Research Challenge” (2000) 287:5457 *Science* 1427-1428.

⁹¹³ Derek Morgan & HFEA supra note 735; See also Nicole le Douarin, Catherine Puigelier, “Avant-propos, Le Douarin” in N & C Puigelier. *Science, Éthique et Droit* (Paris: Editions Odile Jacob, 2007) at 22-25.

The UNESCO International Bioethics Committee further commented that:

The goal of enhancing individuals and the human species by engineering the genes related to some characteristics and traits [...] impinges upon the principle of respect for human dignity in several ways. It weakens the idea that the differences among human beings, regardless of the measure of their endowment, are exactly what the recognition of their equality presupposes and therefore protects. It introduces the risk of new forms of discrimination and stigmatization for those who cannot afford such enhancement or simply do not want to resort to it.

UNESCO, International Bioethics Committee, *Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights* (Paris, UNESCO, 2015) sub 111.

Attempts to improve the genetic design of humans could potentially create a number of novel long-term risks to the human species. Section 16-4 of the French Code Civil⁹¹⁴ specifically recognizes that “eugenic practices” could be potentially harmful to the “human species” as a whole.⁹¹⁵ The Explanatory Report to the Oviedo Convention regarding Article 13 further states that inheritable modification of the human genome “may endanger not only the individual but the species itself”.⁹¹⁶ The human species is the largest group ever protected under the law. The sheer breadth of the legal protection shows the scale and magnitude of potential long-term impacts of human genetic modification. Genetic enhancement (such as those involving transgenic and synthetic genomics) raises the unique risk of transcending the biological limits of the human species.⁹¹⁷ Furthermore, the UNESCO IBC report specifically warns that genetic enhancement could have “long-term and possibly irreversible implications for the continuing evolution of the human species.”⁹¹⁸ Not only legal

⁹¹⁴ Code Civil, Art. 16-4 supra note 25. The article specifically stipulates that “No one may infringe upon the integrity of human species. Any eugenic practice which aims at organizing the selection of persons is forbidden.”

⁹¹⁵ Similarly, the French Constitutional Council has stated, in reference to human genetic modification ban, that one of the Bioethics Law key objectives of the act is to “preserve the biological integrity of the human species” See France, Conseil Constitutionnel Décision n° 94-343/344 DC du 27 Juillet 1994 Loi Relative Au Respect du Corps Humain et Loi Relative Au Don Et À L'utilisation Des Éléments et Produits du Corps Humain, À L'assistance Médicale À La Procréation et Au Diagnostic Prénatal, para 18

⁹¹⁶ Explanatory Report to The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, Section 89.

Hottois argues that a wide-ranging protection for the human species as a whole is derived from the Oviedo Convention's rationale that tinkering with human genetics has far-reaching transformative effects well beyond the individual, to the human species as such. See Hottois, supra note 900.

⁹¹⁷ UNESCO IBC supra note 907, See also Robert Andorno, ‘Biomedicine and International Human Rights Law: in Search of a Global Consensus’ (2002) 80:12 Bull World Health Organ 959-963, 961. Andorno notes that at the time of writing he was a Member of the UNESCO International Bioethics Committee.

See for instance the INSERM Bioethics committee, which explained that France prohibited animal-human transgenesis is contrary to human dignity and raises novel ethical question about crossing species boundaries. See Comité d'éthique de l'Inserm Questions Éthiques Associées aux Applications Cliniques Utilisant Des Cellules Souches L'actualité Thérapeutique des Cellules Souches Séance dédiée de l'académie de pharmacie Salle des Actes 06/10/2017 online : http://www.acadpharm.org/dos_public/Cellules_souches_Acadpharm.pdf

⁹¹⁸ UNESCO IBC supra note 907 at 6.

sources, but eminent life scientists share the view that genetic modification and enhancement could affect in the long term the species' evolution.⁹¹⁹

Human Genetic Modification and the Slippery Slope to Eugenics

Key legal documents and committee reports have repeatedly flagged over the years the issue that inheritable genetic modification poses a particular risk of a slippery slope to eugenics.⁹²⁰ Overall, key French and UK legal documents and committee reports placed less attention on attempts to eliminate disease related genes (negative eugenics) and placed greater attention on the ethical and human rights concerns relating to genetic enhancement (positive eugenics).⁹²¹ Nevertheless, one of the key rationales in favour of a complete ban or a very restrictive approach is that therapeutic genetic modification could eventually lead to prohibited practices of human genetic enhancement. Attempts to genetically improve the child's genome by preventing disease and disability can eventually cross the line to endow them with "desirable" and "enhanced" traits.⁹²² As early as 1984, the UK Council of Science and Society, which was tasked to advise the Parliament on legislation, has warned that genetic modification technology can eventually come to be used for eugenic purposes of endowing future generations with desirable "intellectual or physical characteristics".⁹²³ The 1984

⁹¹⁹ Campbell et al. *supra* note 45.

⁹²⁰ As I explained in chapter 3, lawmakers were also concerned about a slippery slope from genetic diagnosis to genetic modification. The risk highlighted in parliamentary debates and the committees that the use of one genetic technology for trait selection – genetic diagnosis can legitimize and serve as a precedent for genetic modification. However, parliaments were convinced that such a slide down the slope is not likely because genetic diagnosis would be a safer alternative to the much riskier methods of human genetic modification.

⁹²¹ For instance, the CCNE Opinion no.8 has warned that embryo experimentation and the potential use of biotechnology for genetic enhancement purposes could reawaken the spectre of eugenics. See CCNE, Opinion No. 8 *supra* note 36.

⁹²² Philosopher of technology Jacques Ellul has remarked that the possibility of the slippery slope to eugenics is intrinsically tied to the state of technological development. He predicted that the true challenges would emerge when the technology finally becomes feasible. Once technological means would become available to control reproduction, employing it to that ends will eventually become possible. Jacques Ellul & Patrick Chasteney, *A Contre-courant : Entretien* (Paris : Editions de la Table Ronde, 2014).

⁹²³ Council on Human Reproduction Science and Society, *Human Procreation: Ethical Aspects of the New Technologies* (Oxford: Oxford University Press 1984), 80-81.

Despite the slippery slope concerns it raised, the Council of Science and Society has recommended that genetic modification research on surplus embryos should not be prohibited. The committee cited in its reasons that it believes

Warnock report explicitly voiced a concern that genetic manipulation of the embryo for the purpose of genetic enhancement can revive eugenic tendencies in society. Once again, a new potent technology could serve the eugenic aim of improving humans, eliminating traits deemed as defective and selecting in traits deemed useful and desirable.⁹²⁴ Similarly, Baroness Warnock explained that one of the deepest concerns in the field is the slippery slope to eugenics as inheritable genetic modification could be used to create children and future generations with more “ideal” enhanced traits and characteristics.⁹²⁵ Geneticist Jean-François Mattei, a former Minister of Health and one of the main drafters of the 1994 Bioethics law⁹²⁶ opposed the future extension of the law to allow genetic modification. Mattei explained that inheritable genetic modification would lead to genetic enhancement under the pretense of therapeutic benefits.⁹²⁷ Owing to considerable concerns about the slippery slope to eugenics and human enhancement, French and British parliaments decided to legally ban inheritable genetic modification.

More recently, the 2017 UK Parliamentary Committee on Gene Editing and its French counterpart both stated that one of the primary objectives of any future regulation of inheritable genetic modification is to prevent a slippery slope to the creation of genetically enhanced individuals.⁹²⁸ This newer, emerging position is based on an assumption that fewer precautions are needed because the regulations limiting genetic

that exploratory research into human genetic modification is unlikely to lead to clinical applications in the foreseeable future.

⁹²⁴ Warnock Report supra 24 at para 11.13.

⁹²⁵ Mary Warnock supra note 379.

⁹²⁶ Jean-François Mattei is also frequently dubbed the “father of the Bioethics Law”. See Catherine Vincent, “La brevetabilité du vivant en quête d’éthique ; Un Rapport Parlementaire Souligne Les Lacunes D ’ Une Directive Européenne Sur La Protection Juridique Des Inventions Biotechnologiques” *Le Monde*, (July 4, 1996) 23.

⁹²⁷ Jean-François Mattei, *La vie en Questions : pour une Éthique Biomédicale, Rapport au Premier Ministre, La Documentation Française* (Paris : coll des Rapports Officiels, 1994) 230.

⁹²⁸ See United Kingdom, House of Commons, Science and Technology Committee, “Oral evidence - Genomics and Genome-Editing - 29 Mar 2017”, HC 854 online : <http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/genomics-and-genomeediting/oral/49725.html>. Assemblée Nationale et Sénat Rapport Au Nom De l’office Parlementaire D’évaluation des Choix Scientifiques Et Technologiques sur les Enjeux Économiques, Environnementaux, Sanitaires Et Éthiques des Biotechnologies À La Lumière des Nouvelles Pistes De Recherche tome II : Comptes Rendus Et Annexes par m. Jean-Yves, Et Mme Catherine Procaccia, le 14 avril 2017.

modification to “serious conditions” will prevent its eugenic misuse. The legal position established in the 1980s and 1990s shares the concern of the slippery slope to genetic enhancement but placed less confidence in the ability of regulatory mechanisms to set and maintain appropriate limits. I will show that this concern is well justified due to a number of critical flaws and loopholes. The failure to set effective legal limits could very well result in the use of genetic modification to produce children with more “desirable” and enhanced bodily and mental characteristics – the very eugenic outcomes that the law intends to prohibit.

II) An Overview of the Legal Change Concerning Inheritable Genetic Modification

The UK – The First Jurisdiction in the World to Permit a Form of Inheritable Genetic Modification

After two decades of a complete ban,⁹²⁹ in 2015, the UK partially reversed its long-standing ban on inheritable genetic modification. The UK parliament debated and eventually approved the HFEA Regulations.⁹³⁰ Following the approval, the HFEA has promulgated the HFE (Mitochondrial Donation)⁹³¹ Regulations 2015.⁹³² By permitting the modification of mitochondrial DNA, the UK has become the first jurisdiction in the world to legalize and regulate a form of human inheritable genetic modification.

Before we examine the regulations, let us first take a moment to understand what the procedure of mitochondrial genetic modification entails. The mitochondrion is a cell organelle (specialized cell part) often dubbed the “cell powerhouse”. The mitochondrion is responsible for several cellular metabolic functions

⁹²⁹ See HFE Act 1990, Schedule 2, paragraph (1) (4).

⁹³⁰James Gallagher supra note 51.

⁹³¹ Note that the name chosen for the regulations – mitochondrial donation is scientifically inaccurate. The process involves not only a donation of a mitochondrion, but also the modification of the mitochondrial germline DNA.

Geneticist Jeff Nisker points out that the popular monikers “Mitochondrial Donation” and “Three Parents IVF” sound as if the technique is simply yet another form of IVF or gamete donation. These softer monikers tend to defuse the public’s concerns about the idea of genetically modified babies. Nevertheless, and despite being termed as “mitochondrial donation”, the technique is a form of human germline modification. See Jeff Nisker, “The Latest Thorn by Any Other Name: Germ-Line Nuclear Transfer in the Name of “Mitochondrial Replacement” (2015) 37:9 J Obstetrics & Gynecology Can 829.

⁹³²The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 No. 572.

and programmed cell death.⁹³³ The most common technique to modify the mitochondrial DNA involves transferring the cell nucleus from the egg of one woman into an enucleated egg of another woman. The genetically modified egg cell contains genetic material from the two women, the nuclear DNA of the intended mother, and the mitochondrial DNA of the egg donor.⁹³⁴ The mitochondrial DNA encodes about 0.2% of the human genes.⁹³⁵ The mitochondrial DNA does not encode traits such as hair and skin colour (those and many other traits are encoded in the nuclear DNA, which contains about 99.8% of the human genes). As such, at least in theory, the potential of a slippery slope to eugenics is more limited with mitochondrial modification.⁹³⁶ Dr. Fishel, a geneticist who applied for an HFEA license, defends mitochondrial modification by suggesting that the child's genome would not be dramatically altered. Dr. Fishel suggests that the process of modifying the mitochondrial DNA of a future child is "like fixing a car". He adds: "You recognise the car, it's got the same brand, heritage and appearance. All you've changed is a fuel cell in the engine."⁹³⁷ Yet, Fishel's analogy between human genetic modification and car repair fails to capture this complicated technology's various medical, ethical and legal challenges.

⁹³³ Sabzali Javadov & Andrey Kuznetsov, "Mitochondrial Permeability Transition and Cell Death: The Role of Cyclophilin D" (2013) 4 *Frontiers in Physiology* 59.

⁹³⁴ Eunju Kang et al., "Mitochondrial Replacement in Human Oocytes Carrying Pathogenic Mitochondrial DNA Mutations" (2016) 540:7632 *Nature* 270.

⁹³⁵ The mitochondrial DNA consists of 37 genes inherited from the mother. The nuclear DNA contains between 20,000-30,000 genes inherited from both parents. See National Academies of Sciences, Engineering, and Medicine, *Mitochondrial Replacement Techniques: Ethical, Social, and Policy Considerations* (Washington DC: National Academies Press, 2016) 33-35.

⁹³⁶ However, note that a research team from the University of Alabama recently demonstrated that modifying mammalian mitochondrial DNA can affect the onset and the development of visible aging characteristics such as hair loss and wrinkles. The research team is working on developing anti-aging mitochondrial gene therapies to prevent hair loss and skin aging. Bhupendra Singh et al., "Reversing Wrinkled Skin and Hair Loss in Mice by Restoring Mitochondrial Function" (2018) 9:7 *Cell Death & Disease* 735.

⁹³⁷ Carl O'Brien, "Irish Clinic Says it will offer "Three Parent IVF", *Irish Times* (June 20, 2013) online: <http://www.irishtimes.com/news/health/irish-clinic-says-it-will-offer-three-parent-ivf-procedures-1.1447060>

Mitochondrial Modification Sets Several Precedents for More Extensive Genetic Modification

While advocates insist the technique's narrow application would prevent a slippery slope,⁹³⁸ further examination reveals that the HFEA's licensing of mitochondrial modification nevertheless sets several precedents that could broaden the application of genetic modification technologies. First, mitochondrial modification does not involve changing only one but 37 genes simultaneously.⁹³⁹ The high number of genes modified in one procedure could potentially set a precedent for the editing of multiple genes at the same procedure.⁹⁴⁰ Multi-gene editing can be used to change multiple traits in the embryo or to edit complex traits that are encoded in multiple genes such as height. Second, as I will later show, the regulatory approval of mitochondrial modification is cited as a precedent to reverse the ban on nuclear genetic modification. As Tetsuya Ishii further explains, the approval of mitochondrial modification is the first step towards the potential reversal of the ban on nuclear genetic modification. Once the principle of banning inheritable genetic modification has been compromised, there are seemingly no reasons not to keep on making concessions in the name of advancing cutting-edge biomedical technologies.⁹⁴¹ Hence, mitochondrial modification licensing has potentially far-reaching implications as it sets several precedents for nuclear genetic modification and the editing of multiple genes.

⁹³⁸ See for instance, Editorial, "Power Play the Replacement of Mitochondria Does Not Signal Ethical Problems" (2015) 525:7570 *Nature* 425.

In contrast, fertility expert David Keefe explains that "extensive experimental data demonstrates profound effects of mtDNA in a wide array of human conditions, including autism, aging, psychiatric diseases, immune response, response to ototoxic antibiotics, and risk for cardiomyopathy, among others. MTDNA, therefore, does contribute to many facets of "humanness" and to genetic identity, so MT does constitute germ-line genetic engineering." In David L. Keefe, "Easing US Restrictions on Mitochondrial Replacement Therapy Would Protect Research Interests but Grease the Slippery Slope" (2019) 36:9 *J Assisted Repro & Genetics* 1782.

⁹³⁹ Lucía Gómez-Tatay, José M Hernández-Andreu & Justo Aznar, "Mitochondrial Modification Techniques and Ethical Issues" (2017) 6:3 *J Clinical Med* 25.

⁹⁴⁰ For more about new technology to edit the genome at multiple locations, See Bernd Zetsche et al. *supra* note 204.

⁹⁴¹ Ishii, *supra* note 359 at 160.

Will the HFEA Mitochondrial Modification Regulation Mitigate the Slippery Slope to Eugenics?

John Harris, one of neo-eugenics' key proponents, argues that the approval of mitochondrial modification, a form of inheritable genetic modification, will not lead to a slide down the slope to eugenics. Harris, who was once one of the key opponents of regulation in general and the HFEA specifically,⁹⁴² has recently moved to defend the HFEA's policies once the agency took a more permissive stance towards genetic modification. Harris writes:

Slippery slopes can be approached by wearing skis or crampons. We have proved adept in the UK at using crampons to negotiate such slippery slopes as those around embryonic and reproductive technologies. The Human Fertilisation and Embryology Authority (HFEA) was set up as a regulator to deal with these technologies as they are developed, engaging scientific and public audiences in parallel.⁹⁴³

Harris's new line of argumentation echoes the prevalent narrative that the seemingly robust regulations will prevent a slippery slope to eugenics. One must consider a more preliminary question: is Harris correct to assume that the HFEA's regulation of mitochondrial modification is robust in the first place?

Old Problems in a New Context: The HFEA Regulation of Mitochondrial Genetic Modification

The mitochondrial modification regulations are not only based on the same rules applied to genetic diagnosis that are prone to overextensive legal change but are in fact even laxer. One might assume that the HFEA would impose more stringent requirements on mitochondrial modification than genetic diagnosis given that the former potentially poses greater ethical and health risks. However, the mitochondrial modification regulations entirely omit the age of onset and the untreatability requirements. Without these

⁹⁴² John Harris, "Sex Selection and Regulated Hatred" (2005) 31:5 J Med Ethics 291; John Harris *supra* note 275 at 150-157.

⁹⁴³ Quoted in Government Office for Science and Professor Sir Mark Walport, "Gene 'edits' and other words that don't help - GOV.UK" (23 March 2016), online: <https://www.gov.uk/government/speeches/gene-edits-and-other-words-that-dont-help>.

two requirements, mitochondrial modification could be used to modify embryos with treatable conditions or those with a susceptibility gene linked to an often lower risk rate of developing a late-onset condition. Article 8 of the HFEA mitochondrial modification regulations only require a “particular risk” to develop a “serious mitochondrial condition”.⁹⁴⁴ The use of the term “serious mitochondrial condition” repeats the various problems relating to the ambiguity, subjectivity and overbreadth of the seriousness standard in the more controversial context of inheritable genetic modification. To illustrate, consider the HFEA’s recent decision to classify Optic Atrophy Type 1 as a serious mitochondrial condition.⁹⁴⁵ Optic Atrophy Type 1 results in varying degrees of visual field impairments and problems with colour vision, but otherwise entails a normal life span and good health.⁹⁴⁶

The HFEA mitochondrial modification regulations repeat the line drawing flaws demonstrated with genetic diagnosis, but with greater ethical and health risks stemming from the modification of the human genome. It is important to question the prudence of modifying the germline genome, a technique that entails various potential health risks,⁹⁴⁷ to treat partial visual field impairment and colour blindness. Does colour blindness and partial visual field impairments truly justify taking the various and unpredictable risks arising from inheritable genetic modification? Is it prudent to omit the restriction to early-onset condition and allow modification of the genome to potentially prevent a late-onset condition that the time of onset decades from

⁹⁴⁴ Article 8 (a) HFEA, Mitochondrial Donation Regulations 2015 No.572.

⁹⁴⁵ HFEA, “Conditions Licensed by the HFEA”, online: <http://guide.hfea.gov.uk/pgd/>

⁹⁴⁶ Cécile Delettre-Cribaillet, Christian P Hamel & Guy Lenaers, “Optic Atrophy Type 1” in Margaret P Adam et al., eds, *GeneReviews* (Seattle (WA): University of Washington, Seattle, 2015).

⁹⁴⁷ For a general summary of the potential health risks posed mitochondrial gene replacement see Quebec, Commission De L’éthique En Science Et En Technologie, “Genetically Modified Babies: Ethical Issues Raised by the Genetic Modification of Germ Cells and Embryos Summary and Recommendations) (Québec: Gouvernement du Québec, 2018) 13.

For more about the risk of epigenetic damage as a result of modification of the mitochondrial DNA see a meta-analysis: Klaus Reinhardt et al., "Mitochondrial Replacement, Evolution, and the Clinic" (2013) 341:6152 *Science* 1345-1346. See also Jacques HM Cohen & Mina Alikani, “The Biological Basis for Defining Bi- Parental or Tri-Parental Origin of Offspring from Cytoplasmic and Spindle Transfer” (2013) *Reprod. Biomed.* online 26, 535 – 53; Ralph Dobler et al. "A Systematic Review and Meta-Analysis Reveals Pervasive Effects of Germline Mitochondrial Replacement on Components of Health" (2018) 24:5 *Human Reproduction Update* 519-534.

now, where it could potentially be treated with safer, more advanced technologies? The HFEA's mitochondrial modification regulations are problematic because they do not take sufficient measures to promote the use of safer alternatives and restrict the application of an experimental technology that generated a considerable controversy regarding the health risks it may entail. Furthermore, despite the formal restriction to "serious mitochondrial conditions", the HFEA has already approved an arguably non-serious, mild condition consisting of visual difficulties with the individual's field of vision and ability to see colour. Regulatory approval of non-serious conditions such as Optical Atrophy type 1 not only raise legal issues but important ethical and clinical questions regarding the ratio between benefits and risks in a form of inheritable genetic modification. The mitochondrial modification regulations exhibit many of the same line drawing flaws with genetic diagnosis, but this time with greater ethical and health issues are at stake.

Does the French Legal Ban Prohibit all Human Genetic Modification or Only "Non-Therapeutic" Genetic Modification?

While the French law seemingly prohibits genetic modification, its provisions could be interpreted along the lines of the problematic therapy/enhancement distinction.⁹⁴⁸ The Assemblée Nationale and the ABM have interpreted Article 16-4 of the French Code Civil as a complete prohibition on inheritable genetic modification.⁹⁴⁹ A deeper examination of Article 16-4's text reveals that the article itself stipulates that "no person may undermine the genetic integrity of the human species"⁹⁵⁰ and prohibits "carrying out a eugenic

⁹⁴⁸ I will examine the therapy/enhancement distinction and the sheer difficulty in line drawing using these two nebulous concepts later in this chapter.

⁹⁴⁹ See Assemblée Nationale Constitution *supra* note 37 ; ABM, "Rapport d'information au Parlement et au Gouvernement – décembre 2015" (2015) Agence de la Biomédecine, at 44 online : https://www.agence-biomedecine.fr/IMG/pdf/2016_ripg_vdef.pdf

⁹⁵⁰ The approach of criminalizing genetic modification as a crime against the human species is based on a Council of Europe's doctrine that holds that the human genome is the shared heritage of the human species. In particular, the doctrine holds that attempts to practice genetic modification for eugenic purposes in hope of improving gene pools can end up affecting the human species as a whole. The Explanatory Report to the Oviedo Convention addresses these concerns, stating that:

practice aimed at organizing the selection of persons”.⁹⁵¹ However, a number of academics,⁹⁵² as well as the Assemblée Nationale itself⁹⁵³ contend that terms such as the “genetic integrity of the human species” and “eugenic practices” have never been defined and their interpretation remains unclear. The unclear wording of Article 16-4 continues as the text further excludes interventions: “aimed at the prevention and treatment of genetic disease”. Several academics argued that Article 16-4 implicitly allows for the modification of the human genome for therapeutic or preventative purposes.⁹⁵⁴ The flipside of Article 16-4 allowing genetic modification for therapeutic and preventative purposes is its prohibition of genetic enhancement. According to this textual interpretation, Article 16-4 regarding genetic modification could be read as the heavily criticized distinction between therapy and enhancement.

France would first have to overcome one major international law “roadblock” in order to permit genetic modification for “therapeutic” purposes”, its ratification of the Oviedo Convention that seemingly prohibits inheritable genetic modification. Article 13 of the Oviedo Convention has been widely interpreted as banning all forms of inheritable genetic modification.⁹⁵⁵ This interpretation primarily relies on Section 91

The third and final concern relates to the human species ... There are reasons to hope that (genetics) could also enable therapeutic progress to take place. However, the risks associated with this growing area of expertise should not be ignored. It is no longer the individual or society that may be at risk but the human species itself. The Convention sets up safeguards, starting with the preamble where reference is made to the benefits to future generations and to all humanity, while provision is made throughout the text for the necessary legal guarantees to protect the identity of the human being.

Explanatory Report to The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, S14.

⁹⁵¹ Code Civil, art. 16-4 (Inséré par la Loi No 94-653 du 29 juillet 1994 art. 1 1, II, art. 3 J Officiel du 30 juillet 1994 ; Loi no 2004-800 du 6 août 2004 art. 21 J Officiel du 7 août 2004) ; Loi nO 2004-800 du 6 août 2004 relative à la bioéthique, J.O. 6 août 2004.

⁹⁵² Catherine Bachelard-Jobard, *L'eugénisme, La Science Et Le Droit* (Paris : Presses Universitaires de France, 2001) 241; Salat-Baroux, Frédéric, *Les Lois de Bioéthique* (Paris : Édition Dalloz, 1998) 18.

⁹⁵³ Supra note 949.

⁹⁵⁴ See Declan Butler, “WHO's Bioethics Code Likely to Stir Debate” (1999) 398:6724 *Nature* 179. See also Anne-Sophie Paquez supra note 426 at 194.

⁹⁵⁵ Roscam Abbing, “The Convention on Human Rights and Biomedicine: An Appraisal of the Council of Europe Convention” (1998) 5 *Eur J Health L* 383-384. See also Herman Nys, “The Biomedicine Convention as an Object and a Stimulus for Comparative Research” (2008) 15:3 *Eur J Health L* 277; see also Roberto Andorno, “The Oviedo Convention:

of the Explanatory Report to the Oviedo Convention, which states that “interventions seeking to introduce any modification in the genome of any descendants are prohibited.”⁹⁵⁶

However, an ambiguity in the actual text of Article 13 of the Oviedo Convention means it could be read as allowing genetic modification for therapeutic and preventative purposes while disallowing genetic enhancement.⁹⁵⁷ The text of Article 13 reads “an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.”⁹⁵⁸ The reason for Article 13’s ambiguous wording could be traced back to the drafting committee’s wishes not to prohibit somatic gene therapy that may inadvertently change the germline genome.⁹⁵⁹ Yet, the drafting committee’s transcripts from the early 1990’s reveal that certain delegates have expressed concerns that Article 13’s vague text might eventually be interpreted as the

A European Legal Framework at the Intersection of Human Rights and Health Law" (2005) 2:4 J Int’l Biotech L 133-143.

⁹⁵⁶ However, section 91 of the explanatory report further reads “Medical research aiming to introduce genetic modifications in spermatozoa or ova which are not for procreation is only permissible if carried out in vitro with the approval of the appropriate ethical or regulatory body “. See Explanatory Report to The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, Section 91.

The CDBI (Steering Committee on Bioethics), the ethics committee of the council of Europe has reiterated that view Convention on Human Rights and Biomedicine which states that "an intervention seeking to modify the human genome may only be undertaken if its aim is not to introduce any modification in the genome of any descendants" See CDBI Working Party on Human Genetics, Working Document on the Applications of Genetics for Health Purposes, 2003) CDBI/INF, 3, 7.

⁹⁵⁷ Norberto N G De Andrade, “Human Genetic Manipulation and the Right to Identity: The Contractions of Human Rights Law in Regulating the Human Genome” (2010) 7:3 Scripted 437. See Katrine S Bosley et al., “CRISPR Germline Engineering—the Community Speaks” (2015) 201 Nature 482. See also Ana Nordberg et al., "Regulating Germline Editing in Assisted Reproductive Technology: An EU Cross-Disciplinary Perspective" (2020) 34:1 Bioethics 21-22.

⁹⁵⁸ Article 13, The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997.

⁹⁵⁹ CDBI supra note 956.

Note that Article 13 sets specific limits on the application of germline, not somatic gene-therapy. Section 92 of the Explanatory Report states:

“On the other hand the article does not rule out interventions for a somatic purpose which might have unwanted side-effects on the germ cell line. Such may be the case, for example, for certain treatments of cancer by radiotherapy or chemotherapy, which may affect the reproductive system of the person undergoing the treatment.”

Section 92, Explanatory Report supra 905.

controversial distinction between genetic therapy and enhancement.⁹⁶⁰

The Council of Europe has recently given a clear indication that it is seriously considering adopting a textual interpretation of Article 13 that would allow for human germline genetic modification for the broad purposes of “prevention” and “therapy”. A 2015 statement by the Council of Europe’s Committee on Bioethics suggested that if a “social agreement” would form around the legitimacy of the genetic modification, there would be sufficient justification for interpreting Article 13’s ban more permissively.⁹⁶¹ Only two years later in 2017, and without any indication of a social agreement that inheritable genetic modification is legitimate,⁹⁶² the Parliamentary Assembly, the legislative organ of the Council of Europe, had unanimously agreed on advancing a resolution to allow the alteration of the human genome for therapeutic and preventative purposes.⁹⁶³ With a new, much laxer interpretation of Article 13 of the Oviedo Convention, France is able to proceed with its potential plans to reverse its long-standing ban on inheritable genetic modification. Before turning to review the forming plans to reverse the ban, I will first examine a more

⁹⁶⁰ *Ibid.* See also CDBI, Preparatory Work (n24) CORED14–16/12/92 62-66.

⁹⁶¹ Council of Europe Committee on Bioethics(DH-BIO) “Statement on Genome Editing Technologies”, 8th Meeting 1-4, December 2015 Strasbourg, online: <https://rm.coe.int/168049034a>

⁹⁶² At the time of the announcement, public opinion studies indicated that only about 25% of the public views human genetic modification acceptable. See Commonsense Says, “STAT-Harvard Poll: Americans Say no to ‘Designer Babies’”, *STAT* (11 February 2016), online: <https://www.statnews.com/2016/02/11/stat-harvard-poll-gene-editing/>.

A French survey indicates a similar percent of the French public (24 percent) are in favour of using gene editing to modify the human germline of future children. In that poll, 76 percent of the French public did not approve of legalizing this form of human genetic modification. See Denis Sergent, “Les Français Contre L’utilisation Du Crispr-Cas9 Sur L’embryon Humain”, *Le Croix*, (23/05/2016) online : <https://www.la-croix.com/Sciences/Ethique/Les-Francais-contre-utilisation-Crispr-Cas9-embryon-humain-2016-05-23-1200762246>

⁹⁶³ Council of Europe Committee on Social Affairs, Health and Sustainable Development the Use of New Genetic Technologies in Human Beings (Belgium, SOC). at 2 Online: <http://website-pace.net/documents/19855/3313570/20170426-recours-nouvelles-technologies-génétiques-EN.pdf/75b25d58-a122->

The Council of Europe’s Parliamentary Assembly recognized that the human genetic modification “crosses lines that would be ethically inviolable”. Nevertheless, it has voted to move ahead with a proposal to reverse a ban on a technology that crosses such ethically inviolable lines. The Council of Europe General Assembly further called to “develop a common regulatory and legal framework which is able to balance the potential benefits and risks of these technologies aiming to treat serious diseases, while preventing abuse or adverse effects of genetic technology on human beings.”

Council of Europe Parliamentary Assembly, “Recommendation 2115 (2017) Provisional version the use of new genetic technologies in human beings”. online: <http://assembly.coe.int/nw/xml/XRef/Xref-XML2HTML-EN.asp?fileid=24228&lang=en>

preliminary stage, the legalization of research involving genetically modified human embryos. I will put forward that contrary to claims that such research may be confined to the lab, the development of technologies to alter genes linked to “serious” conditions sets facts on the ground and ultimately leads to increased pressure on decision-makers to approve applications in the clinical context.

Examining the Distinction between Research and Clinical Applications of Inheritable Genetic Modification in a World of Rapid Technological Developments

While nuclear genetic modification for reproductive purposes has not been approved yet, the work on developing the technology to edit the human nuclear genome advances in the research labs. Human genetic modification for research purposes has been made legal after nearly two decades of being banned. French and UK laws prohibited inheritable genetic modification research due to concerns that such research would lead to the development of genetic modification technologies for reproductive purposes – a key outcome of the slippery slope to eugenics.⁹⁶⁴ The previously banned genetic modification research has been made legal with amendments in Section 3A (2) in Schedule 2 of the HFE Act 2008⁹⁶⁵ and the 2013 amendments in Section L. 2151-5 of the French Public Health Code.⁹⁶⁶ The HFEA and the ABM have been issuing licences for labs to carry on research on the modification of human embryos’ DNA.⁹⁶⁷ Consequentially, hundreds of human embryos have been genetically altered as a part of experimental studies.

⁹⁶⁴ See the discussion in chapter 3.

⁹⁶⁵ Section 3A (2) of Schedule 2, HFE Act 2008.

⁹⁶⁶ L. 2151-5 du Code De la Santé Publique. See the amending act Loi n° 2013-715 du 6 août 2013 Modifiant La Loi N° 2011-814 Du 7 Juillet 2011 Relative À La Bioéthique En Autorisant Sous Certaines Conditions La Recherche Sur L’embryon Et Les Cellules Souches Embryonnaires (JO (07/08).

The French Constitutional Council has approved an amendment L 2151-5 to the Code de la Santé Publique to allow for clinical trials in human genetic modification. See Conseil Constitutionnel “Décision n° 2015-727 DC du 21 Janvier 2016 Loi de Modernisation De Notre Système De Santé” online: <https://www.conseil-constitutionnel.fr/actualites/communiqu%C3%A9/decision-n-2015-727-dc-du-21-janvier-2016-communiqu%C3%A9-de-presse>

⁹⁶⁷ The ABM notes France’s international law obligations under the Oviedo convention to ensure the adequate protection of embryos in the research context. See ABM, Encadrement International de la Bioéthique - Actualisation 2016 (Paris : Promoprint, 2016) 54.

Laws in the UK and France authorize regulatory agencies to issue research licenses for inheritable genetic modification in circumstances in which the research could lead to therapeutic advances.⁹⁶⁸

Advocates of research involving genetically modified human embryos imply that such research would not lead to genetic modification for reproductive purposes later down the line. The French National Medical Academy report argues that a strong distinction can be maintained between genetic modification for research and reproductive purposes.⁹⁶⁹ A 2008 HFEA report suggested that research involving genetic modification of human embryos does not necessarily entail the approval of reproductive applications later down the road because the regulatory safeguards are robust.⁹⁷⁰ Scientists involved in such projects profusely deny that such research would lead to a slippery slope to creating “GM babies”.⁹⁷¹ Kathy Niakan, who received an HFEA license to edit the germline genome of human embryos, insists that the regulatory license her team received require that their work will remain confined to the research setting. However, there are reasons to question whether inheritable genetic modification will remain confined to the lab.

Will Resource Intensive Research on Inheritable Genetic Modification Stay Indefinitely in the Lab?

One ought to critically reflect on the implicit assertion that inheritable genetic modification will remain confined to the lab and will not eventually be used for reproductive purposes. Mitochondrial modification provides an obvious precedent of research moving from the lab to the clinic. The HFEA 2005

⁹⁶⁸ For a broader discussion of embryo research policies in the UK and France see Davor Solter et al., *Embryo Research in Pluralistic Europe* (Berlin: Springer Science & Business Media, 2013).

⁹⁶⁹ Académie Nationale De Médecine, “Genetic Editing of Human Germline Cells and Embryos” (2016), online: <http://www.academie-medecine.fr/wp-content/uploads/2016/05/report-genome-editing-ANM-2.pdf>

⁹⁷⁰ HFEA Ethics & Law Advisory Group, HFE Bill (Genetic Modification of Human Embryos in Research) Discussion Paper (9 October 2008).

This line of argumentation itself has shifted. When the HFEA later in 2013 recommended allowing modifying the mitochondrial DNA, it denied such approval is a first step down a slippery slope to modifying the nuclear DNA.

See HFEA (2013) *supra* note 34.

⁹⁷¹ See for instance Alice Park, “UK Approves First Studies Using New Gene Editing Technique”, *Time* (1 February 2016) online: <http://time.com/4200695/crispr-new-gene-editing-on-human-embryos-approved/>.

license for pre-clinical research in mitochondrial modification paved the way to the 2018 first pregnancies with embryos with modified mitochondrial genomes. In the pre-clinical research stage, scientists and the HFEA itself argued that inheritable genetic modification research does not inevitably lead to the use of the technology for reproductive purposes.⁹⁷² Yet over time, the push to commercialize the technology has shown that the regulators' claims are not accurate. The HFEA gave a research license to the applicants at Newcastle University to conduct pre-clinical trials and then clinical trials in mitochondrial modification.⁹⁷³ When the HFEA weighed in on changing the law to allow for mitochondrial modification for reproductive purposes, they relied extensively on the applicants' pre-clinical and clinical trials as proof of safety.⁹⁷⁴ The HFEA decided to dismiss independent animal and human embryological studies that have shown that the technique causes multigenerational epigenetic damage, congenital malformation, behavioural irregularities and potentially cancerous translocations.⁹⁷⁵ Instead, the HFEA decided the technology is safe for use for human reproductive purposes, primarily relying on a few studies, most of which were produced by the applicant or associated research teams.⁹⁷⁶ In 2017, the HFEA granted the first licenses to the applicant's clinic to bring to the world babies whose mitochondrial genome had been altered to prevent myoclonic epilepsy.⁹⁷⁷ In 2018, two women were chosen for the implantation of embryos with the modified mitochondrial DNA for the purpose of producing pregnancies.⁹⁷⁸ The HFEA license to use mitochondrial modification for reproductive

⁹⁷² BBC News, "Embryo with Two Mothers Approved", *BBC* (8 September 2005), online: <http://news.bbc.co.uk/2/hi/health/4225564.stm>.

⁹⁷³ See Human Fertilisation and Embryology Authority, Strategy and Information Directorate. "HFEA Grants Licence to Newcastle Centre at LIFE for Mitochondrial Research - HFEA press release", online: <http://hfearchive.uksouth.cloudapp.azure.com/www.hfea.gov.uk/671.html>.

⁹⁷⁴ See HFEA, "Third Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception: 2014 Update" (London: HFEA, 2014) 34-35.

⁹⁷⁵ *Supra* note 34.

⁹⁷⁶ HFEA *supra* note 965. Also see HFEA (2013) *supra* note 34 at 13-14.

⁹⁷⁷ HFEA, Licensing Committee – Minutes – Centre 0017 (Newcastle Fertility at Life) Variation of Licensed Activities to Include Mitochondrial Pronuclear Transfer (PNT) 9/03/2017.

⁹⁷⁸ Jessica Hamzelou, "First UK Three-Parent Babies Could Be Born This Year", *New Scientist*, (08 February, 2018), online: <https://www.newscientist.com/article/2160120-first-uk-three-parent-babies-could-be-born-this-year/>

purposes provides the first incontestable proof of inheritable genetic modification research that has moved from the laboratory to the clinic. This case sheds light on the market forces and regulatory dynamics that could play a similar role in the potential transition of nuclear genetic modification from the lab into the clinic.

Official sources and senior industry figures further explain how laboratory research is a necessary first step towards developing and commercializing inheritable genetic modification technology. The 1996 European Parliament resolution on genetic modification noted "that there is a close connection between the question of the legality of the research on embryos, and that the development of such interventions [as they] require countless experiments on embryos"⁹⁷⁹ Similarly, Jacques Testart, a geneticist and a former director at the medical research institute INSERM opines that the distinction between research regarding genetic modification and its applications is naïve because it fails to recognize that research is the requisite first step towards clinical applications. The kind of research regulators greenlight often indicates the future direction in which the technology will develop.⁹⁸⁰ Fellow geneticist and also a former director of INSERM, Axel Kahn goes further to criticize the broad remit given under Article 25 of the Bioethics Law for the ABM to approve research. Kahn points out that the wording of Article 25 of the Bioethics Law, which requires research to "likely to lead to major therapeutic progress" is illusory and has been interpreted by the ABM in a very permissive manner. Kahn further argues that this broad remit given to the regulator to approve therapeutic research is a "semantic tactic" to circumvent challenges with ethically problematic biomedical experiments and lets labs set facts on the ground.⁹⁸¹

⁹⁷⁹ The European Parliament resolution affirmed that:

"We must reject and prohibit such interventions [human embryo genetic modification research], which would open definitely the door to eugenics and the instrumentalization of human beings."

European Parliament, Resolution of 20 September 1996 (Official J of 28 October 1996, No. 320, 268 et seq.)

⁹⁸⁰ Jacques Testart, "Résister au Transhumanisme, Pour quoi ? Comment ?" (2/3) *Génétique* (31 May 2017) online : <http://www.genethique.org/fr/jacques-testart-resister-au-transhumanisme-pourquoi-comment-23-67665.html>

⁹⁸¹ Génétique, "Vers L'autorisation D'un Nouveau Diagnostic Pour Améliorer Le Taux De Succès Des FIV En Éliminant Les « Embryons Mal Fichus ?", *Génétique* (14 November, 2015), online : <http://www.genethique.org/fr/vers-lautorisation-dun-nouveau-diagnostic-pour-ameliorer-le-taux-de-succes-des-fiv-en-eliminant-les>.

When global competitiveness to innovate drives research to progress at an accelerating rate, the distinction between research and clinical applications is becoming even blurrier than ever.⁹⁸² The European Commission's statement on gene editing technologies calls into question how relevant is the legal distinction between research and clinical applications when the field of human genetic modification advances so rapidly.⁹⁸³ Geneticist Dominique Stoppa-Lyonnet, a former ABM advisor and CCNE member, commented that genetic modification technology now moves at such a high pace that the boundary between research and clinical applications is rapidly disappearing. Stoppa-Lyonnet comments concerning the disappearing, yet crucial line between research and clinical applications underscores the issues with genetic experimentation with too few safeguards.⁹⁸⁴

The Nuffield Council on Bioethics, an institution with considerable influence over UK biomedical policy,⁹⁸⁵ suggests that research into nuclear DNA modification may subsequently lead to the technology's legalization. The Nuffield Council report reviewed the 2016 HFEA research license⁹⁸⁶ granted to the Francis Crick Institute,⁹⁸⁷ to carry out the first of its kind embryological study using CRISPR-Cas9 gene editing

If research on genetically modified embryos is not intended to be carried in a clinical setting, why is the remit of the license so broad? Laws could have specifically set that licenses will be only granted for basic embryological research without clinical application involving the modification of the human genome.

⁹⁸² See for instance, Netherlands, Commission on Genetic Modification (COGEM), Update to policy report Editing human DNA (31.01.2019) at 8-9. Online: <https://cogem.net/app/uploads/2019/07/190131-02-Update-to-policy-report-Editing-human-DNA.pdf>

⁹⁸³ European Commission *supra* 884.

⁹⁸⁴ Sandrine Cabut, "Dominique Stoppa-Lyonnet, Militante en Gène-éthique" *Le Monde* (21 December, 2014) online : https://www.lemonde.fr/sciences/article/2013/12/23/dominique-stoppa-lyonnet-militante-en-gene-ethique_4339193_1650684.html

I will provide more examples later in this chapter that show how pure research into the technology has been or is in the process of being translated into applications.

⁹⁸⁵ Academics and UK government officials often liken the Nuffield Council on Bioethics to National Bioethics commissions, such as the CCNE. See for instance, Jonathan Montgomery, "The Virtues of National Ethics Committees" (2017) 47:1 Hastings Ctr Rep 24-27.

⁹⁸⁶ HFEA, Licensing Committee – Minutes - Centre 0246 (The Francis Crick Institute at Mill Hill) – Application for Research License Renewal for Research Project R0162) – 14/01/2015 (London, HFEA, 2016).

⁹⁸⁷ In a matter of historical irony, the newly created Francis Crick institute was named after an ardent supporter of eugenics. While being remembered for his key role in describing the DNA molecule double helix structure (which earned him the 1962 Nobel Prize in Physiology), Francis Crick was also a supporter of mass sterilization of people with intellectual and

technology. The report stresses that the lab team can go far beyond basic embryological research into developing future clinical applications. The broad HFEA license gives the Francis Crick Institute a mandate to carry out research into “developing treatments for serious diseases or other serious medical conditions.” The report argues that once genetic modification becomes technically feasible, the laws too are likely to be changed to allow for genetic modification for “serious conditions”. The report foresees potential pressures on the regulatory system to reverse the ban on germline genetic modification. The author of the Nuffield Council’s report, Dr. Andy Greenfield, has a particular knowledge of regulatory and legislative dynamics, as well as research work in the field.⁹⁸⁸ Greenfield is the Chair of the HFEA Licensing Committee (responsible for licensing the Francis Crick lab), a Regional Manager at the Medical Research Council (the public funder of the lab), and a former paid advisor to the Wellcome Trust (the private funder of the lab). In his capacity as the Chair of the HFEA’s Licensing Committee, Greenfield has granted Francis Crick Institute the license to carry out its research. According to Greenfield in his capacity as the Nuffield Council member, the HFEA research license⁹⁸⁹ (granted by Greenfield in his role as a regulator) is a major step towards legalizing inheritable genetic modification for reproductive purposes. Greenfield’s predictions that genetic modification research may lead to changes in the legal status of the technology could very well turn into a reality.⁹⁹⁰

Senior UK officials call for the eventual reversal of the ban on inheritable genetic modification for

physical disabilities. See Francis Crick, “Letter from Francis Crick to Bernard D. Davis” (1970) Original Repository: Wellcome Library for the History and Understanding of Medicine. online: <https://profiles.nlm.nih.gov/ps/access/SCBBPG.pdf>

⁹⁸⁸ In addition, Andy Greenfield is a member of the Hinxton Group, which was co-founded by Julian Savulescu and John Harris and calls the HFEA to deregulate human genetic modification. The bodies Greenfield is involved in (Hinxton Group and Nuffield Council), which call his employer (the HFEA) to deregulate genetic modification technology are funded by his former employer (The Wellcome Trust).

See Sarah Chan et al., “Genome Editing Technologies and Human Germline Genetic Modification: The Hinxton Trust Consensus Statement” (2015) 15:12 Am J Bioethics 44-46. See also HFEA, “Andrew Greenfield”, HFEA online: <http://www.hfea.gov.uk/Andrew-Greenfield.html>.

⁹⁸⁹ HFEA Licence Committee *supra* note 986.

⁹⁹⁰ In a later, 2018 report, the Nuffield Council on Bioethics officially called the UK to reverse its ban on nuclear genetic modification and let the HFEA regulate the technology. The Nuffield Council report cites mitochondrial modification as a precedent for legalizing nuclear genetic modification. See Nuffield Bioethics (2018) *supra* note 147.

reproductive purposes. Much of the argumentation in favour of legalizing inheritable genetic modification relies on the questionable assumption that inheritable genetic modification will relatively soon prove to be safe to be used to bring to term children with altered genomes. Such an assumption regarding the technique's safety is questionable in light of the extensive evidence that inheritable genetic modification is presently not safe.⁹⁹¹ In addition, the embryological research that the HFEA and ABM approve and rely upon do not and cannot examine some of genetic modification's most significant health risks – long-term and multi-generational risks.⁹⁹² Nonetheless, these senior UK officials call the parliament to advance on the path towards legalizing clinical applications in humans. Sir Mark Walport, the UK Chief Scientific Advisor, who has a key role in the HFEA and the government's policy, opined that the UK government should continue its work to remove the legal hurdles to the applications of nuclear genetic modification.⁹⁹³ As a reason for allowing nuclear genetic modification, Sir Walport cited the HFEA's approval of mitochondrial modification.⁹⁹⁴ Sir Walport further explained his reasons by stating that the UK should become a world leader in the cutting edge technology of inheritable genetic modification.⁹⁹⁵ Dr. Rob Buckle, the Chief Science Officer at the UK Medical Research Council has praised the research at the Francis Crick Institute, suggesting the research will eventually move from the lab to the clinic. Dr. Buckle has expressed his support of plans to advance towards clinical applications of inheritable genetic modification in what he calls an "ethical and legally rigorous way".⁹⁹⁶ Further, the five key British public research agencies, including the Medical Research Council, expressed interest in translating research into modifying embryos from the lab to reproductive

⁹⁹¹ Supra note 884.

⁹⁹² See Edward Lanphier et al., "Don't Edit the Human Germ Line" (2015) 519:7544 *Nature News* 410.

⁹⁹³ Sir Mark Walport is also one of the key scientific advisers to the HFEA.

⁹⁹⁴ Sarah Knapton, "Britain Should Lead Way on Genetically Engineered Babies, Says Chief Scientific Adviser", *Guardian*, (9 December 2015) online: <http://www.telegraph.co.uk/news/science/science-news/12042178/Britain-should-lead-way-on-genetically-engineered-babies-says-Chief-Scientific-Adviser.html>.

⁹⁹⁵ *Ibid.*

⁹⁹⁶ James Gallagher, "UK Scientists Edit DNA of Human Embryos", *BBC News* (20 September 2017), online: <http://www.bbc.com/news/health-41269200>.

applications later down the line. As such, they issued a statement encouraging the UK Parliament to consider allowing clinical application after research demonstrates that inheritable genetic modification is safe and has no adverse effects.⁹⁹⁷ The UK parliament is in the process of conducting committee work with the intent of potentially passing a bill to reverse the ban on nuclear genetic modification.⁹⁹⁸

French research agencies acknowledged that research that intends to establish safety and efficacy could pave the way to changing the legal status of the technology.⁹⁹⁹ The scientific and regulatory agencies have been encouraging and funding research into inheritable genetic modification to develop the technology and pave the way to potential clinical applications in the future.¹⁰⁰⁰ A 2016 INSERM report argued that the current government's cautious position is a temporary measure until research indicates that inheritable genetic modification technology is safe and has no considerable adverse effects. INSERM has stated that its research agenda in the field prioritizes improving the safety profile of inheritable genetic modification as a step towards an eventual translation to the clinical setting.¹⁰⁰¹ The ABM recently funded and encouraged pre-clinical research into mitochondrial modification to study the health profile of such modified embryos.¹⁰⁰² Similarly, the French National Medical Academy recommended publicly funding research into embryonic genetic

⁹⁹⁷ The Academy of Medical Science et al., *Genome Editing in Human Cells – Initial Joint Statement*, online: <https://wellcome.ac.uk/sites/default/files/wtp059707.pdf>

⁹⁹⁸ I will discuss this work of the parliamentary committee in the next section.

⁹⁹⁹ Note that the European Commission's Bioethics Advisory Board "cautions against reducing the debate to safety issues and the potential health risks or health benefits of gene editing technologies." "See European Commission *supra* 884

¹⁰⁰⁰ See for instance the funding process for genetic modification research in France, see: European Research Council, *CRISPR-Cas9 research in ERCEA Ethics Process* Filipa Ferraz de Oliveira ERCEA Scientific Officer, (2016) Online: https://www.inserm.fr/sites/default/files/media/entity_documents/Inserm_ComiteEthique_Atelier_201603_Presentation5_MFFerraz-De-Oliveira_0.pdf; See also CCNE, *Avis 129 Contribution du Comité Consultatif National D'éthique À La Révision De La Loi De Bioéthique* (Paris : CCNE 2018-2019) at 36 online: http://www.ccne-ethique.fr/sites/default/files/avis_129_vf.pdf

¹⁰⁰¹ INSERM, "Les Enjeux Éthiques De La Technologie CRISPR-Cas9" INSERM, (30 June 2016) online : <https://www.inserm.fr/index.php/espace-journalistes/les-enjeux-ethiques-de-la-technologie-crispr-cas9>

¹⁰⁰² Génétique, "L'Agence de Biomédecine Encadre Ou Encourage La Recherche Sur L'embryon ? Génétique (2 June 2016), online : <http://www.genethique.org/fr/lagence-de-biomedecine-encadre-ou-encourage-la-recherche-sur-lembryon-63315.html>

modification, including research into creating (chimeric) transgenic human-animal embryos.¹⁰⁰³ The French National Medical Academy report states that as research progresses and the technique is shown to be safe, there could be a need to revisit the French ban on inheritable genetic modification.¹⁰⁰⁴ The parliament could legalize inheritable genetic modification in a manner that is consistent with Article 16-4 of the Code Civil, which would mean allowing genetic modification for “therapeutic” purposes.¹⁰⁰⁵ As one can tell, research on inheritable genetic modification does pave the way to eventual application in humans. As such applications are beginning to become more technically feasible, legal positions are starting to shift with a view to gradually reversing the ban and allowing the inheritable alteration of the human genome. The remaining key question is will this potent technology be regulated effectively to prevent eugenic misuse?

III) The Emerging Regulatory Model: The Use of the Genetic Diagnosis’s Requirements

While the particulars of the regulation of genetic modification have not been fully revealed yet,¹⁰⁰⁶ all evidence strongly indicates that the regulatory model is likely to be very similar to that used for genetic diagnosis. The French Parliamentary Committee on Gene Editing has spent two years reviewing the 2011 Bioethics Law with a view to adding provisions to legalize mitochondrial and nuclear genetic modification. The committee heard testimony from officials at ABM and INSERM as well as the UK’s HFEA, the Francis

¹⁰⁰³ Académie Nationale De Médecine supra note 969 at 15.

Additionally, note the discussion among ethicists about the incalculable long-term psychological, societal and political ramifications of the insertion of animal genes into the human genome. See Françoise Baylis, “‘Babies with Some Animal DNA in Them’: A Woman’s Choice?” (2009) 2:2 Int’l J Fem Approaches Bioethics, 70-72. See also Autumn Fiester, “Ethics” in Jochen Tarpits & Marion Weschka eds., *CHIMBRIDS - Chimeras and Hybrids in Comparative European and International Research: Scientific, Ethical, Philosophical and Legal Aspects* (Berlin: Springer, 2009) 61-77.

¹⁰⁰⁴ Ibid. In its 2018 annual report, the ABM commented that the revised INSERM Ethics Committee and the Academy of Medicine positions are opening the door for the legalization the use of germline genetic modification. See Agence de la biomédecine - Rapport sur l’application de la loi de bioéthique – janvier 2018 at 58 online : https://www.agence-biomedecine.fr/IMG/pdf/rapport_complet_lbe_2017_vde_f_12-01-2018.pdf

¹⁰⁰⁵ Académie Nationale De Médecine supra note 969 at 14.

¹⁰⁰⁶ In the field of technology law, a scholar must look beyond the present into the foreseeable future and examine the potential benefits and risks of new technologies. An important issue such as genetic modification requires a careful examination of the proposed regulatory model in advance, to prevent or to alert about its potential pitfalls.

Crick Institute, Nuffield Council and Medical Research Council, all of which recommended using the exact same regulatory model currently being used for genetic diagnosis.¹⁰⁰⁷ After hearing the testimony, the Committee recommended amending the law to reverse the ban and to give the ABM statutory authority to license genetic modification for conditions that are regarded as serious.¹⁰⁰⁸ Furthermore, the ABM is considering, after the act is revised to give them the authority, to potentially approve mitochondrial modification using the HFEA regulations as a model, which contains the same requirements of genetic risk and the seriousness standard.¹⁰⁰⁹ A similar position has been taken by the French National Medical Academy,¹⁰¹⁰ which recommended regulating inheritable genetic modification in a similar manner to genetic diagnosis - by restricting the technique to editing out genes associated with serious and untreatable conditions. The report, however, does not mention the age of onset requirement, nor does it explicitly mention the considerable risk requirement.¹⁰¹¹

Official UK sources strongly indicate that the regulatory requirements applied to genetic diagnosis technologies will be used to regulate genetic modification. They cite practical reasons such as usefulness and familiarity. As early as 1998, the UK Department of Health's Gene Therapy Advisory Committee Report stated that if genetic modification's safety and ethical challenges were ever to be overcome, the technology could be restricted to serious conditions with no treatment.¹⁰¹² The HFEA has later used genetic diagnosis's

¹⁰⁰⁷ France, Assemblée Nationale et Sénat *supra* note 928.

¹⁰⁰⁸ *Ibid* at 303-304.

¹⁰⁰⁹ Council of Europe, CDDH (R85 Appendix IX Draft Outline for the Analysis On Civil Society and National Human Rights Institutions in View of the Work of the Cddh-Insp. 552016), 12 online: [http://www.coe.int/t/dghl/standardsetting/cddh/CDDH-DOCUMENTS/CDDH\(2016\)R85%20Report%2085th%20meeting%2015-17%20June%202016.pdf](http://www.coe.int/t/dghl/standardsetting/cddh/CDDH-DOCUMENTS/CDDH(2016)R85%20Report%2085th%20meeting%2015-17%20June%202016.pdf)

¹⁰¹⁰ In addition, the US National academy of Sciences and academics in the field argue that genetic modification is likely to be regulated using the same requirements applied to genetic diagnosis. See National Academies of Sciences et al *supra* note 49 at 6. See also Tetsuay Ishii, *supra* note 906 at 48-49. And see Rosario Isasi et al. *supra* note 50 at 337.

¹⁰¹¹ Académie Nationale De Médecine *supra* note 969 at 6.

¹⁰¹² The Gene Therapy Advisory Committee (GTAC), Department of Health, "Report on the Potential Use of Gene Therapy in Utero" (London: GTAC, 1998).

regulatory requirements for mitochondrial modification (albeit, as reviewed above, these regulations are even laxer).¹⁰¹³ Presently, the UK government is in the early stages of considering reversing the ban on nuclear genetic modification. The discussions in the Special House of Commons Committee on Gene Editing similarly indicate that genetic diagnosis's regulatory requirements would be used for genetic modification.¹⁰¹⁴ Moreover, senior HFEA officials such as Andy Greenfield and Joyce Harper further indicate that a similar model of screening for serious conditions will be applied to regulate nuclear genetic modification.¹⁰¹⁵ James Lawford Davis, a senior HFEA legal consultant, reaffirmed this position and further asserted that the "key to that regulatory framework is the distinction between therapeutic and non-therapeutic use".¹⁰¹⁶ However, can the law truly distinguish between the broad and ambiguous concepts of genetic therapy and genetic enhancement? An inability to make this distinction could very well compromise the key legislative goal of preventing human genetic enhancement and eugenics.

IV) Critical Shortcomings in Distinguishing between Genetic Therapeutic and Enhancement

New Wine in Old Bottles: The Regulatory Problems with Using Old Laws for New Technologies

The older genetic diagnosis rules are ill-adapted to handle the new, substantially different genetic modification technologies. The legal theory literature highlights the problems with using older laws to regulate newer, substantially different technologies. Old rules that are specifically tailored to older technologies are not well suited to address the unique challenges and complexities that arise with newer technologies.¹⁰¹⁷ The

¹⁰¹³ See The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

¹⁰¹⁴ House of Commons, Science and Technology Committee *supra* note 49.

¹⁰¹⁵ House of Commons *supra* note 49. Joyce Harper *supra* note 49.

¹⁰¹⁶ *Ibid.*

¹⁰¹⁷ See Lyria Bennett Moses, "Recurring Dilemmas: The Law's Race to Keep Up with Technological Change" (2007) U. Ill. JL Tech. & Pol'y 239; Gary E Marchant, Braden R. Allenby & Joseph R. Herkert, eds, *The Growing Gap Between*

same is true in the case before us, where the genetic diagnosis rules do not, and cannot address the unique technological aspects and challenges with inheritable genetic modification. Unlike genetic diagnosis's embryo selection process, genetic modification actually alters the embryo's genetic material. In the process of genetic modification, certain genes are deleted from the embryo's genome and new genes are inserted in their place.¹⁰¹⁸ Applying genetic diagnosis' rules to genetic modification only regulates the deletion of DNA segments linked to a serious condition. These rules, however, do not pertain to any genes that are inserted into the embryo's genome in the process of genetic modification. As I will soon explain, this legal gap has significant ramifications, since the genes inserted through genetic modification can enhance the child's physical and cognitive traits and abilities.

Therapeutically Enhancing Genes: From Preventing Disability to Creating Superior Ability

Genetic modification can simultaneously both potentially prevent a disease and enhance the child's bodily and physical performance. MIT geneticist George Church argues that genetic modification challenges traditional medical and ethical paradigms by being therapeutic and enhancing simultaneously. Church explains that there are rare, naturally occurring gene alleles that are associated with a significantly lower probability of developing later-onset conditions. These genes, often termed "protective genes", not only

Emerging Technologies and Legal-Ethical Oversight: The Pacing Problem" (New-York: Springer Science & Business Media, 2011).

Moses explains that new technological developments challenge existing regulatory legal structures:

H.L.A. Hart described legal rules as having a penumbra of uncertainty, created in part by the open texture of language. Technological change thus enters onto a stage occupied by an already uncertain law. While it does not create the problem of uncertainty, it may exacerbate it by revealing latent ambiguities in the law and raising new legal questions for which there are no clear answers.

Lyria Bennett. Moses, "Understanding Legal Responses to Technological Change: The Example of in Vitro Fertilization" (2004) 6 Minn. JL Sci. & Tech. 528.

¹⁰¹⁸ In a 2001 report, the HFEA broadly recognized the ethical and technological differences between genetic diagnosis and genetic modification warrant prohibiting the latter. The HFEA has written that genetic modification techniques "represent the real horizon of 'designed' rather than merely 'selected' babies." HFEA, "Ethical Issues in The Creation and Selection of Preimplantation Embryos to Produce Tissue Donors" (London: HFEA, 2001).

potentially prevent diseases but can enhance the performance of a biological system. Church lists a number of such gene variants that can be edited in including LRP2, which can potentially reduce the risk of osteoporosis (while also giving the child extra dense bones that are less breakable) and the A673T allele, which reduces the risk of neurodegenerative diseases like Alzheimer (while also cognitively enhancing the person). The PSCK9 gene can reduce the risk of developing cardiovascular disease in 88 percent below general population levels, while also increasing athletic abilities.¹⁰¹⁹ Additionally, Church's MIT faculty colleague, Eric Lander further highlights that synthetic biology breakthroughs enable the creation of lab-synthesized artificial genes that can both simultaneously treat and enhance individuals by endowing them with novel traits that do not exist in nature.¹⁰²⁰ Genetic modification and artificial gene synthesis, in particular, create novel ways to extend, manipulate and control human traits in ways that are unprecedented. Genetic modification presents a convergence of therapy and enhancement in a way that defies traditional medical and ethical paradigms. I will turn to describe two loopholes in the emerging regulatory model that are likely to enable genetic modifications that are simultaneously therapeutic and enhancing.

A Front Door to Enhancement: Interpretations of the Seriousness Standard to Allow the Insertion of Therapeutic Enhancing “Protective Genes”

Preliminary discussions about genetic modification in France indicate how the law could come to blur the already murky lines between therapy and enhancement. In its submission to the parliament, the ABM has advanced a position that genetic modification could potentially be used to insert protective genes into the child genome.¹⁰²¹ Inserted protective genes would potentially enhance future children's immunity to

¹⁰¹⁹ Supra note 874.

¹⁰²⁰ Eric S. Lander, supra 206 at 6-7.

¹⁰²¹ Assemblée Nationale, “Office Parlementaire D'évaluation Des Choix Scientifiques Et Technologiques -” online : [http://www2.assemblee-nationale.fr/15/les-delegations-comite-et-office-parlementaire/office-parlementaire-d-evaluation-des-choix-scientifiques-et-technologiques/\(block\)/24976](http://www2.assemblee-nationale.fr/15/les-delegations-comite-et-office-parlementaire/office-parlementaire-d-evaluation-des-choix-scientifiques-et-technologiques/(block)/24976)

communicable diseases such as HIV¹⁰²² or increase their physiological resistance to developing a susceptibility to an older age disease (such as Alzheimer).¹⁰²³ The protective gene approach goes significantly beyond susceptibility screening, by not only reducing the genetic risk but at the same time enhancing the person's immunity to certain risk factors above the population's baseline.¹⁰²⁴ The French National Academy of Medicine's report further discusses the potential clinical uses of protective genes to reduce the susceptibility to later-onset conditions such as cancer and neurodegenerative diseases. The report explains that inserting into the embryo's genome protective genes could potentially reduce the risk to develop late-onset conditions that are caused by a multitude of environmental factors and various genes. Inserting into the embryo's genome protective genes could be an alternative to editing the genome numerous times at multiple locations, which is a very risky procedure. Yet, the report explains that there could be considerable ethical challenges with using genetic modification by inserting protective genes because this technique goes far beyond the realm of medicine into the territory of Transhumanism, which aims to transcend the biologic limits of the human species. Inserting protective genes have two "transhuman" goals, of making people more immune to

¹⁰²² The CCR5 gene is associated with reduced risk rates of contracting HIV, but also increased risk to develop other disease, such as West Nile Virus. In addition, most people who may supposedly benefit from germline genetic modification to prevent HIV are living in poor countries where HIV rates are low. In developed countries, where most of those who can afford genetic modification live, the risk of contracting HIV is about 0.3 percent (which is significantly lower than current risk rates that genetic modification would cause a harmful off-target gene mutation). Hence, the clinical benefits of such genetic modifications are highly questionable. See Lander *supra* note 206. See also Hildegard Büning et al., "Consensus Statement of European Societies of Gene and Cell Therapy on the Reported Birth of Genome-Edited Babies in China" (2018) 29:12 *Human Gene Therapy* 1337-1338.

For greater detail see the discussion in chapter 8, which examines the 2018 case of two baby girls that their genome was edited to have the CCR5 gene. The discussion in chapter 8 also examines commentary by biomedical scientists who argue that while editing in the CCR5 gene could also result in the enhancement of human cognitive abilities. If the above described genetic modification ever approved, it would be a significant shift in the interpretation of the seriousness standard because it would set a precedent for genetic modification that does not attempt to prevent a pre-existing condition, but to reduce the possibility of acquiring a condition.

¹⁰²³ See a King's College London Genomic discovery that could potentially both prevent neurodegenerative disease and increase cognitive abilities. Sylvane Desrivieres, et al., "Single Nucleotide Polymorphism in the Neuroplastin Locus Associates with Cortical Thickness and Intellectual Ability in Adolescents" (2015) 20:2 *Molecular Psychiatry* 263.

¹⁰²⁴ Lander *supra* note 206.

prevalent late age conditions (in an attempt to defy the ageing process);¹⁰²⁵ and enhancing these individuals' overall physiological performance beyond normal levels.¹⁰²⁶

The seriousness standard could be potentially read as permitting genetic modification with enhancing and protective inserted genes to potentially prevent late-onset conditions. Since the law does not provide even the most basic definition or guidance regarding the unclear seriousness standard, regulators have no formal impediments that would prevent them from approving editing into the germline genome protective genes. The ABM and the French National Academy of Medicine rather favourable treatment of the topic of inserting protective genes could indicate that such a permissive interpretation of the seriousness standard is not off the table. The Federation of European Academies of Medicine further stated that the current legal position should be re-examined with a view to considering inserting into the human genome protective genes.¹⁰²⁷ The broad regulatory requirements could be interpreted to allow for the approval of the insertion of protective genes on similar grounds to susceptibility screening. That ground would be to further reduce the risk a future child might develop a serious condition later in life. The ABM and HFEA have already approved screening against Alzheimer's and Hypercholesterolemia susceptibility genes on the grounds that they are statistically linked to a risk that a future child would develop a serious disease later in life.¹⁰²⁸ Susceptibility screening attempts to reduce the risk of developing a late-onset condition by selecting against genes that are statistically linked to an increased probability of developing a condition. An entirely different approach to reducing the susceptibility-related risks is by modifying the genome to insert "protective genes" that give the person increased resistance to a particular condition much beyond the average population levels.

¹⁰²⁵ Transhuman medicine's long-term goals of going beyond normal health would be profoundly hard to realize because of the numerous biological, environmental and life style factors involved in the onset of disease.

¹⁰²⁶ Académie Nationale De Médecine *supra* note 969 at 12-13.

¹⁰²⁷ The Federation of European Academies of Medicine - The Application of Genome Editing in Humans" (2017) FEAM, online: <https://www.feam.eu/wp-content/uploads/HumanGenomeEditingFEAMPositionPaper2017.pdf>

¹⁰²⁸ See also HFEA, *supra* note 465; ABM, *supra* note 465.

While the method is different, the overall goal of preventing late-onset, serious conditions exists in both susceptibility screening and inserting protective genes. The ABM could make the case for inserting protective genes as reducing the risk of a serious condition, by reading the regulatory parameters together with the broad Article 16-4 of the Code Civil, which stipulates that genetic modification could be used for therapeutic and preventative purposes.¹⁰²⁹ Regulators can approve inserting protective genes into the child's genome by regarding such enhancing genetic modifications as a form of preventative medicine. Such potential interpretations of the unclear and overbroad seriousness standard to allow editing in protective genes would further blur the lines between therapy and enhancement.

Isasi et al. conflictly argue that the regulation of inheritable genetic modification will avoid the ethical pitfalls of genetic enhancement, while at the same time contending that the new regulations will allow for interventions that have significant enhancing effects. The authors suggest that editing the child's genome to insert the MSTN gene (the "Schwarzenegger" gene) should be regarded by regulators as giving the child immunity from a serious muscle degeneration disease later in life.¹⁰³⁰ What the authors fail to mention is that inserting the MSTN genes would considerably enhance the future child's athletic abilities and muscle mass. While Isasi et al. argue that the law will distinguish therapy from enhancement,¹⁰³¹ their example clearly illustrates the opposite of their claim – of how easy it is to classify impermissible genetic enhancements as permissible gene therapy. If the seriousness standard is interpreted to allow using inserted genes with enhancing properties, such interpretations could very well blur the lines between permissible and impermissible.

¹⁰²⁹ Supra note 25.

¹⁰³⁰ Rosario Isasi supra note 50 at 337.

¹⁰³¹ *Ibid.*

Picture: MSTN “Schwarzenegger” Whippet Dog Compared to a Non-modified Counterpart¹⁰³²



A Backdoor to Genetic Enhancement: A Legal Gap Regarding the Inserted Genes Can Enable Genetic Enhancement

Irrespective if regulators interpret the seriousness standard to enable the approval of editing into the genome “protective” genes, such forms of enhancement could still legally take place. The proposed

¹⁰³² Picture taken from MIT Technology Review, See Antonio Regalado, "First Gene-Edited Dogs Reported in China" *MIT Tech Rev* (October, 19 2015) online: <https://www.technologyreview.com/s/542616/first-gene-edited-dogs-reported-in-china/>

The above picture can also illustrate the potential of using genetic modification such as with the MSTN gene for the purpose of human genetic enhancement.

regulatory model only stipulates that genes linked to a serious disorder may be deleted. It does not make any requirements regarding the genes that are inserted in their place. The law is effectively silent on which new genes may be inserted into the future child's genome in place of those removed, thus opening the door for the insertion of alleles that may give rise to the genetic enhancement of the future child's bodily and cognitive performance. For instance, consider the example of genetic modification for an indication that was already approved by regulators, Alzheimer's susceptibility.¹⁰³³ Prospective parents can attempt to edit out a gene (or genes) linked to increased susceptibility to Alzheimer's while replacing it with variants of the M3 genes that can enhance the child's cognitive abilities.¹⁰³⁴ While such a genetically modified child may or may not eventually develop the disease in question later on in life, they may nevertheless be cognitively enhanced. The backdoor to genetic enhancement loophole could enable practices the law seeks to disallow.

The backdoor to enhancement loophole has considerable abuse potential. Virtually every embryo could be genetically susceptible to a number of serious conditions, which would open the door for replacing relevant genes with protective and enhancing variants. With whole-genome sequencing and the over expansive legal notion of genetic risk,¹⁰³⁵ virtually every embryo could be a candidate for genetic modification to eliminate susceptibilities to conditions such as cancers, neurodegenerative and coronary heart disease. Dr. Andy Greenfield, the Chair of the HFEA Licensing Committee, has commented that attempts to eliminate genes linked to susceptibilities could mean a wide application of genetic modification technologies to prevent conditions that typically appear in old age.¹⁰³⁶ MIT geneticist Eric Lander further indicates that rising medical standards and consumer expectations in the era of genomics could motivate synthetic biologists (like himself)

¹⁰³³ See ABM, *supra* note 465; HFEA, PGD 465; See also HFEA, "Regulation Activity Report", 3 December 2008, online: http://www.hfea.gov.uk/docs/AM_Item9a_Dec08.pdf

¹⁰³⁴ See for instance, See Michael R Johnson Desrivieres et al. *supra* note 182.

¹⁰³⁵ See chapter 5 for a more extensive discussion about the legal change to the risk and age of onset requirements and how it led to creating a highly expensive notion of genetic risk.

¹⁰³⁶ See Oxford Martin School *supra* note 719.

to engineer novel artificial genes that could potentially protect people from older age conditions, while also conferring enhanced properties early on in life.¹⁰³⁷ The status of using artificially synthesized genes, much like any other genes inserted in the process of germline genetic modification is not presently addressed by British and French laws. With the backdoor to enhancement loophole, prospective parents will be able to use a legal gap regarding the inserted genes, thus circumventing the prohibition on human genetic enhancement. To better understand the abuse potential of the two loopholes, one needs to first examine the emerging market to see that much of the demand for the technology will not be in treating single-gene disorders, but rather in interventions for enhancement purposes.

The Market Potential for Inheritable Genetic Modification is in Genetic Enhancement

To fully grasp why prospective parents would turn to therapeutic enhancements, one must first understand consumer demand in these novel markets. Prospective parents will very rarely need genetic modification to prevent disease because the IVF embryos would first routinely undergo genetic diagnosis to screen for congenital malformations or susceptibilities to late-onset conditions.¹⁰³⁸ If as a requisite of the procedure, genetic diagnosis is already employed to screen for a baby free of such mutations, what is the need for genetic modification then? The answer given by a number of life scientists is that rather than to treat, genetic modifications' main market is for genetic enhancement. Biotech CEO Edward Lanphier,¹⁰³⁹

¹⁰³⁷ Lander *supra* note 206 at 5-8.

¹⁰³⁸ See comments by geneticist Eric Lander *supra* note 206 at 4-5.

¹⁰³⁹ Lanphier's company has examined the commercial potential of human germline genetic modification. He explains that:

We've looked at [germ-line engineering] for a disease rationale, and there is none ... You can do it. But there really isn't a medical reason. People say, well, we don't want children born with this, or born with that—but it's a completely false argument and a slippery slope toward much more unacceptable uses.

Quoted in Antonio Regalado, "Rewriting Life - Engineering the Perfect Baby", MIT Tech Rev, (March 5, 2015) online: <https://www.technologyreview.com/s/535661/engineering-the-perfect-baby/>

physician Jeffery Botkin,¹⁰⁴⁰ and molecular biochemist Steven Phillips¹⁰⁴¹ all agree that by already utilizing the cheaper and safer genetic diagnosis technology, genetic modification for disease prevention is not something prospective parents would really need.¹⁰⁴² Similarly, Robert Sparrow explains that parents would not spend hefty sums of money on genetic modification to prevent disease when they already use genetic diagnosis, which is considerably safer and more effective. Prospective parents, however, will spend the money to enhance their future children's mental and physical traits.¹⁰⁴³ Prospective parents' interest in genetic enhancements and non-medical trait selection can already be seen through current examples of sperm donor selection for height and intelligence,¹⁰⁴⁴ as well as, genetic diagnosis in the US for eye colour and certain facial characteristics.¹⁰⁴⁵ Further, the first clinician to perform germline genetic modification resulting in a birth of a child, says he will not stop at treating congenital disease but he intends to use genetic modification to "enable parents to choose their baby's hair or eye colour, or perhaps to improve the child's IQ."¹⁰⁴⁶ Clinics seeking lucrative practice¹⁰⁴⁷ and prospective parents seeking children with more desirable physical and cognitive traits would seemingly benefit from laws that allow a legal way to practice some forms of genetic enhancements. The laws' difficulty in drawing essential lines would enable prospective parents to stress that the

¹⁰⁴⁰ Jeffrey R. Botkin supra note 569 at 25-26.

¹⁰⁴¹ Steve Phillips, "The Goal of Human Embryonic Gene Editing Is Enhancement", *Bioethics.Net*, (August 2, 2017) online: <http://www.bioethics.net/2017/08/the-goal-of-human-embryonic-gene-editing-is-enhancement/http://blogs.tiu.edu/bioethics/2017/08/02/the-goal-of-human-embryonic-gene-editing-is-enhancement/>

¹⁰⁴² Supra notes 1039-1041.

¹⁰⁴³ Robert Sparrow, "Genetically Engineering Humans: A Step Too Far?" (2018) 13:1 *Stroke* 57.

¹⁰⁴⁴ Another indication about the potential market for custom trait selection and genetic enhancement could be seen in certain women who seek particular genetic characteristics in a sperm donor. A study by Sawyer et al. showed that 1,597 women chose sperm for their future child based on non-medical traits such as intelligence (42.7%) and height and ethnicity (40.7%). See Sawyer Neroli et al., "A Survey of 1700 Women Who Formed Their Families Using Donor Spermatozoa" (2013) 27:1 *Reprod Biomed Online* 436-47.

¹⁰⁴⁵ See the discussion in chapter 2. Carolyn Abrahm supra note 158.

¹⁰⁴⁶ Mullin supra note 171.

¹⁰⁴⁷ A Physician survey undertaken by the America College of Physicians states that: "[g]enetic enhancement is certain to be lucrative. In an era of dwindling professional incomes, caused in part by the shift to managed care, physicians and other health care providers may be unable to resist the economic incentives to provide genetic enhancements to those willing to pay for them." Quoted in Maxwell J Mehlman, "How Will We Regulate Genetic Enhancement" in Frances H Miller, *Rights and Resources* (Dartmouth: Ashgate, 2018) at 272.

intended goal of modifying their future child's genome is therapeutic; while still effectively enhancing their future child's looks, athletic and cognitive abilities. As I will be discussing later, the commercial interests in inheritable genetic modification reveal that the technology's market potential is in human genetic enhancement, which raises considerable ethico-legal questions and concerns.

Why Therapeutic Enhancements Are Problematic from an Ethico-Legal Standpoint

A deeper examination of therapeutic enhancements reveals a number of deep ethico-legal problems with such practices. Therapeutic enhancements are *prima facie* at odds with the normative considerations underlying the law for a number of reasons. First, one ought to question the therapeutic benefits of the rather risky procedure of genetic modification to possibly reduce the risk of a communicable disease or susceptibility to late-onset conditions that the child may never even develop.¹⁰⁴⁸ NIH Director, geneticist Francis Collins explains that the likelihood a future child would develop communicable or later-onset conditions (such as HIV, diabetes, or non-familial Alzheimer's) depends much more on environmental rather than genetic factors. This is owing to the fact that genetics only play a small role in the acquisition of these conditions. As such, inserting "protective genes" into the embryo's genome would have very questionable clinical value.¹⁰⁴⁹ Second, while therapeutic enhancements can be seemingly classified as both therapeutic and enhancing, as noted above, consumer interest in the technology is not likely to be driven by therapy (given cheaper and safer methods), but rather enhancement. To illustrate, a future child may never develop the late-onset susceptibility to develop neurodegenerative or muscle disease, but they will have augmented athletic or cognitive performance throughout life. Third, therapeutic enhancements threaten to further blur the lines between therapy and enhancement and essentially create a pathway for regulators to

¹⁰⁴⁸ For a critical review of the ratio between risks and benefits of gene-editing to prevent polygenetic traits, see Elisabeth Hildt, "Human Germline Interventions—Think First" (2016) 7 *Frontiers in Genetics* 81.

¹⁰⁴⁹ Patrick Skerrett, "Experts Debate, are we Playing with Fire We Edit Human Genes?" *STAT* (November 17, 2015) online: <https://www.statnews.com/2015/11/17/gene-editing-embryo-crispr/>

officially or unofficially (through the Backdoor to Genetic Enhancement loophole) permit human genetic enhancement. As a result, regulators would fail to give real effect to the underlying normative considerations of preventing neo-eugenic practices,¹⁰⁵⁰ neo-eugenic related human rights risks and novel ethical and societal concerns. Finally, if regulators give therapeutic enhancements their seal of approval, such approvals could produce a legitimizing and normalizing effect, despite that such practices could be highly contentious.¹⁰⁵¹ Regulatory approval of therapeutically enhancing genetic modifications could be an ethically and legally problematic mission creep ever deeper into the territory of endowing children with “desirable” traits.

Regulators’ Acknowledgments that Lines between Therapy and Enhancement Cannot Be Drawn

How would regulators deal with the loopholes that will allow for using genetic modification for the prohibited purpose of genetic enhancement? A deeper examination of authorities’ comments reveals that even if they were to attempt to close the loopholes described here, regulators would not necessarily be able to accomplish this vital legal task and prohibit genetic enhancement. Regulators themselves have repeatedly commented that drawing effective legal lines between genetic therapy and enhancement is a particularly difficult, and perhaps even an unfeasible task. Baroness Deech, the former Chair of the HFEA suggested that “[a]ny efforts to create logical boundaries between serious and non-serious conditions may be vulnerable to attack. Even distinctions between therapeutic interventions and enhancements are difficult to draw.”¹⁰⁵² The HGC, the HFEA’s ethical advisor, similarly states that it “may be difficult to determine where the lines

¹⁰⁵⁰ The CCNE has opined regarding the insertion of “protective genes” (such as to reduce HIV contraction) that: “Apart from the fact that the indication for this gene editing seems medically unjustified and likely to result in related diseases, this constitutes an intervention in the absence of any disease in embryos the progeny of which will also be modified, and can therefore be likened to a eugenic practice.”

CCNE opinion no. 133 *supra* note 717.

¹⁰⁵¹ For a sociological perspective of how legal institutions could use their power and prestige to legitimize socially contentious practices see Pierre Bourdieu, “The Force of Law: Toward A Sociology of the Juridical Field” (1987) 38:5 *Hastings L J* 814.

¹⁰⁵² Ruth Deech & Anne Smajdor *supra* note 726 at 59.

between preventing harm, and enhancement, is to be drawn.”¹⁰⁵³ The Council of Europe Steering Committee on Bioethics writes: “[t]he Working Party appreciates how difficult it is to draw the line between attempting to perfect the human being and attempting to eliminate recognized abnormalities and diseases.”¹⁰⁵⁴ A European Parliament study writes that: “all attempts to use the therapy-enhancement distinction for delineating medical treatments from human enhancement and for restricting the latter notion to non-medical practices are problematic.”¹⁰⁵⁵ The CCNE further adds that any attempts to draw lines between therapy and enhancement are prone to various criticisms, which threaten the distinction and cast doubts on its ability to set meaningful boundaries.¹⁰⁵⁶ If authorities’ opinions are that this legal distinction cannot be made, how would regulators close the loopholes that would enable human genetic enhancement?

IV) Why Regulators Would Encounter Tremendous Challenges in Distinguishing Genetic Therapy from Enhancement

This section highlights a number of key impediments that will significantly hinder any potential attempts to distinguish therapy from enhancement. Such impediments include a large overlap of the therapy and enhancement categories, the subjectivity of these two elusive social constructs and that their meaning is in constant flux. Moreover, like with the terms “serious” and “high-risk” before them, the subjective notions of therapy and enhancement have proven to be difficult to define by academic experts and by legal institutions (as noted above). Law and policymakers are unlikely to succeed in developing a binding legal definition of these nebulous terms to restrain their interpretation and the application. Attempts to rely on

¹⁰⁵³ HGC (2006) supra note 131 at para 1.25.

¹⁰⁵⁴ Council of Europe Steering Committee on Bioethics, “Convention on the Protection of Human Rights and Dignity of the Human Being with Regard to the application of Biology and Medicine: Convention on Human Rights and Biomedicine” (Ets N°164) (Strasbourg: Council of Europe, 2000) 63.

¹⁰⁵⁵ European Parliament, Science and Technology Options Assessment, *Human Enhancement Study* (Brussels: European Parliament, 2009) 17.

¹⁰⁵⁶ CCNE, Opinion No. 122, the Use of Biomedical Techniques for Neuroenhancement in Healthy Individuals: Ethical Issues, 2-3 online: https://www.ccne-ethique.fr/sites/default/files/publications/ccne.avis_ndeg122eng.pdf.

academic or theoretical approaches are neither probable nor particularly feasible as the literature is highly complicated, contains numerous and often contradictory approaches,¹⁰⁵⁷ hard to operationalize and is prone to significant criticisms. After four decades of intense debate, there is an overall consensus among academics that a stable and coherent distinction between therapy cannot be made.¹⁰⁵⁸

Difficulties in Distinguishing Therapy from Enhancement because of these Notions' Conceptual Uncertainty and Excessive Reliance on Normalcy as a Benchmark

One of the greatest challenges with the therapy/enhancement distinction is its overall reliance on the elusive concept of normalcy. Virtually every variant of the therapy/enhancement distinction uses normalcy as a baseline to assess whether an intervention is therapeutic or enhancing.¹⁰⁵⁹ If a genetic intervention brings an individual with sub-par performance to normal levels, then it is regarded as therapeutic. If a genetic modification brings an individual's performance beyond normal levels in society, then it would be regarded as genetic enhancement.¹⁰⁶⁰ The problem with the reliance on elusive notions of normalcy is that what is considered "normal" in certain social contexts highly depends on the evaluators' subjective viewpoints, belief system, cultural norms and expectations of essential bodily and mental performance.¹⁰⁶¹ Further, the state of available technology also tends to raise expectations of normal bodily and mental performance. Therefore, assessments of whether a particular intervention is therapeutic or enhancing would vary across time, place,

¹⁰⁵⁷ See for instance Ruth Chadwick, "Therapy, Enhancement and Improvement" (2009) 2 Int'l Library of Ethics, Law and Technology 28; Vincent Menuz, et al., "Is Human Enhancement also a Personal Matter?" (2013) 19:1 Sci & Engineering Ethics 173.

¹⁰⁵⁸ For more about the inability of the ethics literature to articulate a defensible distinction between therapy and enhancement see for instance Carl Elliott, "Enhancement Technologies and Identity Ethics" (2004) 41:5 Society 28. See also Eric T Jungest, "Can Enhancement Be Distinguished from Prevention in Genetic Medicine?" (1997) 22 J Med & Phil 125. And see Nuffield Council on Bioethics, 2018 *supra* note 147.

¹⁰⁵⁹ The President's Council on Bioethics, *Beyond Therapy: Biotechnology and the Pursuit of Happiness* (Washington D.C., The President's Council on Bioethics, 2003) 14-15. See also Ruth Chadwick *supra* note 1057 at 22.

¹⁰⁶⁰ *Ibid*

¹⁰⁶¹ Vincent Menuz, Thierry Hurlimann & Béatrice Godard, "Is Human Enhancement also a Personal Matter?" (2013) 19:1 Sci & Engineering Ethics 173.

cultural norms and the state of technological development.¹⁰⁶² For instance, the same intervention of increasing height, making a hairline fuller, boosting sexual performance, improving memory and making a person calmer in social settings could be regarded as either therapeutic or enhancing, depending on the evaluator's subjective viewpoint.¹⁰⁶³ The subjectivity and fluidity of what counts as therapy and enhancement are very likely to lead to inconsistent and potentially arbitrary regulatory classifications.

Approaches that suggest using biostatistical measurements to classify which interventions bring an individual to a “species-typical functioning” or above this baseline¹⁰⁶⁴ have been widely criticized. Critics point out that the seemingly objective “species-typical function” approach is conceptually unclear, inaccurate, arbitrary and reliant on the problematic notion of bodily normalcy. Wasserman and Campbell critique the species-typical functioning approach as misguided as disability and functioning are not really assessed and judged from a purely objective standpoint, but are always dependant on a broader social context and performance expectations.¹⁰⁶⁵ Kingma further continues this line of thinking by showing how according to the species-typical approach, homosexuality could be regarded as a disorder because of the assumption that it interferes with statistically-typical reproduction in healthy men. Species-typical advocates’ attempts to address such criticisms by changing the reference group only highlight that the underlying concept of a reference group is a non-objective, value-laden notion that is prone to biases and manipulations.¹⁰⁶⁶ As a President’s Council of Bioethics report on the topic concludes: “enhancement” and “therapy” are bound up

¹⁰⁶² See Eric T Juengst supra 1058 at 126.

¹⁰⁶³ See for instance Carl Elliot, *Better than Well: American Medicine Meets the American Dream* (New York: W.W Norton, 2004) 124-127.

¹⁰⁶⁴ See Christopher Boorse, “Health as a Theoretical Concept” (1977) 44:4 *Phil Sci* 542; Norman Daniels, “Normal Functioning and the Treatment-Enhancement Distinction” (2000) 9:3 *Cambridge Q of Healthcare Ethics* 309.

¹⁰⁶⁵ David Wasserman & Stephen M. Campbell, “A More “Inclusive” Approach to Enhancement and Disability” in *The Ethics of Ability and Enhancement* (New York: Palgrave Macmillan, 2018) at 25-28.

¹⁰⁶⁶ Elselijn Kingma, “What is it to Be Healthy?” (2007) 67:2 *Analysis* 128-133.

with, and absolutely dependent on, the inherently complicated idea of health and the always-controversial idea of normality.”¹⁰⁶⁷

Most Genetic Enhancements Can be passed off as Therapeutic, Bypassing Legal Restrictions

Regulators would encounter a particular difficulty in distinguishing therapy from enhancement by examining the outcomes of such genetic interventions. Distinguishing between therapy and enhancement based on the interventions’ outcomes would be profoundly difficult because many enhancing interventions have therapeutic outcomes and many therapeutic interventions have enhancing outcomes. Many enhancing interventions can directly or indirectly contribute to the person’s health, while therapeutic interventions can enhance the person’s looks and bodily performance. To illustrate, consider how even a seemingly “easy case” of preventing a congenital malformation that would supposedly be classified as therapeutic can also have strong enhancing outcomes. Genetic modification used to prevent congenital conditions such as Neurofibromatosis (tumours that grow on the nervous system) not only prevents skin lesions and bumps, hearing loss and cataracts but can also be viewed as enhancing the child’s looks, attractiveness, social success and even earning prospects.¹⁰⁶⁸ In such cases, genetic modification can be regarded as both therapeutic and enhancing based on its outcomes. In addition, genetic enhancements can also have therapeutic outcomes. IQ levels are correlated with better health outcomes. Causal explanations suggest that people with higher IQ levels tend to take better care of their health (such as maintaining a better diet and exercising) than their peers and take fewer risks that would adversely affect their health (such as smoking and drinking).¹⁰⁶⁹ Hence, even cognitive enhancement can be presented as having therapeutic outcomes. Even purely cosmetic traits such

¹⁰⁶⁷ The President's Council on Bioethics, *supra* note 122 at 15.

¹⁰⁶⁸ Cases that are less clear cut than Neurofibromatosis exhibit the difficulty of how a seemingly therapeutic intervention has enhancing outcomes. Such cases include genetic interventions on genes responsible for ‘medicalized conditions such as male pattern balding, short stature, tendency to develop skin pigmentation, and secondary sexual characteristics.

¹⁰⁶⁹ Linda S. Gottfredson & Ian J. Deary, "Intelligence Predicts Health and Longevity, But Why?" (2004) 13:1 *Current Directions in Psychological Science* 1-4; Batty, G. David, Ian J. Deary, & Linda S. Gottfredson, "Premorbid (early life) IQ and Later Mortality Risk: Systematic Review" (2007) 17:4 *Annals of Epidemiology* 278; David G. Batty et al., "IQ in Early Adulthood and Mortality by Middle Age: Cohort Study of 1 Million Swedish Men" (2009) 20:1 *Epidemiology* 100.

as height are statistically correlated to better earning and health outcomes. Therefore, when examining cases that are seemingly are “purely therapeutic” or “purely enhancing” interventions through the lens of their outcomes, one can see how blurry and malleable the distinction between these two artificial categories is. Regulators would face tremendous difficulties in setting limits to genetic modification based on their therapeutic or enhancing outcomes.

Problems in Classifying Therapeutic Enhancements – Are they Therapeutic or Enhancing?

In contrast to the assumption that therapy and enhancement are mutually exclusive categories, certain interventions can be both therapeutic and enhancing. The literature often refers to this overlap between therapy and enhancement as “therapeutic enhancements”.¹⁰⁷⁰ Therapeutic enhancements have a dual function – they are both therapeutic and enhancing at the same time.¹⁰⁷¹ First, a therapeutic enhancement prevents a disability (such as modifying the MSTN gene to potentially prevent muscle degeneration), and second, it brings the organism to a state of “super-ability” (such as that the MSTN “Schwarzenegger” gene leads to highly abnormal muscle growth). Therapeutic enhancements show the flawed assumption of the distinction, that therapy and enhancement are mutually exclusive, when in fact they can coincide. The question of how to classify therapeutic enhancements that fall in both categories is not only a difficult academic question but will soon become a difficult challenge for regulators.

Therapeutic enhancements present a particular problem for regulators who will need to classify them as either therapeutic or enhancing. Regulators would need to make a binary decision – can the genetic

¹⁰⁷⁰ Maartje Schermer, “The Dynamics of the Treatment-Enhancement Distinction: ADHD as A Case Study” (2007) 79 *Philosophica* 25.

Industry and consumer interest in therapeutic enhancement can be shown from its parallels in other biomedical industries. The most notable example is the pharmaceutical industry, which is interested in occupying the grey area between therapy and enhancement. The pharmaceutical Industry has aggressively attempted to occupy the territory of therapeutic enhancements in the case of pharmaceuticals such as Viagra and Ritalin.

¹⁰⁷¹ Gregor Wolbring et al., “Emerging Therapeutic Enhancement Enabling Health Technologies and Their Discourses: What Is Discussed Within the Health Domain?” (2013) 1:1 *Healthcare* 20.

modification be approved or not. If the intervention is therapeutic or preventative it would be seemingly approved and if it is enhancing it would be not. However, regulators would find it particularly perplexing to clearly determine which interventions are permissible and which are not in respect to therapeutic enhancements, which could be classified either enhancing or therapeutic. As explained above, the classification of an intervention as either belonging to the therapy or enhancement categories is not done by using objective assessment methods but rather by heavily relying on the assessor's subjective viewpoints, cultural norms and biases. Therapeutic enhancements create a particularly challenging situation for regulators because instead of dealing with a real distinction, regulators would find two categories with considerable overlap. Many therapeutic enhancements could be passed off as either enhancing and impermissible or therapeutic and permissible, based on the adjudicator's subjective views, beliefs, biases and political considerations. This ability to potentially classify therapeutically enhancing genetic modifications as therapeutic opens the door to pressure and manipulation of regulatory decisions.

Regulatee Pressures to Classify Therapeutic Enhancements as “Therapeutic”

Even if regulators attempted to close the therapeutic enhancement loopholes, prospective parents and the industry could still put great pressure on the malleable regulatory classifications and broaden the notion of therapy so it includes therapeutic enhancements. Consistent industry and consumer pressure can result in the interpretation of unclear and overbroad legal standards in a very lax and permissive manner. Hence, even if regulators were ever to attempt to restrict genetic modification only to “therapeutic” inserted genes, the industry and consumers could still try to make the case that therapeutic enhancements should be regarded as therapeutic. Interested parties can argue that despite the enhancing effects (on muscle mass, athleticism, and cognitive performance), building genetic immunity of the unborn child to older age diseases,

should be nevertheless regarded as therapeutic. Geneticist Bertrand Jordan,¹⁰⁷² warns of the likely attempts to classify genetic modification for enhancement purposes as therapy, writing that:

“Strictly therapeutic applications are virtually non-existent. But interventions to reduce the risk of a given disease by introducing protective alleles are quite possible: their promoters will be able to present them as an act of preventive medicine, and thus lead us to a slippery slope which leads to genetic enhancement.”¹⁰⁷³

In an age in which the notion of therapy is being redefined, regulators could come under growing pressure to classify therapeutic enhancements as therapeutic based on arguments that such genetic modifications could purportedly offer new ways to promote public health and generate savings on rising healthcare costs. Such arguments are unproven and questionable (due to the unclear benefits of editing out genes linked to susceptibilities and the technique’s health risks),¹⁰⁷⁴ but nevertheless have been made by academics.¹⁰⁷⁵ Regulators and ethics commissions would be able to present genetic modification with enhancing elements as therapeutic. For instance, the HGC has pointed out that “it could be argued that there is no line [between therapy and enhancement] and that the two are one and the same thing, with the common objective of ensuring that a child is born with a few disadvantages as possible.”¹⁰⁷⁶ According to this logic expressed in the HGC report, many enhancements of the child’s traits could be argued to have redeeming qualities and benefits that seemingly warrant making them allowable. Hence, even if regulators

¹⁰⁷² Bertand Jordan is the discoverer of the human leukocyte antigen (HLA) gene complex and a pioneer in DNA microarray technology. See Bertrand Jordan, “Histoire de l’Inserm”, INSERM online : histoire.inserm.fr/les-femmes-et-les-hommes/bertrand-jordan

¹⁰⁷³ Bertrand Jordan, “Thérapie Génique Germinale, le Retour ? Chroniques Génomiques” (2015) 31 :6/7 Médecine/Sciences 691.

¹⁰⁷⁴ See Patrick Skerrett, “Experts Debate, are we Playing with Fire We Edit Human Genes?” STAT (November 17, 2015) online: <https://www.statnews.com/2015/11/17/gene-editing-embryo-crispr/>.

¹⁰⁷⁵ Eric T. Juengst *supra* 1064 at 125; David B. Resnik & Pamela J. Langer, “Human Germline Gene Therapy Reconsidered” (2001) 12:11 Human Gene Therapy, 1451; LeRoy Walters & Julie Palmer, *the Ethics of Human Gene Therapy* (Oxford University Press, New York 1997); Laura Yenisa Cabrera, “Reframing Human Enhancement: A Population Health Perspective” (2017) 2 Frontiers in Soc 4.

¹⁰⁷⁶ HGC *supra* note 131.

attempted to close the therapeutic enhancement loopholes, prospective parents and the industry could still put great pressure to broaden the notion of therapy so it includes therapeutic enhancements.

Therapy and Enhancement: Changing Social Constructs in a Changing World

The already daunting task of drawing and holding lines would become particularly more challenging as notions of therapy and enhancements themselves would change over time as rapidly advancing technologies redefine expectations of bodily performance. Health anthropologist Linda Hogle explains that the very notion of what is socially considered therapy or enhancement is itself in flux because relentless technological progress changes societal standards, which are commonly used to evaluate the baseline of normalcy. As technologies elevate expectations about physiological and cognitive performance, the baseline for normalcy keeps on being raised to meet ever higher expectation levels until what was previously considered normal falls below the bar and eventually becomes defective.¹⁰⁷⁷ Wolbring points out that more people currently deemed as normal would come to be viewed as “technologically disabled”, due to their failure to keep up with the rising standards of bodily and mental performance in the age of technological enhancement.¹⁰⁷⁸ Similarly, the European Parliament report writes “Moreover, today’s enhancement might become tomorrow’s disease, and what is perceived as a plus today may be seen as compulsory tomorrow.”¹⁰⁷⁹ Prospective parents could feel compelled to genetically enhance their children if they know that a child who fails to meet rising societal expectations might fall behind and be in a disadvantageous position.¹⁰⁸⁰ As the relentless progress of biomedical technology further blurs the faint lines between therapy and enhancement, regulators would face a monumental challenge. Regulators would face difficulties in drawing and holding

¹⁰⁷⁷ Linda F. Hogle, “Emerging Medical Technologies” in *The Handbook of Science and Technology Studies* Hackett et al., eds, (Cambridge: MIT Press, 2008) at 854-859.

¹⁰⁷⁸ Gregor Wolbring, “Therapeutic, Enhancement Enabling, Assistive Devices and the UN Convention on the Rights of Persons with Disabilities: A Missing Lens in the Enhancement Regulation Discourse” (2009) 6:1 J Int’l Biotech Law 198.

¹⁰⁷⁹ European Parliament, *supra* note 1055 at 196-197.

¹⁰⁸⁰ Sandel *supra* note 287.

legal lines to consistently govern a rapidly changing technological field using two social constructs that themselves are in constant flux. In sum, the various challenges flagged above would make it profoundly challenging to close the two loopholes described here as concrete lines between therapy and enhancement are particularly hard, if not nearly impossible to draw and hold.

V) Reflections on the Critical Flaws in Distinguishing Genetic Therapy from Enhancement

The key risk with the line between therapy and enhancement becoming even blurrier is that laws will be ineffective in setting meaningful limits for inheritable genetic modification, a technology with potentially profound long-term ethical, societal and policy ramifications. The two therapeutic enhancement loopholes identified here show the regulatory task of governing inheritable genetic modification will be profoundly challenging. This analysis indicates that the regulation of genetic modification is unlikely to succeed at drawing meaningful and effective lines to distinguish between seemingly permissible genetic therapy and impermissible genetic enhancement. Over time, genetic therapy and enhancement risk of becoming even less distinct terms and their convergence would intensify the major problems in regulating these technologies. The risk, therefore, is that the regulatory system could be marching over time deeper into the legally and ethically problematic human enhancement territory. Human genetic enhancement and the long-term Transhumanist goals of creating people with “custom-tailored”, “desirable” or “superior” traits are the exact eugenic outcomes that parliaments, national ethics committees and regulators worked for decades to prevent. French and UK laws consistently regarded human genetic enhancement as an objectionable eugenic practice that might have detrimental effects on future generations and society. The underlying considerations behind the laws are that heritable genetic modification does not only present unknown adverse health risks to the future generations but also various ethical, human rights and societal risks.¹⁰⁸¹ Yet, the two therapeutic enhancement loopholes could very well mean laws may not be successful

¹⁰⁸¹ See discussion above in section 1 and in chapter 3.

in setting appropriate limits to a technology that has highly transformative effects for human individuals, and as some scholars more broadly suggest — humanity.¹⁰⁸²

Conclusion

This chapter has shown that the regulation of genetic modification would suffer from several problems that would make it particularly prone to overextensive legal change and eugenic misuse. This examination exposed three particular ways in which the use of overbroad, unclear legal standards such as “serious” and “therapeutic” are likely to result in the very same overextensive legal change and eugenic outcomes legislators seek to prevent. The use of genetic diagnosis’s unclear and overbroad regulatory requirements will import a number of line-drawing weaknesses such as the approval of interventions on mild and treatable conditions to the context of genetic modification, which is far more ethically contentious. Furthermore, this chapter has identified and described two new, hard to close loopholes that will enable licensing genetic modifications that are simultaneously therapeutic and enhancing. These three critical shortcomings in the proposed governance model for inheritable genetic modification raise considerable doubts about the laws’ ability to set proper and meaningful limits to such rapidly evolving biotechnologies. Therefore, without effective legal mechanisms to limit genetic modification, fewer hurdles will be left in the way of those seeking to improve upon human heredity.

¹⁰⁸² See Lee M. Silver, “Reprogenetics: Third Millennium Speculation: The Consequences for Humanity When Reproductive Biology and Genetics Are Combined” (2000) 1:5 EMBO Rep 375-378; Jürgen Habermas *supra* note 41.

Chapter Eight

Critical Reevaluation of Genetic Intervention Laws Paves the Way to a Reform

The findings of significant shortcomings in setting effective legal limits call for a critical re-evaluation of genetic intervention laws. This chapter offers three general lessons that are essential for decision-makers, institutions and civil society to advance towards addressing the growing challenges with genetic interventions' governance. First, the lack of awareness about the legal shortcomings among decision-makers, experts and the public hinders a law reform solution. A sober and meaningful political and public discourse requires awareness of the growing problem of overextensive legal change and the regulatory flaws in order for an ameliorative action to be taken. Second, to grasp what is at stake and identify motivations for a law reform, stakeholders require a better understanding of the potential medical, human rights, political and societal ramifications of laws not setting effective limits to these transformative biotechnologies. This chapter highlights some of these potential ramifications such as ineffectiveness in accomplishing the key legislative goal of preventing the gradual emergence of neo-eugenic practices and misuse, the associated ethical and human rights risks, and the risk of state involvement in market-driven neo-eugenic practices. Third, decision-makers should recognize that while the political window of opportunity for a law reform to address the issue at hand is still open, it is rapidly closing. The fast pace at which genetic intervention technologies and markets progress require equally expedient efforts if a law reform is to address this growing problem in a timely and effective manner.

D) The Potential Ramifications of Genetic Intervention Laws Shortcomings in Setting Limits

The Current Rules Are Ineffective in Accomplishing the Key Legislative Goal of Preventing Gradual Emergence of Neo-Eugenics

This thesis's findings of a pattern of overextensive legal change call for a critical re-evaluation of whether genetic intervention laws have achieved their intended goals. As shown in chapter 3, legislatures,

committees and later, regulators worked for decades to create a regulatory system that prevents the growing risk of eugenic misuse of genetic interventions. Lawmakers and regulators have worked to set appropriate limits that would prevent the application of genetic technologies to non-life-threatening genetic conditions. And yet, over time, shifting interpretations of the unclear regulatory standards have significantly weakened their ability to set meaningful boundaries. As a result, regulators frequently approved the very same interventions that each of the rules intended to prohibit (i.e., screening against conditions that are mild, have safe and effective treatment options, not predominantly determined by genes and have an age of onset in the seventh decade of life and beyond). In addition, this thesis has identified two loopholes in the proposed regulatory model for inheritable genetic modification that could enable some of the very same types of eugenic interventions sought to be prohibited - human genetic enhancements. This thesis shows that the legal change pattern risks bringing about many of the same outcomes explicitly sought to be prevented by committees, lawmakers and ethics commissions. In light of these findings, the legal and policy communities would benefit from examining the various regulatory weaknesses exposed in this thesis with the view of correcting these flaws.

Regulators Cannot Both Facilitate Pattern of Overextensive Legal Change and Prevent it at the Same Time

The legislative goal of preventing a gradual emergence of eugenics puts genetic intervention laws in a rather “tight space” in which there is room for some legal change,¹⁰⁸³ but a pattern of accumulative, overextensive legal changes would often run contrary to this goal. Generally speaking, legal change is essential in many legal fields to adjust rules to changing social, economic, and political circumstances,¹⁰⁸⁴ but in the

¹⁰⁸³ Very carefully planned legal change does not necessarily have to compromise the rules’ ability to set meaningful boundaries. Chapter 9 discusses how to accommodate certain legal changes that are consistent with key legislative objective while maintaining the rules’ ability to set meaningful limits.

¹⁰⁸⁴ See for instance, Alan Watson, *Society and Legal Change 2nd Ed* (Philadelphia: Temple University Press, 2010).

specific context of genetic intervention laws, overextensive legal change runs contrary to the laws' very foundational principle of preventing a gradual transition to neo-eugenics and preventing associated medical, human rights and societal risks. Regulators cannot be both inadvertently promoting the overextensive legal change pattern and prevent it at the same time. The two largely contradict each other. The regulators' actions of bringing about overextensive legal change cannot be truly reconciled with the legislative goals of preventing such pattern from occurring.

Recognize the Mission Creep and How It Negatively Impacts Regulators' Ability to Perform their Key Duties

One of the greatest overarching risks is regulators' inadvertent failure to notice the gradual pattern of overextensive legal change and the manner in which it may facilitate the emergence of neo-eugenics. Langdon Winner's concept of technological somnambulism sheds light on how constant advances in genetic intervention technologies can make regulators lose track of the regulation's trajectory and its ramifications. Winner's technological somnambulism concept explains that technological change restructures nearly every aspect of human life from individual habits to larger political and economic conditions. In the process, the focus often gets directed towards improvements in functionality and efficiency of new technologies, while attention is shifted away from their negative implications.¹⁰⁸⁵ However, the ethical and human rights risks, flagged since the early 1980s by leading jurists and ethicists do not all suddenly disappear into thin air. Ethically troubling aspects such as the devaluation of the lives of people with "faulty genes", child commodification and intergenerational harms to the genome and health do not become less relevant but rather more relevant and salient with time. These issues become more salient as the legal change enables controversial applications of reproductive biotechnology to become a reality. The mission creep becomes more pronounced as

¹⁰⁸⁵ Langdon Winner, "Technology as Forms of Life" in David M. Kaplan, ed., *Readings in the Philosophy of Technology* (Oxford: Rowman & Littlefield, 2004) at 107.

decision-makers refocus their attention on facilitating rapid technological advancements and move further away from the normative goals they were tasked to perform. Regulators suggest they have prevented the re-emergence of neo-eugenics,¹⁰⁸⁶ and yet they themselves are those who could be gradually opening the door for its re-emergence. Technological somnambulism could be redirecting regulators' perception to see technological progress as a goal in itself¹⁰⁸⁷ and away from negative outcomes - thus rendering the legal system much less effective in safeguarding the public interest and preventing negative ramifications.

Risks Arising from Indication Expansion of Gene Editing to Interventions with Questionable Risks to Benefits Ratio

The shortcomings of inheritable genetic modification's proposed regulatory model could result in an extension of this techniques' indications to arguably mild, low-risk or treatable conditions, instances in which the purported benefits could be outweighed by its clinical risks.¹⁰⁸⁸ Several factors could drive indications to expand to interventions with lower benefit-risk ratios including the availability of cheaper and safer methods for disease prevention (such as genetic diagnosis) and that genetic modification's main market potential is in "genomic immunizations", therapeutic enhancements and non-medical enhancements.¹⁰⁸⁹ Chapter 7 examined the weaknesses of the proposed regulatory model, which is

¹⁰⁸⁶ See a lengthier discussion about the narrative of the robust boundaries in the introductory chapter. Also see CCNE, Opinion n°107 supra note 48; HFEA 2006, supra note 747.

¹⁰⁸⁷ A shining example of such framing of novel technologies as progress is with looming approval of genetic modification in the UK and France, despite being far much less effective than genetic diagnosis in preventing genetic disease, but far riskier for the health of the future descendants of genetically modified children.

¹⁰⁸⁸ The German ethics committee commented that the editing germline genes linked to susceptibilities, late-onset conditions or those that can be effectively treated or prevented using other methods could raise risk-benefit imbalance problems. See Germany, Deutscher Ethikrat supra note 353 at 30-32.

The principle that benefits must outweigh the risks is core regulatory requirement in biomedical regulatory regimes such as those of the EMA and FDA in the context of authorizing medical products. See for instance the FDA common rule, Code of Federal Regulations (CFR), Title 45 Public Welfare Part 46: Protection of Human Subjects §111(a)(2).

¹⁰⁸⁹ The UK the Parliamentary Office of Science and Technology suggested that scientific and technological developments could eventually lead to the regulatory licensing of germline gene-editing for susceptibilities to develop multi-factorial conditions and even non-medical genetic enhancements. UK Parliament - Parliamentary Office of

particularly prone to indication expansion as it is likely to come under industry and consumer pressure to broadly interpret vague terms such as “serious” and “therapeutic”. These dynamics can be seen in an early illustrative example of the HFEA approval of mitochondrial modification to potentially prevent colour blindness. The HFEA license raises the question of whether the purported benefits (of being able to see all colour shades) justify the potential adverse health effects of modifying the germline genome (such as cancer).¹⁰⁹⁰ Such concerns regarding a benefit-risk imbalance are more likely to plague germline modifications for mild, low risk or treatable conditions (which is where many of the applications of the technology are).

An illustrative example of a likely risk-benefit imbalance is gene-editing to reduce the probability of HIV contraction. This was the stated motivation¹⁰⁹¹ behind the first known case of nuclear germline modification resulting in live births.¹⁰⁹² In late 2018, the He Jiankui affair became an international media sensation after the announcement that the scientist edited the germline genome of two baby girls. The stated purpose of editing the genome of the two baby girls was to reduce (but not eliminate)¹⁰⁹³ their risk of contracting the HIV virus in the future.¹⁰⁹⁴ Scientists, clinicians and ethicists condemned the

Science and Technology, “Human Germline Gene Editing” POSTNOTE Number 611 (London: The Parliamentary Office of Science and Technology, 2020).

¹⁰⁹⁰ See the discussion in chapter 7 about the HFEA approval of mitochondrial modification to prevent colour blindness.

¹⁰⁹¹ Commentators raised questions about the motivations behind He-Jiankui editing CCR5 genes of the two baby girls. Neuroscientific evidence suggests that the CCR5 gene plays an important role in neuroplasticity, learning and memory. A Nature article further suggests that the insertion of the CCR5 gene into the two babies’ genomes may have given them certain cognitive advantages. See David Cyranoski, “Baby Gene Edits Could Affect a Range of Traits” (2018) 10 Nature; See also Miou Zhou, et al. “CCR5 is a Suppressor for Cortical Plasticity and Hippocampal Learning and Memory” (2016) Elife 5: e20985; Mary T Joy, et al. “CCR5 is a Therapeutic Target for Recovery After Stroke and Traumatic Brain Injury” (2019) 176:5 Cell 1143-1157.

¹⁰⁹² Owen G Schaefer, “Rogue Science Strikes Again: the Case of the First Gene-Edited Babies” The Conversation (27 November 2018) online: <https://theconversation.com/rogue-science-strikes-again-the-case-of-the-first-gene-edited-babies-107684>

¹⁰⁹³ The CCR5 deletion mutation only confers resistance to certain strains of HIV. See Lucia Lopalco, “CCR5: From Natural Resistance to A New Anti-HIV Strategy” (2010) 2:2 Viruses 574-600.

Li et al. further note that “HIV is a highly mutable virus and CCR5 is not the only chemokine co-receptor for HIV virus entry.... This result suggests that CCR5 knockout does not necessarily prevent Lulu and Nana [the gene-edited girls] from getting HIV infection.” In Jing-ru Li, et al. “Experiments that led to the First Gene-Edited Babies: The Ethical Failings and The Urgent Need for Better Governance” (2019) 20:1 J Zhejiang U 33.

¹⁰⁹⁴ David Cyranoski & Heidi Ledford, “Genome-Edited Baby Claim Provokes International Outcry” (2018) 563:7733 Nature News 607-608.

irresponsibility of using gene editing techniques when the purported benefits (such as reducing the risk of HIV contraction)¹⁰⁹⁵ are outweighed by the techniques' profound adverse effects.¹⁰⁹⁶ Commentators further argued that germline gene editing is an ineffective method to combat HIV/AIDS because it does not treat existing patients and those who have access to cutting-edge biotechnologies only account for a very small share of HIV carriers worldwide. Additionally, such genomic alterations would not be effective in combatting the AIDS pandemic since they would not be widespread enough to affect gene pools, especially in countries where the HIV virus is more prevalent. Furthermore, other methods offer considerably safer alternatives to editing the germline genome, such as sperm washing to prevent intergenerational transmission and recently developed HIV vaccines to prevent infection.¹⁰⁹⁷ Aside from critiquing the minor and negligible benefits, life scientists also raised the point that intervening on the CCR5 gene poses a number of health risks. Epidemiological studies found the people with the CCR5 gene are more likely to experience severe encephalitis and yellow fever, are twice more likely to die early from multiple sclerosis, more than four times likely to die from influenza¹⁰⁹⁸ and on average have a 3 year shorter

¹⁰⁹⁵ It is also interesting to note that He Jiankui confirmed that he knew that one of the two twin girls, "Nana" only has one functional copy of the CCR5 deletion gene. One copy of the CCR5 deletion gene would not give Nana any immunity to HIV, but may result in her being cognitively enhanced. See Michael La Page, "CRISPR Babies: More Details on the Experiment that Shocked the World" *New Scientist* (28 November 2018) online: <https://www.newscientist.com/article/2186911-crispr-babies-more-details-on-the-experiment-that-shocked-the-world/>

¹⁰⁹⁶ Carrie D Wolinetz & Francis S. Collins, "NIH Supports Call for Moratorium on Clinical Uses of Germline Gene Editing" (2019) 567:7747 *Nature*: 175; Henry T. Greely, "CRISPR'd Babies: Human Germline Genome Editing in The 'He Jiankui Affair'" (2019) 6:1 *J Law and the Biosci* at 154-163. Hervé Chneiweiss, "De Retour De Hong Kong Ou L'éthique À L'heure D'une Génétique D'Augmentation De La Personne Humaine" (2019) 35 :3 *Med Sci* 263-265.

¹⁰⁹⁷ Comité de Bioética de España, "Statement issued by the Spanish Bioethics Committee on Genome Editing in Humans" (2019) CBE, online: <http://assets.comitedebioetica.es/files/documentacion/en/CBE%20On%20Genome%20Editing%20In%20Humans.pdf>; Eric S. Lander, et al., "Adopt a Moratorium on Heritable Genome Editing" (2019) 567:7747 *Nature* 166. Haoyi Wang & Hui Yang, "Gene-Edited Babies: What Went Wrong and What Could Go Wrong" (2019) 17:4 *PLoS Biology* e3000224; Bertrand Jordan, "Bébés CRISPR-Anatomie d'une Transgression" (2019) 35 :3 *Med S* 266-270; Antonio Regalado, "China's CRISPR Babies: Read Exclusive Excerpts from The Unseen Original Research" *MIT Tech Rev*, (December 3, 2019) online: <https://www.technologyreview.com/2019/12/03/131752/chinas-crispr-babies-read-exclusive-excerpts-he-jiankui-paper/>

¹⁰⁹⁸ See David Cyranoski, "Baby Gene Edits Could Affect a Range of Traits" *Nature* (June 25 2020) online: <https://www.nature.com/articles/d41586-018-07713-2>. See also Falcon, A., et al. "CCR5 Deficiency Predisposes to Fatal Outcome in Influenza Virus Infection" (2015) 96:8 *J General Virology* 2074-2078.

life span.¹⁰⁹⁹ In addition, biomedical science experts voiced concerns that germline edited children would be exposed to several significant adverse effects such as congenital malformations, toxicity, weakening the immune system and cancer.¹¹⁰⁰ Moreover, the unpredictable adverse effects of germline modification cannot be fully known at the time or ruled out.¹¹⁰¹ The He Jiankui affair (which ended in a prison sentence)¹¹⁰² illustrates the broader point of the benefit/risk imbalance in editing the genome to reduce HIV contraction, an intervention the UK and French authorities have described as a potentially favourable application.

Regulatory licensing that is not sufficiently attentive to the above challenges can have negative medical, ethical, financial and legal consequences in instances where the purported benefits are outweighed by the clinical risks. First, the ethical principle of non-maleficence is of concern in interventions with a risk-benefit imbalance as the scientific and clinical communities are aware of the potential adverse effects of human germline modification as well as a host of unpredictable outcomes the technique entails. The issue of non-maleficence is further intensified as modifications of the germline genome are inheritable, thus putting at risk the health of not only the first but also successive generations.¹¹⁰³ While technological advances may eventually reduce the likelihood of off-target edits in the embryos,¹¹⁰⁴ challenges would remain in the foreseeable future in regards to long-term and

¹⁰⁹⁹ See also Sara Reardon, "Gene Edits to 'CRISPR Babies' Might Have Shortened Their Life Expectancy" (2019) 570:7759 *Nature* 16.

¹¹⁰⁰ Robert J. Ihry et al., "p53 inhibits CRISPR–Cas9 Engineering in Human Pluripotent Stem Cells" (2018) 24:7 *Nature Med* 939; Michael Kosicki, Kårt Tomberg & Allan Bradley *supra* note 884; Erwei Zuo et al., "Cytosine Base Editor Generates Substantial Off-Target Single-Nucleotide Variants in Mouse Embryos" (2019) 364:6437 *Science* 289-292.

¹¹⁰¹ Certain health risks of the technique may not be known until a later date because unfavourable clinical data may not be published or disclosed. See for instance, Owen Dyer, "Novartis Delayed Notifying about Gene Therapy Data Manipulation until after Approval, FDA Says" (2019) *Brit Med J* 366.

Similarly, Ishii and Beriain note that post-marketing surveillance could be hindered by technical challenges with prenatal testing in detecting off-target effects such as studies do not account for genetic variability of populations. In addition, certain parents may not wish to submit their children to long-term monitoring or may not even disclose to their young children that their genome has been edited. Tetsuya Ishii & Iñigo de Miguel Beriain, "Safety of Germline Genome Editing for Genetically Related "Future" Children as Perceived by Parents" (2019) 2:6 *The CRISPR J* 370-375.

¹¹⁰² Jon Cohen & Dennis Normille, "China Delivers Verdict On Gene Editing of Babies" (2020) 367: 6474 *Science* 130.

¹¹⁰³ Jennifer M Gumer, "The Wisdom of Germline Editing: An Ethical Analysis of the Use of CRISPR-Cas9 to Edit Human Embryos" (2019) 25:2 *The New Bioethics* 137-140.

¹¹⁰⁴ Jennifer A. Doudna, "The Promise and Challenge of Therapeutic Genome Editing" (2020) 578:7794 *Nature* 229-236.

intergenerational health risks.¹¹⁰⁵ Second, the materialization of adverse effects in germline-edited children would create financial costs for families, insurance companies and the public system for treating and tending to the needs of individuals who were negatively impacted.¹¹⁰⁶ Third, legal experts warn that biotechnology companies could be held liable for damages resulting from such procedures as there is readily available knowledge that the modification of the germline genome can cause significant adverse effects.¹¹⁰⁷ Decision-makers can prevent the above-mentioned financial, legal and public health risks by strengthening genetic intervention laws so they are more effective in disallowing germline modifications for mild, low risk or treatable conditions, the very types of interventions more likely to raise concerns regarding risk-benefit imbalance.

Safeguarding Human Rights and Ethics

Overextensive legal change could potentially bring the regulatory system closer to *prima facie* inconsistency with its own underlying ethical and human rights principles. In particular, the regulatory potential trajectory to human genetic enhancement and other novel eugenic interventions has a growing potential of being at odds with international human rights law instruments such as the Oviedo Convention and the UNESCO Universal Declaration of Human Rights and the Genome. These international instruments, as well as British and French legal norms, regard such genetic interventions as potentially derogating from liberty, human dignity and freedom from discrimination. Such risks could intensify as laws gradually change to allow applications such as the selection of traits that have little to nothing to do with the prevention of medical harms or modifying children's genome to enhance their physiological and mental

¹¹⁰⁵ Gumer further adds that early practitioners run the risk of intervening on genes that their function is not fully understood, such as editing-out seemingly deleterious yet beneficial genes, or editing-in genes that may negatively co-interact with the individual's genome and risk their health. See Gumer *supra* note 1103.

¹¹⁰⁶ See for instance see, Barry S. Coller, "Ethics of Human Genome Editing" (2019) 70 *Annual Rev Med* 299.

¹¹⁰⁷ Gary E Marchant, "Legal Risks and Liabilities of Human Gene Editing" (2016) 13:1 *Scitech Lawyer* 26-29; Boston College Law Review Staff, "The Price Tag on Designer Babies: Market Share Liability" (2018) 59 *B.C.L. Rev.* 319, Dorota Krekora-Zajac, "Civil Liability for Damages Related to Germline and Embryo Editing Against the Legal Admissibility of Gene Editing" (2020) 6:1 *Palgrave Communications* 1-8.

performance much beyond the ordinary population levels. To avert human rights and ethical risks arising from neo-eugenics, a law reform can redraw the existing legal lines pertaining to genetic interventions in a clearer, and more effective manner.

A reform to strengthen genetic intervention laws serves the legislative objective of protecting future generations from human rights, ethical and societal risks. Lawmakers, ethical commissions and regulators themselves have identified various risks posed to future generations from the misuse of reproductive biotechnologies. More specifically, authoritative documents identify a host of risks to future generations and society such as negative impacts on equality on inclusion, risks arising from attempts to transcend the biological limits of the human species and the intergenerational health risks inheritable genetic modification pose.¹¹⁰⁸ The restrictions on disallowed genetic interventions (such as on non-serious conditions and genetic enhancements) contribute to protecting future generations and society from these risks by preventing the emergence of neo-eugenic practices. Furthermore, the restrictions on genetic interventions do not limit free and informed choices on whether to seek medical interventions for non-serious conditions such as cosmetic surgeries or somatic gene therapies. Such decisions would give future children a say in matters concerning them, rather than impose on future generations a genetic blueprint of which human characteristics are deemed “desirable” or “undesirable”.¹¹⁰⁹

Preventing the Risk of Future State Involvement in Market-Driven, Neo-Eugenic Practices

The growing genetic intervention market enables the state to intervene on it by incentivizing and nudging parents towards genetic choices that seemingly serve goals such as improving the public health and

¹¹⁰⁸ See the discussion in chapters 3-7.

The risk flagged in authoritative documents illustrate the difference between the interests of future generations and society and the small subset of prospective parents who may wish to select against contentious genetic interventions that are sought to be restricted by the law. As noted throughout the thesis, there is often a poor or questionable medical justification to genetically intervene against mild, treatable and low risk susceptibilities as well as for purposes of human genetic enhancement.

¹¹⁰⁹ Supra notes 14, 907, 912.

productivity of future citizens. As legal change broadens the range of genetic traits offered on the market, so is the state freer to incentivize interventions that supposedly align with public interests. Political theorists warn that state involvement in the heritable characteristics of its future citizens could negatively alter the power relations between the state and the public and constitute a problematic form of social control.¹¹¹⁰ Chapter 2 has argued that one of the most effective safeguards to avoid future state involvement in market-driven neo-eugenics are strong and effective genetic intervention laws that set appropriate limits to genetic trait selection. Hence, a reform of genetic intervention laws is required so that the laws can fulfill their vital function of safeguarding the public's interest by preventing the state from becoming increasingly involved over time in neo-eugenic markets.

II) Lack of Awareness of the Overextensive Legal Changes Hinders a Law Reform Solution

While a considerable part of the public is concerned about the re-emergence of eugenic practices,¹¹¹¹ law reform to draw stronger, clearer legal lines is not anywhere to be seen on the horizon. A key roadblock to a reform is arguably the public's lack of awareness of this growing problem of the regulatory weakness in setting limits. Such awareness is needed to generate sufficient political pressure on decision-makers to set effective legal limits. Without such awareness, growing interest groups relating to genetic intervention technologies will use their power to maintain the status quo of the lenient legal boundaries. The growing economic and political power of the genetic intervention industry over time could make a reform to better regulate the market harder.

¹¹¹⁰ Bertrand Russell *supra* note 41; Francis Fukuyama *supra* note 41.

¹¹¹¹ *Infra* notes -1138-1140.

The public cannot seek a law reform to address the problems with the governance of genetic interventions when it lacks the necessary information for effective engagement and oversight.¹¹¹² With the hectic pace of modern life, limited attention span and the media placing other issues on the daily agenda, it is not easy for the public to gain awareness of the various ways in which our world is rapidly changing. The literature regarding technological literacy and knowledge generally indicates that the public is not aware of the typical technical and complex issues in science and technology governance.¹¹¹³ The lack of public awareness is no different in the rapidly evolving context of genetic intervention technologies.¹¹¹⁴ Research suggests that the public has limited knowledge and information about the topic of genetic interventions in general. For instance, a study amongst 370 patients with hereditary cancer syndrome shows only 24 percent of them knew of the existence of genetic diagnosis.¹¹¹⁵ Another meta-analysis of responses from 4,642 participants shows that only 35 percent are even aware of the existence of genetic diagnosis techniques.¹¹¹⁶ Additional studies indicate that the public not only has limited awareness about genetic intervention technologies but lacks basic information about its benefits, capabilities, limitations and risks.¹¹¹⁷ Furthermore,

¹¹¹² For instance, political theorist Michal Hutchings asserts that even if the public is keenly interested in key policy issues, a lack of essential information impedes public engagement. See V L. Hutchings, *Public Opinion and Democratic Accountability: How Citizens Learn about Politics* (Princeton: Princeton University Press, 2003).

¹¹¹³ See Dietram A Scheufele & Jon Turney, “Messages and Heuristics: How Audiences Form Attitudes about Emerging Technologies” (2006) *Engaging Science: Thoughts, Deeds, Analysis and Action*. See also Dominique Brossard & Matthew C Nisbet, “Deference to Scientific Authority among a Low Information Public: Understanding U.S. Opinion on Agricultural Biotechnology” (2007) 19:1 *Int J Public Opin Res* 24; Dietram A Scheufele, “Communicating Science in Social Settings” (2013) 110:1 Supplement 3 *PNAS* 14040.

¹¹¹⁴ See Cathrine Batias, *Les Risques de l'assistance Médicale à La Procréation : Pourquoi Tant de Mystères ?* (Saint-Denis: Connaissances et Savoirs, 2018) at 32.

¹¹¹⁵ See Thereasa A. Rich, et al., “Comparison of Attitudes Regarding Preimplantation Genetic Diagnosis Among Patients with Hereditary Cancer Syndromes” (2014) 13:2 *Fam. Cancer* 291.

¹¹¹⁶ See Gwendolyn Quinn et al., “High-risk Consumers’ Perceptions of Preimplantation Genetic Diagnosis for Hereditary Cancers: A Systematic Review and Meta-Analysis” (2012) 14:2 *Genetics in Med* 194.

¹¹¹⁷ Celeste M. Condit, “Public Understandings of Genetics and Health” (2010) 77:1 *Clinical Genetics* 1. See also Susanne B Haga et al., “Public Knowledge of and Attitudes toward Genetics and Genetic Testing” (2013) 17:4 *Genetic Testing and Molecular Biomarkers* 327. See also Hudson Kathy, Scott Joan & Andrea Kalfoglou, “Public Awareness and Attitudes about Genetic Technology” *Genetics and Public Policy Center*, Washington DC, 2002).

these studies suggest that considerable parts of the public do not have the requisite technological and scientific literacy skills to evaluate developments in the field of reproductive biotechnology independently.¹¹¹⁸

When most members of the public lack even basic knowledge about genetic intervention technologies, they would find it considerably more challenging to be additionally aware of how these technologies are being regulated.¹¹¹⁹ The technical nature of reproductive biotechnology makes it hard for the public to follow and assess the rapidly changing regulatory landscape of these potent technologies. Understanding the intricacies of this complicated field requires proficiency in ethics, genetic science, technology and the governing laws. Furthermore, the law, industry, and genetic technologies move at such a fast pace that makes it very challenging for all but a small circle of experts to keep abreast of the new developments. Even academics have suggested that the legal boundaries are robust and prevent misuse,¹¹²⁰ so why would the general public, which has much less time and resources, be able to develop proper awareness regarding the regulatory flaws in what seems like a niche, complicated area of the law. With limited knowledge and scientific literacy to assess this complicated topic independently, the public has to rely on intermediaries such as the media to receive information, which is not free from various biases.

The Media and its Biases in Reporting about Genetic Intervention Technologies

The media's reporting about genetic intervention technology tends to oversimplify this complicated topic and to present it in a sensationalist and biased manner.¹¹²¹ Biases in media reporting promotes both

¹¹¹⁸ *Ibid.*

¹¹¹⁹ As an indication of the lack of public knowledge, a Wellcome Trust study found 85 percent of participants did not have basic knowledge about the regulation of somatic germ-line genetic modification. See Wellcome Trust. What do People Think about Gene Therapy? London, *Wellcome Trust* (15 August 2005), 15. online: https://wellcome.ac.uk/sites/default/files/wtx026421_0.pdf

¹¹²⁰ *Supra* note 50.

¹¹²¹ See also Peter Conrad, "Uses of Expertise: Sources, Quotes, and Voice in the Reporting of Genetics in the News" (1999) 8:4 *Public Understanding of Science* 285.

Health sociologist Peter Conrad described the media bias in framing genetic discoveries and innovations in a positive light and dubbed it "genetic optimism". The "Genetic optimism" perspective could distort public perceptions by overemphasizing the benefits of certain genetic technologies while deemphasizing their potential harms and risks.

favourable or unfavourable viewpoints on genetic intervention technologies. As an example of an unfavourable bias, news reporting dubbed HLA typing (creation of a “saviour sibling”) as “designer babies”, a term often reserved for genetic enhancement.¹¹²² Newspapers use metaphors to describe the ethical risk of rampant genetic discrimination using metaphors from popular culture such as references to the futuristic movie *Gattaca*.¹¹²³ In terms of biases in favour of certain interventions, the media has been promoting medicalizing and genetic deterministic views that treat certain bodily and neurological variations as devastating diseases.¹¹²⁴ Further, the media presents the inheritable applications of the CRISPR-Cas9 gene editing technique as safe, effective and cheap¹¹²⁵ when studies have shown it to be presently limited in efficacy, raises considerable safety concerns,¹¹²⁶ and particularly expensive.¹¹²⁷ Such biased and overly simplistic media portrayals of genetic interventions could affect public perceptions of this unravelling biotechnological revolution.

See Peter Conrad, “Genetic Optimism: Framing Genes and Mental Illness in the News” (2001) 25:2 *Culture, Med & Psychiatry* 225.

¹¹²² Alan Petersen, Alison Anderson & Stuart Allan, “Science Fiction/Science Fact: Medical Genetics in News Stories” (2005) 24:3 *New Genetics & Soc’y* 339-340.

¹¹²³ Brigitte Nerlich, Susan Johnson & David D Clarke, “The First ‘Designer Baby’: The Role of Narratives, Cliche’s and Metaphors in the Year 2000 Media Debate” (2003) 12:4 *Science as Culture* 471.

¹¹²⁴ Shah E Mountcastle et al., “Assessing Mass Media Reporting of Disease-Related Genetic Discoveries: Development of an Instrument and Initial Findings” (2003) 24:4 *Science Comm*, 475–478. See also T B. Mepham, *Bioethics: An Introduction for the Biosciences* (New-York: Oxford University Press, 2008) at 137-138. See also Peter Conrad, *The Sociology of Health and Illness* (New-York: Worth Publishers, 2008).

¹¹²⁵ Meaghan O’Keefe et al., “‘Editing’ Genes: A Case Study About How Language Matters in Bioethics” (2015) 15:12 *The Am J Bioethics* 3.

¹¹²⁶ *Supra* note 884.

¹¹²⁷ The high prices of somatic CRISPR/CAS 9 gene editing (generally over 1\$ million USD) are intrinsically tied to the holders’ patent rights pertaining to the technology, see Jacob S. Sherkow, “CRISPR, Patents, and the Public Health” (2017) 90:4 *Yale J Biol Med* 667. See also the US Court of Appeals’ decision about the CRISPR/CAS9 patent dispute: *University of California v. Broad Institute Inc.*, No. 17-1907, Fed. Cir (2018).

See more generally about the expected high costs of germline gene editing, Wilson, Ross C. & Dana Carroll, “The Daunting Economics of Therapeutic Genome Editing” (2019) 2:5 *The CRISPR J* 280-284.

The “Robust” Regulations as the Dominant Narrative in the Media

While the media portrays developments in genetic intervention technologies both positively and negatively, it describes the regulatory system nearly entirely in positive terms. With very rare exceptions,¹¹²⁸ the media portrays the regulation of genetic interventions as a robust control system that was successful in preventing the slippery slope. This over-simplistic, largely inaccurate portrayal of the regulatory system is likely to be a result of the complexity of the subject matter of genetic interventions. Not only is the topic of genetic intervention technologies a highly complicated subject matter, but its regulation adds another layer of complexity. An OECD study about the governance of biotechnologies suggests that the sheer complexity of biotechnology regulation makes people (and journalists alike) accept the narratives promoted by regulators.¹¹²⁹ The complexity¹¹³⁰ of biotechnology regulation and the public’s inability to independently assess the regulators’ statements puts the public (and journalists) in a position that they have to take the regulators’ word.¹¹³¹ Consistent with these observations, the media promotes a simplistic, non-critical portrayal of the regulatory system that nearly exclusively promotes the narrative of the robust legal boundaries. For instance, *Le Monde* describes the ABM’s regulation of genetic diagnosis as a “rigorous

¹¹²⁸ For instance, in a rather rare remark for a person of his stature, the then departing Chair of the CCNE, Didier Sicard remarked: “the practice of PGD progressively leads to the right to have a perfect child.” As he also further commented “Dare we say: France sets up, step by step, a health policy constantly coming closer and closer to eugenics.”

See Didier Sicard, “La France Face au Risque de L’eugénisme”, *Le Monde* 4-5 Février 2007.

Professor Robert Winston, a member of the House of Lords and former genetic diagnosis clinician suggested the HFEA’s failure to regulate will result in a neo-eugenic market in which parents will “modify their children, enhance their intelligence, their strength and their beauty and all the other so-called desirable characteristics.” See Buckland, *supra* note 132.

¹¹²⁹ David E. Winickoff, “Public Acceptance and Emerging Production Technologies” (2017) in *The Next Production Revolution Implications for Governments and Business: Implications for Governments and Business* (Paris: OECD Publishing, 2017) 277.

¹¹³⁰ The literature discussed several cognitive biases that could lead to challenges in the understanding complex subject matter (such as biotechnology regulation) including anchoring, overconfidence and availability biases. See for instance: Amos Tversky & Daniel Kahneman, *supra* note 645; Daniel Kahneman, “Reference Points, Anchors, Norms, and Mixed Feelings” (1992) 51:2 *Organizational Behav & Human Decision Processes* 296-312. For a discussion of these cognitive biases in the public policy context see Colin R. Kuehnhanss, “The Challenges of Behavioural Insights for Effective Policy Design” (2019) 38:1 *Pol’y and Soc’y* 14-40.

¹¹³¹ *Ibid.*

control system”¹¹³² *Libération* magazine published a piece by clinicians René Frydman, Samir Hamamah and Nelly Achour-Frydman, who asserted that slippery slope concerns are simply misguided because of the tight regulatory regime the ABM imposes.¹¹³³ BBC News reinforces the narrative that the approval of mitochondrial modification will be done within a careful, strictly regulated, robust control system.¹¹³⁴ Sky News further echoes the narrative of the robust regime by exclusively presenting statements by regulators and geneticists who argue that the HFEA’s robust regulations of mitochondrial modification (which is surprisingly even laxer than that of genetic diagnosis) will certainly prevent a “slippery slope towards designer babies”.¹¹³⁵ With such a portrayal of the regulations as a robust system that have prevented the slippery slope, the media paints a picture, which is unfortunately inconsistent with the available facts. The public, which lacks the technological literacy to assess this complicated subject matter independently, could put its faith in the media’s overstated claims and the potentially misleading narrative it promotes.

The Public Cannot Object to What It Knows Not Of

The lack of awareness and a belief in the narrative of the robust regulatory boundaries has a chilling effect on critical public discourse and political engagement, which are crucial for a law reform to take place.

The public would not seek a solution if it is not even aware of the problem.¹¹³⁶ The public will have a hard

¹¹³² Paul Benkimoun & Cécile Prieur *supra* note 51.

¹¹³³ René Frydman, Samir Hamamah & Nelly Achour-Frydman “Des Moyens Pour Le Diagnostic Pré-Implantatoire”, *Libération.fr* (1 July 2009), online : http://www.liberation.fr/societe/2009/07/01/des-moyens-pour-le-diagnostic-pre-implantatoire_567916. The clinicians argue that: “PGD is not a eugenic policy because it is not intended to eradicate a mutation. To allow the birth of a child free whether or not it carries the genetic trait.” (However, contrary to this statement, genetic diagnosis at that time was already approved for screening against unaffected gene carriers.) The article ends by stating that genetic diagnosis poses no risk of a slippery slope. In the authors’ eyes, the only ethical problem is prospective parents’ lack of access to this technology.

¹¹³⁴ James Gallagher *supra* note 51.

¹¹³⁵ Thomas Moore, “IVF: ‘Three-Parent’ Babies Hurdle Cleared”, *Sky News* online: <https://news.sky.com/story/ivf-three-parent-babies-hurdle-cleared-10451231>.

¹¹³⁶ Michelle Chowdhury makes a similar argument that the lack of public awareness to the non-competitive state of the economy, and its harmful effects on the prices of goods and services and corruption impedes a law reform in anti-trust law to make the economy more competitive. See Richard Whish & Christopher Townley, *New Competition Jurisdictions: Shaping Policies and Building Institutions* (Cheltenham: Edward Elgar Publishing, 2012) 78-80.

time to mobilize to take political action without a well-informed sober public discourse and an understanding of the problems at hand. The key missing piece of information in the debate about genetic technologies is that the laws are providing ever fewer and weaker safeguards against emerging human heredity improvement practices. Given the public's persistent concerns about the slippery slope, a more critical public discourse would likely have developed had the public had been fully aware of the regulatory weaknesses and its ramifications. However, the public is largely unaware of the considerable challenges with the legal governance of genetic intervention technologies, which intensify over time. And those seeking more information will often encounter the narrative of the robust boundaries, which tends to pacify the audience and create a feeling that a law reform is not required.

Public Disapproval as a Key Driver of a Potential Law Reform

Had the public (and its elected governments)¹¹³⁷ been fully aware of the overextensive legal changes, they could have exercised their democratic rights and worked towards a law reform. Public opinion studies suggest that about 70 percent of the public oppose the selection of non-serious traits,¹¹³⁸ over 85 percent of the public disapproves of genetic enhancement¹¹³⁹ and over 75 percent of the public are concerned about a

¹¹³⁷ Lawmakers are also directly exposed to this narrative of robust regulatory boundaries directly through their contract with regulators. This narrative could create an incorrect impression that regulations set effective boundaries and that no reform is needed to set stronger boundaries. If lawmakers were aware that regulators could enable problematic applications (such as human genetic enhancement), they could have acted and set stronger legal limits.

¹¹³⁸ See Patrick Sturgis, Helen Cooper & Chris Fife-Schaw, "Attitudes to Biotechnology: Estimating the Opinions of a Better-Informed Public" (2005) 4:1 *New Genetics & Soc'y* 42; Chloe Miller, Jenny Hewison & Stephen Morley *supra* note 517; Cara Mand et al., "Genetic Selection for Deafness: The Views of Hearing Children of Deaf Adults" (2009) 35:12 *J Med Ethics* 722.

¹¹³⁹ See Commonsense Says, "STAT-Harvard Poll: Americans Say no to 'Designer Babies'", *STAT* (11 February 2016), online: <https://www.statnews.com/2016/02/11/stat-harvard-poll-gene-editing>; Denis Sargent *supra*; Feighanne Hathaway, Esther Burns & Harry Ostrer, "Consumers' Desire towards Current and Prospective Reproductive Genetic Testing" (2009) 18:2 *J Genet Couns* 137; Mairi Levitt & Fiona K O'Neill, "Making Human Better and Making Better Humans" (2010) 6:1 *Genomics, Soc'y & Pol'y* 10.

slippery slope to eugenics.¹¹⁴⁰ Public opinion studies¹¹⁴¹ further cast considerable doubt on whether the public supports applications approved by regulators, such as screening against gens linked to susceptibilities, treatable conditions and mild conditions.¹¹⁴² These public opinion insights are significant in indicating that regulatory decisions at the time of legal changes had taken place and the potential future change trajectory is lacking in public approval.

With such high numbers expressing disapproval, politicians could not have remained indifferent to the public's discontent. Democratic governments, due to their need to be in tune with public opinion,¹¹⁴³ would have been under greater pressure to respond to the public's concerns¹¹⁴⁴ about the regulations' eugenic

¹¹⁴⁰ See Patricia E. Hershberger & Penny F. Pierce supra note 624 at 61-62.; Andrea L. Kalfoglou, Joan Scott & Kathy Hudson. "Attitudes about Preconception Sex Selection: A Focus Group Study with Americans" (2008) 23:12 Hum Reprod 2733-2735; Alain Graf, "Rapport Final des Etats généraux de la bioéthique. (Part I)", 2009 39-40 online, http://www.sante.gouv.fr/IMG/pdf/Rapport_final_bioethique_2_juillet09.pdf; Hudson, Kathy L. "Preimplantation Genetic Diagnosis: Public Policy and Public Attitudes" (2006) 85:6 Fertility and Sterility 1643; Cary Funk, et al., "U.S. Public Wary of Biomedical Technologies to 'Enhance' Human Abilities", (26 July 2016), Pew Research Center: Internet, Science & Tech online: <http://www.pewinternet.org/2016/07/26/u-s-public-wary-of-biomedical-technologies-to-enhance-human-abilities/>.

¹¹⁴¹ In addition, qualitative research potentially indicates that public disapproval of certain changes is linked to many of the same ethical concerns flagged by the legal system itself including the destruction of embryos, child commodification and instrumentalisation. The qualitative data compliments the quantitative data by potentially offering explanations as to why the public has reservations and concerns about the regulators assuming a more permissive approach to genetic interventions. Infra note 1144.

¹¹⁴² Research conducted for Human Fertilisation and Embryology Authority by MORI, Sex Selection – Public Consultation (2003) Online: http://www.hfea.gov.uk/docs/Appendix_F.pdf; Protière supra note 613, 379-404; Lammens, Chantal et al. "Attitude Towards Pre-Implantation Genetic Diagnosis for Hereditary Cancer" (2009) 8:4 Familial Cancer, 457.

¹¹⁴³ See James S Fishkin, *The Voice of the People: Public Opinion and Democracy* (New Haven: Yale University Press, 1997). See also S N Soroka, & C Wlezien, *Degrees of Democracy: Politics, Public Opinion, and Policy* (New-York: Cambridge University Press, 2010). See also James A. Stimson, "Party Government and Responsiveness" in *Democracy, Accountability, and Representation*, Przeworski, A, S C Stokes & B Manin eds. (Cambridge: Cambridge University Press, 1999) at 197.

¹¹⁴⁴ Several scholars suggested that legislative and regulatory changes should not be hindered by negative public opinion because it is likely the result of ignorance and unfounded fears about the misuse of reproductive biotechnology. Timothy Caulfield, Lory P Knowles & Eric M Meslin, "Law and Policy in the Era of Reproductive Genetics" (2004) 30:4 J Med Ethics 414-416; John Harris supra note 942. See Martin H Johnson & Kerry Petersen, "Public Interest or Public Meddling? Towards an Objective Framework for the Regulation of Assisted Reproduction Technologies" (2008) 23:3 Hum Repro 716.

In contrast to the portrayals of public opinion as being driven by fear and ignorance about biotechnologies, quantitative studies reveal the public does reflect, reason, and grapple with the ethical dilemmas and challenges of reproductive genetics. See Kalfoglou Scott & Hudson supra note 1140; Jackie Leach Scully, Tom Shakespeare & Sarah Banks supra note 308. Tom Shakespeare, "Ethics Watch" (2005) 6:9 Nature Reviews Genetics 666.

trajectory. Otherwise, the public's dissatisfaction with the governments' lack of action could have manifested through other forms such as public protest,¹¹⁴⁵ petitions, direct pressure on parliamentary representatives and citizen groups involved in regulatory and legislative discourse (which would have been relevant given the present revisions of the UK and French laws). If there was sufficient awareness, the public's discontent and potential mobilization could have otherwise pressured governments to act and draw stronger legal lines to correct the problem. Elected governments would have been under greater pressure to scrutinize regulatory decisions. Regulators too, under greater public and political scrutiny, would likely have been under greater pressure to redraw the malleable legal lines.

Is Public Disapproval Sufficient to Propel Governments to Set Stronger Legal Boundaries?

Keen observers could question the degree to which public awareness and engagement has the power to lead to legislative changes. Lawrence Lessig doubts the effect public pressure has on governments in the present state of affairs when even greater counter pressure is operated on them by industry interest groups to block law reform efforts.¹¹⁴⁶ Industry interest groups often have at their disposal well-oiled lobbying machines to reach and affect decision-makers in order to block law reforms that are against their strategic and commercial interests. A variety of proposed reforms to tighten financial regulations, enhance environmental standards and promote healthier food legislation have been trampled by the well-oiled machine of special interest lobbyists.¹¹⁴⁷

¹¹⁴⁵ After the French government held a preliminary hearing on CRISPR/Cas 9, Vita Alliance held a peaceful demonstration against the application of the technology to modify the germline human genome. The protest was a rare occasion and did not receive much media attention. See "Stop Bébé GM : Campagne Citoyenne D'alerte sur CRISPR-Cas9," (May 2016) online : www.alliancevita.org/2016/05/stop-bebe-ogm-une-campagne-citoyenne-dalerte-sur-cispr-cas9/

¹¹⁴⁶ Laurence Lessig, *Republic, Lost: Version 2.0* (New York: Grand Central Publishing, 2015).

¹¹⁴⁷ Ronald J. Hrebenar, & Bryson B Morgan, *Lobbying in America: A Reference Handbook* (Santa Barbara: ABC-CLIO, 2009); Kenneth Ainsworth, Scott H. Ainsworth & Erik Godwin, *Lobbying and Policymaking: The Public Pursuit of Private Interests* (Los Angeles: SAGE Publications, 2012).

Nevertheless, public pressure has already proven itself as a force that has led governments to take action regarding genetic interventions. As discussed in chapter 3, the public's concerns about the slippery slope to eugenics were one of the main drivers for the very enactment of genetic intervention laws in the first place. Despite the public's lack of organization, mobilization and despite industry lobbies pushing for a permissive regulatory environment, genetic intervention laws were passed by parliaments and implemented.¹¹⁴⁸ Hence, public concerns about the misuse of genetic intervention technologies have already proved capable of mobilizing governments to act.

However, interest groups' political weight has grown since the 1980s. What was once a collection of a few private clinics and small start-up biotech companies has grown over the past decades to include large labs and multinational companies (which have deep ties to the well-oiled pharma lobby).¹¹⁴⁹ Nevertheless, the industry's current vested interest in genetic enhancement is still relatively small because the therapeutic applications of gene editing receive a priority at the moment. The industry, which is still seeking support for inheritable genetic modification, is less likely to resist at this time bills that would set stronger limits (than the nebulous "serious" and "therapeutic" standards) to disallow human genetic enhancement. Public pressure could be particularly effective at this critical juncture when governments are seeking to reverse the ban on inheritable genetic modification. If a sufficient degree of public pressure was applied to governments, such pressure could still offset some of the industry influence and result in a reform to draw better, stronger safeguards from the misuse of these potent technologies.

The Need for a Better Informed Discourse about the Flaws of Genetic Intervention Laws

The path to reform goes through greater awareness of the existing laws' various problems and

¹¹⁴⁸ See Melanie Latham *supra* note 90; Svea Luise Herrmann, *Policy Debates on Reprogenetics: The Problematisation of New Research in Great Britain and Germany* (Frankfurt: Campus Verlag, 2009) at 51-61; McLean & Elliston *supra* note 463 at 59-62.

¹¹⁴⁹ See Nicolas Rasmussen, *Gene Jockeys: Life Science and the Rise of Biotech Enterprise* (Baltimore: Johns Hopkins University Press, 2014).

shortcomings. For a reform to happen, the public and its elected officials must first know and understand that genetic intervention laws' ability to set meaningful limits has been significantly weakened over the years. With this thesis, I have attempted to pave the way to a more accurate discourse by pointing the spotlight to the illusory narrative promoted by regulators that the "robust" regulatory regime has successfully prevented the slippery slope to eugenics. This narrative is further echoed by journalists, academics and within policy circles, leading laypersons to incorrectly believe that the regulations are setting robust safeguards and no reform is needed. Understanding the flaws of genetic intervention laws is a critical first step to raise public and political awareness of this important technology governance problem. With greater awareness of the weaknesses of the current regulation of genetic intervention, public and political discourse would be able to reflect in a meaningful way on some of the greatest challenges in the governance of genetic intervention technologies.¹¹⁵⁰ Greater awareness of these significant shortcomings is a vital step towards making better-informed choices with powerful technologies that could have profound and lasting effects on future society.

III) The Pressing Timeline for Reforming Genetic Intervention Laws

If a law reform is to effectively address and ameliorate the regulatory flaws, then the time to do so is short. To advance with reform plans, lawmakers will need to act with expediency, for the landscape of genetic intervention technologies is changing rapidly. The industry and its regulation are changing at a fast pace, charting new grounds and setting more precedents. With every year that passes, regulators are approving more of the contentious intervention the rules intended to disallow. At the same time, democratic and public

¹¹⁵⁰ The Council of Europe, the WHO and UNESCO all recently stressed the importance of a public debate about the regulatory limits to genetic modification. Council of Europe - Committee on Social Affairs, "Health and Sustainable Development the Use of New Genetic Technologies in Human Beings" (Brussels: Council of Europe, 2017) "WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing" (18-19 March 2019) online: <https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Governance-1-paper-March-19.pdf>; UNESCO, "UNESCO Panel of Experts Calls For Ban on "Editing" of Human DNA to Avoid Unethical Tampering with Hereditary Traits," UNESCO (6/10/2015) online: <https://en.unesco.org/news/unesco-panel-experts-calls-ban-editing-human-dna-avoid-unethical-tampering-hereditary-traits>

debates are lagging behind and struggling to catch up with the rapidity of biotechnological innovation.¹¹⁵¹ This rapid rate at which new genetic technologies are launched threatens to exceed the pace of public discourse.¹¹⁵² And yet, the biotechnological revolution keeps on unfolding, moving ever closer to supposedly improving human heredity. The more the market offers greater trait selection and becomes more established and deeper entrenched in economic, political and social structures, the harder it will be to reverse the course that the technology is charting.¹¹⁵³

Interest groups' growing stakes in genetic intervention markets are reducing the likelihood of a law reform to set clear and effective legal limits.¹¹⁵⁴ The more regulators "liberalize" the market in child genetics, the more interest groups' stakes in these markets is likely to grow. The industry stands to profit from those highly lucrative markets, especially as it gradually turns to enhance future children's athletic, physical and cognitive performance. With a growing reliance on this market, the industry is likely to intensely lobby to stifle reform attempts to "turn back the clock" on this lucrative business. The growth of interest groups could undermine political attempts to pass an effective reform.¹¹⁵⁵ As a result, the political window of opportunity for an effective law reform is beginning to close.¹¹⁵⁶

¹¹⁵¹ For instance, Baylis and Ikemoto write that public discourse and engagement "cannot occur while scientists and clinicians forge ahead with germline modifications and disregard the views, interests, and concerns of the many communities to whom germline modification matters." See Françoise Baylis & Lisa Ikemoto, "The Council of Europe and the Prohibition on Human Germline Genome Editing" (2017) 18:12 EMBO rep 2084.

¹¹⁵² Azria & Grangé supra note 53.

¹¹⁵³ Technology philosopher and historian Thomas P Hughes developed the theory of technological momentum, which explains how the more technology becomes entrenched in social structures and transforms them, the harder it is to control the course of technological evolution. See Thomas P. Hughes, "Technological momentum" in Merritt Roe Smith and Leo Marx, eds, *Does Technology Drive History? The Dilemma of Technological Determinism* (Cambridge: MIT Press, 1994) at 101–113.

¹¹⁵⁴ Even an anonymous Spanish regulator has commented on the situation that "there are economic interests would prefer avoiding setting real limits." See Pavone & Arias supra note 653 at 244.

¹¹⁵⁵ For a more detailed analysis of how the growth of interest groups are responsible for blocking law reform attempts, See Jeffrey M Berry & Clyde Wilcox, *The Interest Group Society* (Oxford: Routledge, 2015) at 16–21.

¹¹⁵⁶ For more about the importance of the timing of regulating emerging technology before the political window of opportunity closes, See Gaia Bernstein, "Regulating Reproductive Technologies: Timing, Uncertainty, and Donor Anonymity" (2010) 90 BUL Rev. 1198–1201.

Conclusion

Biomedical regulators, which were entrusted with a mandate of preventing a mission creep, have arguably played a noteworthy role in its very materialization. Despite consistent warnings by lawmakers and official commissions over the years, regulators' licensing policy gradually shifted from the prevention of lethal congenital malformation to interventions that have increasingly less to do with the future child's health. On the horizon, the shortcomings in the proposed regulatory model for genetic modification could potentially enable the approval within the broad remit of "therapy", the genetic enhancement of human physiological and cognitive traits. Yet, the lack of awareness that overextensive legal change is happening and this pattern's ramifications hinders a law reform solution. A meaningful and sober political and public discourse requires awareness of the growing problem of overextensive legal change in order for ameliorative action to be taken. Legal decision-makers will find important reasons to consider a reform, as the existing legal governance of genetic intervention technologies presents a number of considerable problems. Legal institutions should consider the various ramifications of the regulatory insufficiency including ineffectiveness in accomplishing the key legislative goal of preventing a mission creep, the associated ethical and human rights risks and the growing risk of state involvement in neo-eugenic markets.¹¹⁵⁷ Equally, decision-makers should recognize that while the political window of opportunity for a law reform to correct the problem is still open, it is rapidly closing. To effectively correct the critical flaws in the regulation of genetic intervention technologies, law reform efforts must commence soon, for our rapidly changing world will not wait.

¹¹⁵⁷ These above mentioned risks underscore the importance of strengthening the governance of genetic interventions by setting clearer and effective legal limits. The next chapter offers a blueprint for a reform intended to address the above flagged challenges.

Chapter Nine – Recommendations

A Blueprint for a Reform to Genetic Intervention Laws

This chapter provides a newly developed blueprint for a law reform. The reform aims to offer a new avenue to advance towards the key policy goal of preventing the misuse of genetic intervention technologies by strengthening its governance. The reform is based on two general lessons regarding the qualities genetic intervention laws require in order to set more effective and durable limits. First, to improve on the conceptual design of existing rules, lawmakers need to identify clearer normative and clinical distinctions capable of better determining which genetic interventions are permissible and impermissible. Second, the legislative drafting process needs to place greater attention on making careful language choices that express the laws' underlying conceptual distinctions with clarity, reduced subjectivity and an explicitly delimited scope. This chapter then translates these two general lessons about drawing clearer and more durable legal limits into practical recommendations. Rather than attempting to draw the “ideal” legal lines, it offers practical advice and concrete examples for how to substantially redesign the existing rules to enhance their clarity and to improve their ability to set durable limits. The reform includes specific suggestions for legislative amendments, clearer conceptual distinctions and newly developed legal tests. In particular, a new legal test described here can considerably lower the likelihood of misusing biotechnologies for human genetic enhancement purposes, which is often described as the key unsolved ethico-legal issue with the governance of inheritable genetic modification.¹¹⁵⁸ However, a prudent legislative policy response requires awareness of the inherent weakness of attempts to regulate inheritable genetic modification due to the sheer complexity of drawing and holding legal lines. In light of these inherent challenges, decision-makers need to carefully reevaluate recent suggestions to reverse the long-standing ban on these transformative technologies.

¹¹⁵⁸ This thesis's aim in offering new legislative and regulatory solutions is not to offer support or to endorse the reversal of the ban. Rather, based on a realpolitik view that the ban is eventually going to be reversed, the thesis endeavours to offer decision-makers legal and governance tools to reduce inheritable genetic modification's misuse potential.

Part A: General Lessons for the Development of Stronger Genetic Intervention Laws

I) General Lesson: From Drawing “Lines in the Sand” Using Vague Social Constructs to Developing Clearer Distinctions

A foundational lesson from this inquiry is that in order to set more durable legal limits, legislative developers need to reduce the laws’ current reliance and reference to conceptually unclear constructs. Chapters 4-7 demonstrated how the unclear restrictions to “serious conditions” or a “therapeutic” purpose are ultimately unsuccessful in setting effective limits. These challenges in setting limits stem from the heavy reliance on ambiguous social constructs (such as “bodily normalcy”),¹¹⁵⁹ which have a fluid and changing meaning that is becoming increasingly expansive over time. Ambiguous legal wording such as “serious” and “therapeutic” are prone to be interpreted more broadly as new reproductive biotechnologies tend to raise medical standards and elevate societal expectations. The unclear terms of a “serious condition”, “risk”, and “therapeutic” are co-interpreted and applied by (often self-interested) regulatees, who often push for interpretations that are highly expansive and permissive. Over time, the process of overextensive legal change erodes these unclear requirements’ limit-setting function and blurs the boundaries between permissible and impermissible genetic interventions.¹¹⁶⁰

Setting more durable limits requires going beyond malleable and overbroad standards and requires identifying distinctions that are capable of drawing clearer, sharper and more specific lines. Clearer, more specific legal limits would reduce the regulator’s and regulatee’s very broad margin of discretion and would refocus the interpretation on a more specific, carefully limited group of permissible genetic interventions. More specific limits have the quality of not only being able to more clearly designate which genetic

¹¹⁵⁹ Andrea Arz de Falco *supra* note 781; Isabel Karpin & Roxanne Mykitiuk *supra* note 128.

¹¹⁶⁰ The HFEA itself, in its Ethical Values report warned that inability to demarcate lines between acceptable and unacceptable genetic diagnosis could result in a slippery slope to eugenics. See HFEA (2001) *supra* note 722.

interventions are allowed (as current laws do) but also which genetic interventions are disallowed. This work would require reexamining and improving on the ambiguous theoretical underpinnings of certain rules (such as the nebulous distinction between medical and social trait selection).¹¹⁶¹ Improving on the conceptual design of existing rules requires a considerable investment of intellectual effort to examine and better articulate the rules' guiding principles, their rationales and identify clearer distinctions.¹¹⁶² Legislative developers would do well to first lay the theoretical groundwork for a reform by identifying clearer ethical, clinical and technological distinctions capable of better determining which genetic interventions are permissible and impermissible.¹¹⁶³

In this chapter, I will present a number of clearer normative distinctions and rules which I have identified by conducting a comparative analysis of genetic intervention laws in 20 European countries.¹¹⁶⁴ While most surveyed countries use nearly the same unclear and broad rules,¹¹⁶⁵ I have identified a few rare pieces of legislation that could serve as a useful model for a reform as they employ clearer normative distinctions. For instance, the Austrian Genetics Act, 2015 provides the only known example of a jurisdiction that has limited the otherwise highly ambiguous term serious condition only to cases of an increased risk of death, risk of severe brain damage, unrelievable severe pain or to circumstances in which the child would

¹¹⁶¹ See for instance chapter 6, which discusses how the distinction between medical and social interventions underlays the seriousness standard and the rules on embryo sex selection.

¹¹⁶² See generally, Lon L. Fuller, *The Morality of Law* (New-Haven: Yale University Press, 1969) at 63-65.

Fuller describes the process of making unclear legal standards clearer: "Water from the tainted spring can sometimes be purified, but only at the cost of making it something else that it was."

¹¹⁶³ For instance, later in the chapter, I will discuss the legal, ethical and technological distinction between non-inheritable, somatic genetic modification and the inheritable, germline genetic modification.

¹¹⁶⁴ The countries included in this comparative analysis are the UK, Portugal, Spain, France, Belgium, the Netherlands, Germany, Austria, Switzerland, Denmark, Norway, Sweden, Iceland, Finland, Estonia, Latvia, the Czech Republic, Slovakia, Hungary and Slovenia.

¹¹⁶⁵ Most surveyed legislation restricts genetic diagnosis to instances of a significant risk of developing a serious and untreatable condition.

In addition to similar restrictions, the legislation in most of the countries in this comparative review shares common ethical considerations and seeks to accomplish similar policy objectives.

only survive with intensive medical care.¹¹⁶⁶ The Austrian Parliament's explanatory report clarifies that the rationale behind this unique approach of setting more explicit limits is to restrict genetic diagnosis only to specific cases of well demonstrated medical need, and avoiding reproductive biotechnologies' overuse and misuse.¹¹⁶⁷ I will later examine useful examples of relevant foreign legislation that demonstrate how the efforts of lawmakers can lead to the development of clearer normative distinctions and rules in regards to genetic interventions.

Explicitly Articulate the Rules' Rationales to Better Guide Interpretation and Application

Legislators should consider explicitly articulating the rules' rationales to promote interpretation and application that is consistent with the legislative policy objectives. Explicitly laying out the rule's rationales in authoritative legal documents (such as the act's interpretation clause, explanatory reports or background documents) would guide regulators to interpret the rules in a manner that is more consistent with the policy objective of preventing a mission creep.¹¹⁶⁸ This lesson directly follows from the thesis's analysis that has shown that the regulators' initial fidelity to the rules' rationales resulted in a restriction to a well-specified group of single-gene caused, life-threatening congenital malformations. However, over time, regulators' interpretations have drifted further away from the underlying normative considerations to eventually approved genetic interventions that are *prima facie* in contrast with the rules' rationales. Explicitly articulating the rules' rationales can address this problem by guiding regulators towards appropriate interpretations and

¹¹⁶⁶ Fortpflanzungsmedizinrechts-Änderungsgesetz 2015 – das Allgemeine bürgerliche Gesetzbuch und das Gentechnikgesetz geändert werde (Fortpflanzungsmedizinrechts-Änderungsgesetz 2015 – FMedRÄG 2015) that came into force on the 24th of February, 2015, Art 2 (a) (1) (2) [Hereafter: The Genetics Act].

¹¹⁶⁷ Republik Österreich, Auf der das Österreichische Parlament Erläuterungen - Fortpflanzungsmedizinrechts-Änderungsgesetz 2015 (445 d.B.). Bundesgesetz, mit dem das Fortpflanzungsmedizinrecht, das Allgemeine Bürgerliche Gesetzbuch, das Gentechnikgesetz und das IVF-Fonds-Gesetz geändert werden Fortpflanzungsmedizinrechts-Änderungsgesetz 2015.

The Austrian Parliament explained that it revised its legislation that originally prohibited genetic diagnosis to be in conformity with the ECHR ruling in *Costa and Pavan v Italy*. The ECHR decision in *Costa* affirmed that the Italian ban on genetic diagnosis was contrary to Articles 8 and 14 of the European Convention of Human Rights. See *Costa and Pavan v. Italy* [GC] [2012] App. No. 54270/10, Judgment of 28 August 2012.

¹¹⁶⁸ For a more comprehensive discussion about the importance of stating the purpose and objectives of the legislation in order to guide statutory interpretation, see Aldo Z Borda, *Legislative Drafting* (Oxford: Taylor & Francis, 2011) xi-xii.

help them steer clear from overly expansive interpretations that can bring about undesirable ethical, societal and medical outcomes. For instance, official legal documents could clearly and explicitly state that a condition is regarded treatable if it has safe and effective treatments. If official legal documents have made such statements, regulators would have a hard time ignoring this guidance and approve genetic diagnosis against a host of conditions with safe and effective treatments (such as PKU, webbed hands and cross-eyes). Another manner to guide interpretations is to amend the act's preamble to include a statement that discourages an overly permissive licensing policy that could promote overextensive legal change or the misuse of reproductive biotechnologies. One unique example can be found in the preamble of the Swiss Medical Assisted Reproduction Act 2017, which specifically states that the purpose of the act is to “protect human dignity, personhood, and the family, as well prohibit abusive applications of biotechnology and genetic engineering”.¹¹⁶⁹ Explicitly stating the rules' rationales in authoritative legal documents will guide interpretations and will help prevent a situation in which regulators gradually move away from the specific rules' rationales and the law's normative objectives.

II) General Lesson: The Significance of Clearer Legislative Drafting and Limit Setting

A second general lesson from this inquiry is that the legislative drafting process needs to articulate the conceptually clearer normative distinctions (identified in lesson no.1) using more precise language. For the legal boundaries to be more durable, they ought to have the qualities of a) greater clarity b) reduced reliance on subjective terms such as “risk” and “serious” and c) explicit limits on the scope in a manner that distinguishes permissible from impermissible interventions. By incorporating these lessons about the role of

¹¹⁶⁹ See Art 1 (b) Bundesgesetz über die Medizinisch Unterstützte Fortpflanzung (Fortpflanzungsmedizingesetz, FMedG) vom 18. Dezember 1998 (Stand am 1. September 2017). [Hereafter: The Medical Assisted Reproduction Act]

language in the process of legal change, a law reform can address some key underlying causes of overextensive legal change and progress towards setting clearer, more effective limits.¹¹⁷⁰

The Significance of Clearer Legislative Drafting and Limit Setting in Addressing Overextensive Legal Change

Legislative clarity has an important role in keeping legal change in check by guiding interpretations and setting more precise limits as to which genetic interventions are permissible and which are impermissible. Legal theoretical explanations shed light on the importance of legislative clarity in achieving the legislature's goals and in preventing the law from evolving in undesirable ways. Legal theorist Frederick Schauer explains that in cases in which there is a concern of a slippery slope, clearer and better-defined rules will help to avert a slide down the slope.¹¹⁷¹ Similarly, Lon Fuller stresses the significance of legislative clarity, especially in instances in which an unclear legal text can give adjudicators the ability to change the legal policy too rapidly and steer it in undesirable directions that could be contrary to the legislature's intent.¹¹⁷² Critical legal scholar Duncan Kennedy views unclear and overbroad legal language as giving adjudicators the power to shape and effectively make laws, often in a manner that serves the interest of privileged groups.¹¹⁷³ Fellow legal theorist Ken Kress, agrees with Kennedy's analysis about the manner in which unclear and overbroad language can produce undesirable legal changes, but contends that clearer legislative drafting could, at least in part, remedy this problem and enable laws to achieve their intended objectives.¹¹⁷⁴ These theoretical insights regarding

¹¹⁷⁰ For more about the key role of clear, unambiguous legislative drafting in developing legislation that is more effective in furthering the intended policy objectives, see Helen Xanthaki, *Drafting Legislation: Art and Technology of Rules for Regulation* (Oxford: Hart Publishing, 2014) 1-20.

¹¹⁷¹ Frederick Schauer *supra* note 616.

¹¹⁷² See Fuller *supra* note 1162.

Fuller also explains that "to put a high value on legislative clarity is not to condemn out of hand rules that make legal consequences depend on standards such as "good faith" and "due care". There are instances, in which broad terms are justified, and other instances in which the importance of legislative clarity is paramount."

¹¹⁷³ Duncan Kennedy, "Legal Formality" (1973) 2:2 J.K Stud 351- 361.

¹¹⁷⁴ Ken Kress *supra* note 127.

legislative and legal clarity are particularly useful in addressing some of the core issues underlying the overextensive legal change problem. Clearer legislative drafting and more distinct legal limits would help correct the present situation, in which the ambiguous legal language gives regulators and regulatees an overly broad discretionary range. Using clearer legal language would help reduce what H.L.A Hart calls the laws' "penumbra of uncertainty"¹¹⁷⁵ and guide adjudicators towards a more specific set of outcomes that are consistent with the legislative objectives.

Greater Normative Clarity Promotes Accountability

Legislative clarity has an important function of facilitating external scrutiny and promoting regulatory accountability. Regulators could be made more accountable for their decisions if those decisions can be assessed against a more explicit and specific set of policy objectives and evaluation criteria. A reform to genetic intervention laws brings about an opportunity to enhance regulatory accountability and oversight by enabling more detailed reviews and scrutiny against well-established, clearer legal criteria. Under the current laws, critical scrutiny of regulatory decisions is a particularly difficult task because of the laws' use of overbroad and highly ambiguous legal constructs, which can very often be invoked to justify a genetic intervention in question. Even genetic interventions against mild conditions or for human enhancement can be passed off as permissible under the unclear and malleable "seriousness" or "therapeutic" standards. Such broad and ambiguous legal language can conceal the extensive changes to the law and the manner in which it diverges from the key legislative objective that seeks to prevent such developments.¹¹⁷⁶ These challenges, however, can be addressed with clearer and less unambiguous legal limits. Clearer laws would enable various parties,

¹¹⁷⁵ Herbert Lionel Adolphus Hart, "Positivism and the Separation of Law and Morals" (1958) 71 Harv. L. Rev 593, 606-607.

¹¹⁷⁶ See analysis in chapter 3.

including, courts, governments¹¹⁷⁷, parliaments¹¹⁷⁸ and civil society to evaluate and critique whether or not the regulatory licensing policy is consistent with the law and its normative objectives. Government and court oversight is particularly important in this highly sensitive legal context that is rapidly changing as a result of genetic interventions' fast-paced technological evolution. In *S.H and Others v. Austria*, the Council of Europe's highest court, the Grand Chamber, emphasized the importance of constant state vigilance, stating that "in this area, in which the law appears to be continuously evolving and which is subject to a particularly dynamic development in science and law needs to be kept under review by the Contracting States".¹¹⁷⁹ The Grand Chamber's decision in *Parrillo v. Italy* stressed the significance of judicial oversight of genetic experimentation given the inherent risks of eugenics "precisely because this domain [of reproductive genetic technology] may evolve in a manner seriously dangerous to humankind".¹¹⁸⁰ Regulators knowing there is more effective external scrutiny of their decisions are more likely to exercise greater caution and restraint in approving controversial genetic interventions. Clearer legislative drafting and better articulated normative objectives would enable the courts, governments, parliaments and civil society to perform a critical oversight task. Clearer rules and rationales would strengthen external oversight and help to keep regulatory decisions in check, and better aligned with the legislative policy.

Complementary Regulatory and Policy Measures to Strengthen Genetic Interventions' Governance

While the proposed reform offers a way forward in strengthening the governance of genetic interventions, pressures are likely to persist in terms of interpreting even the clearer, more specific rules in a

¹¹⁷⁷ Government reviews of genetic diagnosis law has existed in France until 2009. In 2009, the CCNE recommended discontinuing these reviews since, in their view, the regulatory requirements led to the prevention of the slippery slope.

See CCNE, Opinion n°107 supra note 48; See also Conseil D'État supra note 35.

¹¹⁷⁸ The German Embryo Protection Act requires specific parliamentary review of genetic diagnosis every two years in light of novel development in genetic intervention technologies. See Deutscher Bundestag, Gesetzentwurf Entwurf eines Gesetzes zur Regelung der Präimplantationsdiagnostik (Präimplantationsdiagnostikgesetz – PräimpG) Drucksache 17/5451. 12. 04. 2011.

¹¹⁷⁹ *S.H and Others v. Austria* supra note 441 at para 95.

¹¹⁸⁰ *Parrillo v. Italy* [GC] [2015] App No. 46470/11, Judgment of 27 August 2015 at para 26.

somewhat laxer manner. A primary strategy to further address these potential drivers of the overextensive legal change pattern would be to adopt, in addition to a law reform, a suite of complementary regulatory and policy measures. A key policy measure is to conduct periodic reviews of regulatory licensing practices by the government and the parliament. Such periodic reviews of regulatory licensing practices are legally required in Switzerland and in Germany.¹¹⁸¹ To further strengthen the review process, it would be beneficial to officially designate in authoritative policy documents that a main purpose of such evaluations is to examine regulatory licensing practices and determine if they might contribute to overextensive change. Identifying and taking corrective action close to the time would promote regulatory afterthought and restraint, particularly given that regulators are often accountable to their respective departments. Furthermore, additional measures would contribute to curtailing overextensive legal change such as encouraging greater transparency, increasing regulatory independence, addressing potential biases and challenges with the public consultation process.¹¹⁸² Together with the law reform, these complementary policy and regulatory measures would contribute to the overarching strategic objective of preventing overextensive legal change by strengthening the governance of genetic interventions.

Part B: Providing Examples of Legislative Amendments to Genetic Intervention Laws

Part B is dedicated to translating the above general lessons into practical advice by offering suggestions and concrete examples of legislative amendments. The suggestions and examples provided are based on the analysis of the existing rules' specific shortcomings and the general lessons above on how to

¹¹⁸¹ See Deutscher Bundestag, supra note 1178 and see Art 14-1, the Medical Assisted Reproduction Act supra note 1169.

¹¹⁸² See for instance commentary about issues with the HFEA's public consultations, Françoise Baylis, "The HFEA Public Consultation Process on Hybrids and Chimeras: Informed, Effective, And Meaningful?" (2009) 19:1 Kennedy Institute of Ethics J 41; David Albert Jones, *Chimera's Children: Ethical, Philosophical and Religious Perspectives on Human-Nonhuman Experimentation* (London: A&C Black, 2012) 129-130; Eric Blyth et al. "No 'Brownie Points' for Ill-Conceived Donation Review" (2011) 593 BioNews.

revise the relevant acts to set clearer and potentially more durable legal limits.¹¹⁸³ It is outside the scope of this thesis to undertake an exhaustive review of strategies of how to develop a perfect set of revised rules or suggest where to precisely draw the legal lines¹¹⁸⁴ Part B provides general suggestions on how to improve on the conceptual design and the wording of the existing rules.¹¹⁸⁵ The proposed legislative amendments and recommendations were developed to strike a finer balance between allowing a degree of flexibility for certain hard cases and providing legal certainty. In this specific context, legal certainty is particularly important due to the particular challenges with setting and maintaining the legal limits to genetic interventions.¹¹⁸⁶ The examples presented here would assist decision-makers in drawing clearer, more durable lines to address the growing problem of overextensive legal change.¹¹⁸⁷

The advice presented here can inform various countries across the globe that their legislative governance response to genetic intervention might be lacking, fragmented or contains unclear provisions. The blueprint for a reform can help Canada¹¹⁸⁸ to address complex legislative and regulatory challenges with

¹¹⁸³ Other advantages of clearer legal requirements would be the simplification of the regulatory decision-making process and a more efficient management of public resources. See Ruth Deech, Anna Smajdor et al, *Saviour Siblings, Designer Babies, and Sex Selection* (Oxford: Oxford University Press, 2008) at 64-67.

¹¹⁸⁴ The sheer complexity of the multifaceted overextensive legal change problem does not allow for the development of perfect legal solutions that can mitigate and prevent the problem in its entirety. Rather than spending years searching for perfect legal solutions, a pragmatic and feasible plan should focus on good, effective and implementable solutions. In these circumstances, Voltaire's words are correct that "the perfect is the enemy of the good." See Voltaire, *Contes En Vers Œuvres Complètes De Voltaire* (Paris : Garnier, 1877) at 50.

¹¹⁸⁵ There are a number of important reasons why improving upon the existing rules is preferable to attempting to drawing an entirely novel set of rules. First, revising the laws is a pressing task with a limited period and developing an entirely novel set of rules might take many years to come to fruition. Second, the literature so far has not offered any entirely de-novo alternatives to the existing rules, so the likelihood lawmakers would be able to develop de-novo rules is highly unlikely. Third, legislatures and regulators are already familiar with the existing rules. Substantially revising the existing rules is the most pragmatic solution given the feasibility of the task, the current needs of the legal system and the pressing timeline for accomplishing the task of reforming genetic intervention laws.

¹¹⁸⁶ Interestingly, the ABM has discussed that genetic intervention laws should ideally balance between a certain degree of flexibility and certainty. The ABM has explained that legal certainty is required in order to prevent a "slippery slope". However, as I have shown throughout this thesis, the ABM did not excel in finding that right point of balance between flexibility and certainty. See "État Des Lieux Du Diagnostic Prénatal En France" (2008) Agence de la Biomédecine, at 50-5 online : <https://www.agence-biomedecine.fr/IMG/pdf/rapport-etats-des-lieux-du-diagnostic-prenatal-en-france.pdf>.

¹¹⁸⁷ See the review in chapter 8 of the challenges and the ramifications of the overextensive legal change problem and the motivations to reform the law.

¹¹⁸⁸ The originally promised regulations regarding genetic diagnosis are not expected in the foreseeable future after the dissolution of the Canadian regulator, the Assisted Human Reproduction Agency. This is largely owing to Supreme Court's

respect to genetic diagnosis¹¹⁸⁹ and germline modification technologies.¹¹⁹⁰ This blueprint can additionally assist over two dozen jurisdictions in Europe and Oceania that have substantially similar laws¹¹⁹¹ to the UK and France¹¹⁹² and could be potentially prone to overextensive legal change. The proposed law reform could aid nations in addressing the growing problem that overextensive legal change poses by offering concrete legislative and regulatory solutions.

I) The Seriousness Standard: The Need to Go Back to the Drawing Board

A key item on the legislative development agenda would be to replace or substantially rework the seriousness standard. Lawmakers would need to take concrete steps to address the seriousness standard's current shortcomings in setting limits by enhancing this standard's conceptual clarity, delimiting its scope and reducing its reliance on subjective viewpoints and biases. Instead of relying on subjective and problematic notions of "bodily normalcy" (as the seriousness standard currently does),¹¹⁹³ the new or improved standard

decision in *Ref re Assisted Human Reproduction Act*, 2010, The Supreme Court ruled that the federal government's legislation was ultra vires and struck down half of the act's provisions, further leading to an unstable climate in the regulation of assisted human reproductive technologies. Moreover, the Supreme Court's decision, which struck down sections 10 and 11, could be interpreted as allowing the provinces to make exceptions to the ban on germline genetic modification. For more details about the decision see for instance, François Baylis, "Supreme Court of Canada Decision on the Assisted Human Reproduction Act Creates Urgent Need for Action" (2011) 33:4 J Obstet Gynaecol Can 317-319. ¹¹⁸⁹With the exception of section 5 (1)(e)'s prohibition on social sex selection, the *Assisted Human Reproduction Act*, 2004 does not draw any line between permissible and impermissible uses of genetic diagnosis. *Assisted Human Reproduction Act*, R.S.C. 2004, s 5(1)(e).

For more about the lack of regulation of genetic diagnosis in Canada see Juliet Guichon, Ian Mitchell & Christopher Doig, "Assisted Human Reproduction in Common Law Canada After the Supreme Court of Canada Reference: Moving Beyond Regulation by Colleges of Physicians and Surgeons" (2013) 25:2 Can J of Women and the Law 315-339

¹¹⁹⁰ Canada might eventually consider reversing the ban on human germline genetic modification. See Zubin Master & Patrick Bedford, "CRISPR Gene Editing Should Be Allowed in Canada, But Under What Circumstances?" (2018) 40:2 J Obstet Gynaecol Can 224-226. See also Canadian Institutes of Health Research, "Human Germline Gene Editing: Points to Consider from A Canadian Perspective" (2016) Online: <http://www.cihir-sc.gc.ca/e/50158.html>

¹¹⁹¹ See Isabel Karpin & Kristin Savell supra note 764; CoE-PGD-PND Council of Europe: Background Document on Preimplantation and Prenatal Genetic Testing, 2015 online [https://www.coe.int/t/dg3/healthbioethic/Activities/07_Human_genetics_en/INF\(2015\)6%20e%20dpi%20dpn.pdf](https://www.coe.int/t/dg3/healthbioethic/Activities/07_Human_genetics_en/INF(2015)6%20e%20dpi%20dpn.pdf)

¹¹⁹² The HGC, UK Department of Health, CCNE, and the Council of Europe have all at certain points called for devising clearer regulatory parameters. See HGC, 2006 supra note 131 at 3; UK Department of Health, *Human Reproductive Technologies and the Law: Government Response to the Report from the House of Commons Science and Technology Committee*, Cm 6641 (London: TSO, 2006) 18; CCNE Opinion No. 122 supra note 1056 at 5; Council of Europe Steering Committee On Bioethics supra note 735 at 34.

¹¹⁹³ Andrea Arz de Falco supra note 781; Isabel Karpin & Roxanne Mykitiuk supra note 128.

should guide regulators towards more consistent and coherent interpretations by putting greater emphasis on more objective assessments of the condition's potential impacts on the child's future health. Lawmakers can look at the common clinical characteristics of permissible genetic interventions in order to develop a new or improved standard that sets more specific limits.¹¹⁹⁴ One exceptionally rare, yet useful model is the Austrian Genetics Act 2015, which narrows the scope of the term serious conditions only to cases of an increased risk of death, the risk of severe brain damage, unrelievable severe pain or to circumstances in which the child would only survive with intensive medical care.¹¹⁹⁵ The Austrian Genetic Act's definition of the term "serious condition" provides an excellent example of how lawmakers can define the term serious conditions by considering the common clinical characteristics (increased risk of death, brain damage, etc.) of permissible diagnoses. The definition found in the Austrian law offers a method to determine with greater certainty which conditions warrant genetic diagnosis (such as Beta-thalassemia, Tay-Sachs and Duchenne Muscular Dystrophy) and which do not (Dwarfism, the Autism spectrum and Intersex). At a minimum, if lawmakers cannot agree on a binding definition, the law should include more legal indications and criteria to narrow the scope of the new or revised rule. To do so effectively, lawmakers can look into clinical indications¹¹⁹⁶ and ethical standards¹¹⁹⁷ to draw inspiration. New definitions, legal indications, and criteria would be particularly

¹¹⁹⁴ A new or reworked standard will still need to be rather broad and general so it covers a number of eligible diagnosis, but not so broad that it loses its meaning and conceptual clarity altogether.

¹¹⁹⁵ Art 2 (a) 2 Bundesgesetz, mit dem das Fortpflanzungsmedizingesetz, das Allgemeine bürgerliche Gesetzbuch, das Gentechnikgesetz und das IVF-Fonds-Gesetz geändert werden (Fortpflanzungsmedizinrechts-Änderungsgesetz (FMedG) 2015.

For more about the general political context surrounding the legislation of the FMedG 2015, see Erich Griessler, & Mariella Hager, "Changing Direction: The Struggle of Regulating Assisted Reproductive Technology in Austria" (2016) 3:1 *Repro Biomed & Soc'y Online*, 68.

¹¹⁹⁶ See for instance, Institute of Medicine Committee on Serious and Complex Medical Conditions *supra* note 767. See also Maggie Liu et al., "Evaluation of Therapeutics for Severely Debilitating or Life-Threatening Diseases or Conditions: Defining Scope to Enable Global Guidance Development" (2020) 107:3 *Clinical Pharmacology & Therapeutics*, 514-520.

¹¹⁹⁷ See for instance a rare attempt to describe the common characteristics of mild conditions, Benjamin S Wilfond *supra* note 750.

useful to narrow the standard's scope, reduce its subjectivity and enhance its conceptual clarity so that the revised rule can set more effective and appropriate limits.

It is not the goal of this thesis to develop an entirely new standard to replace the seriousness standard. This complicated task of revising or replacing the seriousness standard would realistically require drawing on the expertise of various professionals such as lawyers, social scientists, clinicians and disability rights groups.¹¹⁹⁸ I would not embark here on such a colossal task of developing a novel standard to replace genetic intervention laws' primary rule. Instead, this section offers a criterion, a legal indication and a regulatory policy recommendation. These three proposals could serve as the foundations for a new or reworked rule to replace the problematic seriousness standard and add much needed clarity and certainty.

Regulatory Criterion: Assessment of a Condition only based on Its Expected Medical Impacts on the Putative Child

It is recommended that the revised act would clearly state that conditions' assessments would be performed solely based on the condition's expected medical impacts on the putative child.¹¹⁹⁹ This criterion, which places the key focus on the putative child would help disperse a key legal ambiguity: for whom is the condition serious?¹²⁰⁰ Currently, broad interpretations enable classifying conditions with only minor medical impacts on the putative child as serious on the grounds that those conditions could cause negative, social and emotional difficulties to third parties.¹²⁰¹ The regulatory reliance on prospective parents' (and implicitly societal) views on the child's genetic traits may negatively affect their interests not only espouses potentially

¹¹⁹⁸ On the importance of including people with disabilities in the consultation process relating to the governance of genetic intervention technologies see, Jackie Leach Scully, "Disability and Genetics in the Era of Genomic Medicine" (2008) 9:10 *Nature Reviews Genetics* 801.

¹¹⁹⁹ The precise wording of the provision in the act or the regulations will need to be determined by legal drafters in a manner that is consistent with the revised regulatory requirement to replace the seriousness standard.

Legal drafters can also consider adding words like "detrimental" before medical impacts to more specifically designate the gravity of the medical impacts to be considered.

¹²⁰⁰ See Plachot & Cohen *supra* note 702; See also Peter R Brinsden *supra* note 702; Ilja Richard Pavone *supra* note 703.

¹²⁰¹ For arguments in favour of classifying conditions based on their impact on third parties, see Scott Rosamund et al. *supra* note 556 at 344.

unfounded and speculative claims but can also reinforce prevalent biases that people with certain bodily and mental characteristics are better off not born.¹²⁰² Ultimately, over-privileging the interests of third parties¹²⁰³ might continue to push regulatory licensing policy in a problematic direction of further moving away from the key rationales of restricting genetic interventions only to instances in which a condition would have profound medical effects on the putative child.¹²⁰⁴ All of the above is not to say that third parties' viewpoints are not generally important, but their role in the regulatory licensing policy is questionable because the arguments of alleged negative impacts can be invoked to genetically intervene on a wide variety of physiological or cognitive characteristics third parties deem "abnormal" or "undesirable".¹²⁰⁵ Such arguments regarding a condition's potential negative impacts on third parties have been frequently invoked to screen even for conditions that only have minor impacts on the child's health such as PKU, intersex and the autism spectrum.¹²⁰⁶ The initial normative objectives, articulated by parliaments, ethical commissions and regulators themselves have explicitly stated that genetic intervention based on costs, societal preferences or emotional convenience would be unethical and impermissible. This is since this line of reasoning could promote an instrumentalist or a eugenic worldview and be overall a part of a mission creep.¹²⁰⁷ To combat the potential mission creep, it is recommended that the respective acts would clearly state that conditions would be

¹²⁰² See Jeffrey R. Botkin supra note 569 at 36.

¹²⁰³ Christian Munthe argues that decisions to license genetic diagnosis should be based on the medical impact of the condition on the future child and not simply based on parental preferences. See Christian Munthe, "Preimplantation Genetic Diagnosis: Ethical Aspects" *Encyclopedia of Life Sciences* 2006 online publication (doi: 10.1038)

¹²⁰⁴ See for instance, Mattei J.-F, Cherioux J. supra note 423; HFEA supra 447.

¹²⁰⁵ There is a line of argument that the well-being and happiness of parents can affect children's health. In this context of genetic interventions, there is lack of empirical evidence that a) if prospective parents genetically intervene on an embryo to prevent a mild condition (hearing impairment, cross-eyes etc.) the parents will enjoy a sustained sense of well-being as a result and b) that such alleged well-being changes will lead to a notable impact on the child's health. Nevertheless, such unbacked arguments can provide support for the selection against bodily and mental characteristics parents views as more "desirable" and the instrumentalization of children by falsely associating children's and prospective parents' interests.

¹²⁰⁶ HFEA License Meeting Committee, Centre 008 (IVF Hammersmith) Variation to add PGD for Phenylketonuria online: <http://guide.hfea.gov.uk/guide/ShowPDF.aspx?ID=3426>; HFEA Licensing Committee supra note 833; HFEA Licensing Committee, Clubbed Hands and Feet Application online: <http://www.hfea.gov.uk/10252.html>.

¹²⁰⁷ HGC, *Choosing the Future: Genetics and Reproductive Decision-Making* (London: HGC, 2001) at 19; HFEA, 2003 supra note 728. Mattei J.-F, Cherioux J. supra note 423. Noëlle Lenoir supra note 734.

assessed based on their expected medical impacts on the putative child. This explicit legal criterion would make the regulatory licensing policy unambiguous by focusing the attention on the most affected party – the putative child.

The Significantly Reduced Life Expectancy Legal Indication

Adopting a new legal indication, the significantly reduced life expectancy, will to more clearly determine whether a condition has a sufficient level impact on the future child's health to warrant licensing a genetic intervention. The significantly reduced life expectancy indication offers an objective, clear and commonly accepted indication about whether a condition is warranted for genetic intervention. The HFEA originally considered making life expectancy a legal indication to assess the licensing of genetic diagnosis. The rationale behind the HFEA's original idea to use life expectancy was to ensure that the screening policy only applies in circumstances in which the child's health is profoundly impacted.¹²⁰⁸ Life expectancy provides an indication about a person's overall health, as living with conditions that profoundly affect health also tend to be strongly associated with shorter lifespans.¹²⁰⁹ Early and premature death often indicates that a condition is warranted for genetic diagnosis. Some of the clearest cases of warranted genetic diagnosis are when the condition significantly reduces life expectancy, such as the infant onset neurodegenerative disorders of Tay-Sachs and Canavan disease.¹²¹⁰ In such instances, not only will the children die prematurely, but their short

¹²⁰⁸ HFEA supra note 447.

¹²⁰⁹ See European Union - Eurostat – Quality of Life Indicators – Health online: https://ec.europa.eu/eurostat/statistics-explained/index.php/Quality_of_life_indicators_-_health; Final report of the expert group on quality of life indicators 2017 ed. <https://ec.europa.eu/eurostat/documents/7870049/7960327/KS-FT-17-004-EN-N.pdf/f29171db-e1a9-4af6-9e96-730e7e11e02f> OECD, Life Expectancy at Birth online: <https://data.oecd.org/healthstat/life-expectancy-at-birth.htm> See Christian Munthe, *Pure Selection: The Ethics of Preimplantation Genetic Diagnosis and Choosing Children Without Abortion* (Gothenburg: Acta Universitatis Gothoburgensis, 1999), 93; Andrea L. Kalfoglou, Joan Scott & Kathy Hudson, "PGD Patients' and Providers' Attitudes to the Use and Regulation of Preimplantation Genetic Diagnosis" (2005) 11:4 Reproductive Biomed Online 486-496.

¹²¹⁰ See for instance, David Degrazia, *Creation Ethics: Reproduction, Genetics and Quality of Life* (Oxford: Oxford University Press 2012) at 137-141.

lives would be marked by pain and suffering.¹²¹¹ Bioethicists across the board, from disability advocates¹²¹² to transhumanists¹²¹³ view short life expectancy as circumstances in which a genetic intervention would be legitimate and permissible. I would further suggest to build on this rare consensus in the field and make it an explicit legal indication.

Significantly reduced life expectancy can provide a rather clear indication about which conditions should be approved and which should not. I would recommend using the wording “significantly reduced life expectancy” (similar to the wording “reduced life expectancy” in the Norwegian guidelines)¹²¹⁴ as opposed to the more ambiguous wording such as “life-threatening” (used in the Danish act)¹²¹⁵ or “premature death” (used by the Swedish guidelines).¹²¹⁶ It is recommended that an expert committee would convene to issue official guidance regarding the extent that a condition would need to reduce life expectancy to qualify as “significant”.¹²¹⁷ The significantly reduced life expectancy legal indication would enable regulators to better determine whether certain conditions warrant genetic intervention by relying on more objective clinical characteristics. To meet the significantly reduced life expectancy legal indication, the condition would need

¹²¹¹ Shakespeare *supra* note 229 at 670;

¹²¹² Shakespeare *Ibid*; See Erik Parens & Adrienne Asch *supra* note 778; Alicia Ouellette, “Selection against Disability: Abortion, ART, and Access” (2015) 43:2 J L, Med & Ethics 215.

¹²¹³ Christopher Gyngell & Julian Savulescu, “The Simple Case for Germline Gene Editing” *Genes for Life – Future Leaders* online: http://www.futureleaders.com.au/book_chapters/pdf/Genes-for-Life/Christopher-Gyngell_Julian-Savulescu.pdf; Silvia Camporesi & Giulia Cavaliere, “Eugenics and Enhancement in Contemporary Genomics” Gibbon, et al. eds, *Routledge Handbook of Genomics, Health and Society* (New York: Taylor & Francis, 2018).

¹²¹⁴ Bioteknologinemnda, The Norwegian Biotechnology Advisory Board, An Option for Couples at High Risk of Passing on a Serious Hereditary Condition to their Children online: http://www.bion.no/filarkiv/2010/07/pgd_english.pdf

¹²¹⁵ Art. 7.1 Act no. 460 of 10th June 1997 on Artificial Fertilisation.

¹²¹⁶ Regeringens proposition 1994/95: 142 om Fosterdiagnostik and Socialut-Skottet 1994/95: SoU 18. This position is further described in SoU, “Genetik, Integritet Och Etik. Slutbetänkande Av Kommittén Om Genetisk Integritet”, 2004 20 at 292.

¹²¹⁷ An expert committee would be better placed to decide on such complex philosophical, ethical, societal and regulatory matters. In developing this indication, decision makers would do best to set a reasonable, minimal bar of what is considered a reduced life expectancy so that this new indication would effectively guide regulatory decisions. To illustrate, one suggestion that could be repurposed for this legal indication is that life expectancy would be lowered below 50 years to qualify as significant. See Walter Glannon, “Genes, Embryos, and Future People” (1998) 12:3 Bioethics 204.

to: a) have a median life expectancy that is lower than the one required by the indication (as determined by an expert committee); and b) the reduced life expectancy is directly caused by the condition in question or its related complications. To illustrate, conditions such as mild albinism, squint, cleft palate and intersex all do not affect the child's lifespan,¹²¹⁸ and hence would be flagged by the significantly reduced life expectancy legal indication as non-eligible for genetic intervention. As shown in the above example, the significantly reduced life expectancy legal indication would be useful to weed out conditions that have little to no effect on the putative child's health. The significantly reduced life expectancy legal indication would help to better determine which conditions are eligible for genetic intervention and which are not, hence adding another tool to the toolkit of combating overextensive legal change.

Operative Recommendation: Reduce Reliance on Quality of Life Assessments

An operative recommendation would be to reduce the reliance on quality of life assessments, which could be inaccurate, biased and driving the overextensive legal change. Decision-making based on quality of life assessments¹²¹⁹ can promote overextensive legal change owing to the fact this elusive and subjective concept can reflect biases, and encourage negative judgments¹²²⁰ regarding a wide variety of physical and mental conditions and variations.¹²²¹ Quality of life assessments are prone to biases in part because there are

¹²¹⁸ For instance, note that the lifespan of people with intersex is not shortened and is the same as the general population. Hughes & Deeb A supra note 802.

¹²¹⁹ Certain ethicists recommend the use of the quality of life as a way to assess candidate genetic interventions for licensing. See Wertz and Knoppers, supra note 79. Philip Kitcher, *The Lives to Come: The Genetic Revolution and Human Possibilities* (New-York: Simon and Schuster, 1996). See also F. Shenfield, et al., "Taskforce 5: Preimplantation Genetic Diagnosis" (2003) 18:3 Human Repro 649-65.

Shenfield et al. make a somewhat unusual argument as they recognize that it is nearly impossible to assess the quality of life of the unborn because of a number of flaws and lack of objectivity of quality of life assessments, but still suggest relying on such assessments as a primary decision-making tool.

¹²²⁰ For more about the ethical challenges with making quality of life judgments in the genetic interventions context, see United Nations, General Assembly - Human Rights Council "Promotion and Protection of All Human Rights, Civil, Political, Economic, Social and Cultural Rights, Including The Right to Development Rights of Persons with Disabilities - Report of the Special Rapporteur on The Rights of Persons with Disabilities" Forty-third session (24 February–20 March 2020) at 3-6 online: https://www.un.org/ga/search/view_doc.asp?symbol=A/HRC/43/41

¹²²¹ See for instance, David Wasserman & Adriane Asch, "The Uncertain Rationale for Prenatal Disability Screening" (2006) 8:1 Ethics J Am Med Assoc 53-56; See also Philip Moons, Werner Budts & Sabina De Geest, "Critique on the

no objective methods to assess a concept that is so multifaceted, complicated and largely dependent on individuals' subjective viewpoints on bodily and mental abilities.¹²²² Extensive evidence gathered in the past three decades shows that able people tend to view the quality of life of people with disabilities more negatively than the way people with such disabilities view their own quality of life. Multiple studies relating to this phenomenon (known as the disability paradox) have found consistent evidence that despite prevalent viewpoints that people with disabilities have a poor quality of life, a high percentage of individuals with a variety of cognitive and physical disabilities rank their quality of life as high or very high.¹²²³ Wasserman and Asch suggest that negative views held by prospective parents and medical professionals do not necessarily reflect the actual quality of life of a future child and have more to do with inaccurate information, prevalent biases and ableist attitudes.¹²²⁴ Furthermore, a Government of Quebec report on reproductive technologies warns that excessively relying on subjective quality of life evaluations in licensing genetic interventions can result in a "slippery slope".¹²²⁵ This thesis's analysis has shown that negative quality of life judgments played a role in the overextensive legal change pattern. It has shown how regulators', prospective parents' and clinicians' negative quality of life judgments of conditions such as cross-eyes, webbed hands and intersex have played a role in pushing for an increasingly permissive regulatory policy of screening against mild and medicalized conditions. While a law reform can take quality of life assessments into consideration in licensing

Conceptualisation of Quality of Life: A Review and Evaluation of Different Conceptual Approaches" (2006) 43:7 Int'l J Nursing S 891-901; See also Alicia Ouellette, *Bioethics and Disability: Toward a Disability Conscious Bioethics* (Cambridge: Cambridge University Press, 2011) at 86.

¹²²² F Shenfield et al., supra note 1219 at 650; Bobbie Farsides & Robert J. Dunlop, "Measuring Quality of Life: Is There Such a Thing as a Life Not Worth Living?" (2001) 322:7300 Brit Med J 1481.

¹²²³ Peter A Ubel et al., "Misimagining the Unimaginable: The Disability Paradox and Health Care Decision Making" (2005) 24 Health Psychol (4 Suppl): S57-S62; Heather P Lacey et al., "Are they Really That Happy? Exploring Scale Recalibration in Estimates of Well-Being" (2008) 27 Health Psychol 669-675; Catherine E Ross & Marieke, M Van Willigen, "Education and the Subjective Quality of Life" (1997) 38 J Health Soc Behav 275-297; See Also Gary L Albrecht, & Patrick J Devlieger, "The Disability Paradox: High Quality of Life against All Odds" (1999) 48:8 Social Science & Med 977.

¹²²⁴ Wasserman and Asch supra note 1221.

¹²²⁵ Québec, Commission De L'éthique, De La Science and De la Technologie, "Ethics and Assisted Procreation: Guidelines for the Donation of Gametes and Embryos, Surrogacy and Preimplantation Genetic Diagnosis" (Québec: Gouvernement du Québec 2010) at 122 online: <http://www.ethique.gouv.qc.ca/en/assets/documents/PA/PA-avis-et-errata-EN.pdf>

decisions, such a policy is neither particularly ethically sound nor is it free from criticisms that it ultimately draws arbitrary and malleable legal lines. Such arbitrary lines, drawn using subjective quality of life assessments tend to promote the medicalization of conditions and devalue the lives of people with body variations and disabilities. A law reform should minimize the regulatory system's heavy reliance on subjective quality of life assessments to reduce negative biases in decision-making and avoid overextensive legal change.

II) Towards a Better Legal Definition of Untreatable Conditions

To promote clearer, better-focused interpretation and application, it is recommended that the law would require that conditions would be primarily or exclusively assessed whether they are treatable or not based on the treatment's level of safety and efficacy. This recommendation follows from chapter 4, which shows that while the treatment's safety and efficacy were initially primary considerations, overextensive legal change significantly weakened the rule's ability to set meaningful limits and enabled classifying treatable conditions as untreatable. These assessment criteria of safety and efficacy are overall less subjective, less malleable and cannot be invoked in every case. Assessment of quality of treatments based on safety and efficacy is the hallmark of pharmaceutical law, in Europe, Canada and the US.¹²²⁶ In our context, the Swiss Medical Assisted Reproduction Act, 2017, specifically restricts screening only conditions that lack a safe and effective treatment.¹²²⁷ To illustrate, a safety and efficacy centered assessment of the low PHE diet will identify there is a consensus in the clinical literature that the diet is a safe and effective treatment for PKU.¹²²⁸ To promote evidence-based decision-making, it is recommended that regulators would be required to evaluate the safety and efficacy of a treatment course based on the best available data, comprehensive literature reviews, and consider relying on independent expert panels to reduce biases. Focusing the review of the untreatability on objective safety and efficacy considerations will contribute to a more consistent

¹²²⁶ See José Luis Valverde, *Key Issues in Pharmaceuticals Law* (Amsterdam: IOS Press, 2007).

¹²²⁷ Art 2 (c) FMedG supra note 1195.

¹²²⁸ See Donald B Bailey Jr supra note 542.

interpretation and application of the rule and overall clearer, better focused regulatory licensing policy.

Reassessment of Conditions that have become Treatable with the Progress of Medicine

Lawmakers should consider amending the primary or secondary legislation to require periodic reassessments of currently approved conditions to determine whether new advances in biomedicine and therapeutic options have effectively rendered these conditions treatable. Periodic reassessment of whether a condition has become treatable would keep the legal change in check by creating a mechanism to remove conditions from the list that no longer meet the regulatory requirement of being untreatable. The CCNE, in opinions no. 107¹²²⁹ and no. 120,¹²³⁰ has stated that medical advances can warrant a potential revocation of licenses to screen for certain conditions once they have become treatable.¹²³¹ However, there is no known publically available information to indicate that such reassessments have been conducted or that regulators have de-listed conditions in light of new treatment options. All the while, advances in biomedical science and technology are moving towards making more conditions treatable.¹²³² New treatment options could prove to be ethically and clinically preferable alternatives to prenatal genetic interventions, particularly to inheritable genetic modification, which could pose significant health risks.¹²³³ Advances in biomedical technologies such

¹²²⁹ CCNE, Opinion No. 107 supra note 48.

¹²³⁰ CCNE, Opinion No. 120 supra note 493 at 33.

¹²³¹ The Danish report on foetal diagnostics makes similar points that a serious condition may eventually become non-serious because of the progress of biomedical technology see Sundhedsstyrelsen, “Fosterdiag- Nostik og Riskovurdering”, (Copenhagen: Sundhedsstyrelsen 2003) at 84.

¹²³² Advances in biomedical science and personalized medicine help make previously untreatable diseases treatable. About half of the new FDA approvals under the novel drug pathway were for orphan drugs. Moreover, the number of new treatment approvals getting the orphan drug designation is steadily rising over the past four decades. Most of these newly approved orphan drugs are indicated for rare genetic disorders. See U.S. Food & Drug Administration, “New Drug Therapy Approvals 2019 – Advancing Health Through Innovation” FDA.gov (January 6, 2020) <https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2019#conclusion>; Scott Gottlieb, “Taking New Steps to Meet the Challenges of Rare Diseases — FDA Marks the 11th Rare Disease Day” (February 26, 2018) FDA.gov <https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/taking-new-steps-meet-challenges-rare-diseases-fda-marks-11th-rare-disease-day>

¹²³³ Supra note 884.

as stem cell and somatic (non-inheritable) gene therapies,¹²³⁴ could eventually provide new treatment avenues. For instance, the FDA is currently in the process of expedited review of potentially promising treatments for conditions such as hemophilia and spinal muscular atrophy.¹²³⁵ New safe and effective treatments would warrant a reconsideration of whether a condition needs to be removed from the list of approved genetic interventions once it has been shown to have an effective treatment course. In sum, periodic reassessments of whether a condition has become treatable would be essential in modernizing the list of licensed conditions, keeping it in check, and creating a mechanism to address the problem of overextensive legal change.

The Cost Considerations Legal Test

Law reform efforts would benefit from incorporating into the act or its regulations a legal test to determine whether a condition that has a safe and effective treatment should be regarded as untreatable solely due to its cost component. To help address the considerable ethical challenges associated with licensing decisions based on the treatment's costs,¹²³⁶ this new legal test would limit the consideration of costs only to instances in which prospective parents would not be able to access the treatment due to persistent financial impediments. The cost considerations legal test consists of three requirements. First, regulators would consider costs as a reason to license a genetic intervention only in instances when a safe and effective

¹²³⁴ Gunning writes: "The other side of the biotechnological coin is that the more we understand how individual genes operate the more likely we are to be able to correct the effects of a malfunctioning gene product or to insert a correctly functioning gene. And stem cell therapy is a bright light on the horizon." Gunning *supra* note 460.

¹²³⁵ Cynthia E Dunbar et al., "Gene Therapy Comes of Age" (2018) 359:6372 *Science* ean4672.

¹²³⁶ It is recommended that decision-makers would exercise caution when considering costs as a part of the assessment of whether a treatment satisfies the untreatability requirement. As explained in chapter 4, classifying a condition as untreatable solely because of the treatment's cost can raise considerable ethical issues. Such ethical issues include the prevention the potential lives of otherwise healthy children due to costs associated with the treatment and organized cost-containment strategies that seek to encourage genetic interventions on traits associated with high treatment and accommodations costs.

One policy prescription suggested in the literature is for governments to provide adequate coverage of the costs of treatments so that parents with insufficient means would not be forced to prevent the birth of otherwise rather healthy children. See Shakespeare *supra* note 229.

treatment is not funded by public insurance schemes.¹²³⁷ Second, regulators would assess the degree to which the treatment cost may render it inaccessible to the general public by employing affordability thresholds, which will be developed based on relevant economic indicators and adjusted periodically.¹²³⁸ Third, regulators should consider special circumstances in which individual prospective parents can still access the treatment despite lack of public coverage, such as patient assistance programs, the availability of private insurance coverage or personal means.¹²³⁹ The proposed legal test offers a series of steps to examine whether the treatment costs may create a barrier to access to an extent it may render the condition effectively untreatable.

III) Setting Clearer, More Effective Limits for the Legal Notion of Genetic Risk

An operative recommendation for a law reform would be to reinstate a revised version of the rule based on scientific risk assessments (penetrance). Penetrance assessment is a proven method to set durable legal limits, which are essential to address the overextensive legal change pattern. Chapter 5 has demonstrated in detail how regulators' shift from scientific risk assessments (penetrance) to subjective risk assessments (perceived risk) has resulted in a highly expansive and overly permissive legal notion of genetic risk. Under the highly expansive legal notion of genetic risk, regulators have approved susceptibility screening even when the risk rate is only in the realm of single digits or outright 0% (screening against healthy, unaffected gene carriers). Furthermore, chapter 5 explained the reasons why subjective risk assessments are ineffective in setting meaningful legal limits, including clinicians' self-interest, prospective parents' cognitive biases, history of emotional trauma, risk-averse behaviour and overly simplistic, genetic reductionist views.¹²⁴⁰ In contrast

¹²³⁷ This situation would rarely occur in Western European jurisdictions such as the UK and France. Western European medical and pharmaceutical insurance schemes offer a wide range of publicly funded treatments in instances of medical necessity. See note 530.

¹²³⁸ The affordability threshold will be maintained, adjusted and publicized by regulators. If treatment becomes affordable (such as due to the availability of generic versions), regulators will be required to revisit the original decision to regard a condition as untreatable solely due to the costs.

¹²³⁹ It is also worthwhile mentioning the high costs of genetic interventions themselves, especially the projected high costs of inheritable genetic modification. See Kannan & Najjar *supra* note 282. See also note 1126.

¹²⁴⁰ See chapter 5 for a more detailed discussion and analysis.

to subjective risk assessments' overall poor performance in legal limit setting, scientific risk assessment (penetrance) is a calculation of the probability that the putative child carrying the particular gene will develop a certain condition.¹²⁴¹ Since penetrance is a probabilistic hereditary calculation, its results are quantifiable and measured in percentages,¹²⁴² thus enabling lawmakers to set a bright-line rule. The penetrance bright-line rule sets a clear cut-off point regarding which risk rates warrant a genetic intervention and which do not. Chapter 5 has shown that the penetrance bright-line rule has performed an effective boundary-setting function in the period in which it was used between 1998 and 2006. An operative recommendation would be to instate the penetrance bright-line rule as a formal requirement to set clearer and, predictable legal limits.¹²⁴³

Setting Appropriate Risk Rates

The determination of the precise bar of genetic risk should be left to expert legal and policy making bodies. These decision-making bodies should consider an appropriate balance between having a certain degree of flexibility and fulfilling the rule's boundary-setting function. Legislatures, governments and ethics commissions would need to consider the relevant ethical, societal and clinical questions that are essential to determine the appropriate legal bar of genetic risk. The law can set the bar of risk to still allow certain susceptibility screening in a range deemed appropriate, with the benefits of bright-line rules' predictability and reliability. For instance, if the bar of risk is set at 50%, the bar would allow for certain susceptibility screenings such as against the BRCA1, which is statistically linked to a 60% risk of developing breast cancer.¹²⁴⁴ Another option is to use a sliding scale for the bar of risk based on the condition's clinical impacts. To illustrate this

¹²⁴¹ Tom Strachan & Andrew Read *supra* note 613.

¹²⁴² See Anthony Griffiths et al., *An Introduction to Genetic Analysis*, 7th edition (New York: W. H. Freeman, 2000).

¹²⁴³ While bright-line rules cannot set limits that are entirely precise for every given situation, they nonetheless have a particularly important role in setting stable and predictable limits. Such stability and predictability is a prime consideration in this context of developing legislation to effectively address overextensive legal change. For a discussion of bright-line rules' limit-setting function see and *supra* note 616.

¹²⁴⁴ For revised penetrance estimates for BRCA1 and BRCA2 see: Evans D. Gareth et al., "Penetrance Estimates for BRCA1, BRCA2 Based on Presymptomatic Testing: A New Unbiased Method to Assess Risk?" (2018) 55:7 J Med Genetics 442-448.

approach, the bar of risk can be reduced to 25% if the condition is statistically linked to a 10-year shorter life expectancy. As one can tell from the above examples, the bright-line rule of penetrance is not overly restrictive, as some might argue,¹²⁴⁵ and could be set at a point that allows for susceptibility screening that decision-makers view as appropriate.¹²⁴⁶

Decision-makers would do well to set the bar of risk at the point that is not overly low. There are two important reasons to set the bar of risk at a reasonable point, as it has an essential function for the continued ability of the regulatory regimes to set meaningful limits as new genomic technologies reveal that every embryo is susceptible to develop a late-onset condition. First, as explained in chapter 5, setting the bar of risk at a reasonable point serves the regulatory function of preventing unwarranted screening for genes that have a uncertain or statistically very weak links to health outcomes.¹²⁴⁷ The HFEA and the CCNE initially warned that inaccurate marketing and misguided genetic reductionist views would lead prospective parents to push the regulatory bar of risk to become lower and lower, leading to a “slippery slope.”¹²⁴⁸ A second key reason not to set the bar of risk too low is in order to prevent and address an overly expansive legal notion of “genetic risk”. As explained in chapters 5 and 7, the combination of an over-expansive legal notion of genetic risk and whole genome sequencing technology¹²⁴⁹ would reveal that virtually every embryo is “at risk” to develop a

¹²⁴⁵ Guido De Wert et al. *supra* note 862.

¹²⁴⁶ For instance, The Spanish regulator (the CNRHA) has set the bar of risk at 60%, citing the need to allow highly penetrant mutations while disallowing screening against low susceptibility genes, which are particularly prevalent amongst the general population. Pavone & Arias *supra* note 653 at 245.

Similarly, clinical geneticist Shirley Hodgson suggests setting the bar of risk at 60% to prevent a situation in which most, if not all embryos will be found to be “at risk”. See Rice *supra* note 555 at 157.

¹²⁴⁷ See the analysis in chapter 5 regarding the boundary setting function of the significant risk requirement.

See Byk *supra* note 442; CCNE opinion No. 5 *supra* 453. CCNE opinion No.6 *supra* note 561; HFEA and AGCT, *supra* note 567.

¹²⁴⁸ CCNE, Opinion no. 67 *supra* 572.

¹²⁴⁹ Note the review in chapter 5, which explains that while virtually every embryo and person has genes correlated with susceptibilities, such links are often very weak.

See for instance about plans of the UK NHS to become the first world service in the world to routinize whole genome sequencing - UK Department of Health and Social Care “The NHS Genomic Medicine Service is the first National

late-onset condition. As such, a large share of embryos might be eligible for the alteration of their genome to edit-out susceptibility genes or to edit-in “protective genes” in hope of conferring future individuals “genetic immunities” to late-onset conditions. As discussed in chapter 7, such insertion of “protective genes” to future children’s genomes would also often enhance their physiological or cognitive capabilities. Such practices would further blur the lines between genetic therapy and enhancement. Over time, the approval of genomic immunizations and therapeutic enhancements could bring the regulatory system closer to the territory of transhumanism and neo-eugenics.¹²⁵⁰ A reasonable, carefully considered minimal bar of genetic risk could stem this tide by ensuring the legal boundaries can perform a meaningful boundary-setting function.

IV) A New Legal Test to Disallow Human Genetic Enhancement

Law reform efforts need to effectively address one of the greatest challenges with the regulation of genetic interventions – the real possibility of misusing potent reproductive biotechnologies for human enhancement purposes.¹²⁵¹ The operative lessons from this inquiry are that the regulatory system needs effective limit-setting mechanisms if it is to successfully address its current flaws and to fulfill the key legislative task of disallowing human genetic enhancement.¹²⁵² This analysis has shown that the task of effective legal governance of genetic interventions is ever more relevant and pertinent in light of this thesis’s new findings about the critical flaws in the emerging regulation of inheritable genetic modification. In chapter 7, I have identified two new loopholes with high-abuse potential that could enable interested prospective parents and clinics to genetically enhance future children’s physiological and cognitive traits. Thus, these loopholes would essentially enable circumventing the key legislative objective, which holds that such genetic

Genomic Healthcare Service in The World and Will allow Faster Diagnosis and Personalised Care” Gov.UK online: <https://www.gov.uk/government/news/matt-hancock-announces-ambition-to-map-5-million-genomes>

¹²⁵⁰ See Académie Nationale De Médecine supra note 969 at 13-14.

¹²⁵¹ See the review in chapter 2, which shows that genetic interventions for enhancement purposes are in early stages of emergence. The chapter reviews examples of single gene edits to enhance muscle mass, cognitive function and immunity. Other notable examples reviewed are genetic diagnosis for eye colour, the ranking of embryos based on estimated IQ and editing multiple genes at the same procedure, which could make it possible to alter more complex traits such as height.

¹²⁵² See the analysis in chapter 7.

modifications are a prohibited eugenic practice. To address the concerns about inheritable genetic modification's misuse, I propose a newly developed legal test that if implemented properly, could substantially reduce the risk of abusing the two loopholes and prevent circumventing the legislative policy goal of prohibiting human genetic enhancement.

A New Approach to Disallowing Genetic Enhancement

The new legal test proposed here will create an open list of disallowed genetic interventions based on specific categories that would be written into the law. The new legal test draws on this thesis's insights into how to overcome the specific line drawing challenges described in the previous chapters. The first insight embedded into the design of the new legal test is in creating a new regulatory mechanism that for the first time would designate which genetic interventions are disallowed (as opposed to the current system, which only designates which interventions are allowed). For instance, the new legal test would designate certain genetic interventions as disallowed (such as an enhancement of a child's IQ beyond median levels). The second insight embedded into the design of the new legal test is in the direct acknowledgment that the therapy/enhancement distinction would overall be ineffective in demarcating lines for genetic interventions. Deductive reasoning-based attempts (i.e. therapy/enhancement distinction) would face a host of issues in determining which interventions are "therapeutic" (and allowed) or "enhancing" (and disallowed) because the boundaries between these two categories are eminently indeterminate, has fuzzy limits (in a manner that resembles the Sorites paradox)¹²⁵³ and even considerably overlap. I suggest moving away from a deductive reasoning approach (i.e. therapy/enhancement distinction) to an inductive reasoning approach (i.e. a list of categories regarding certain classes of genetic enhancements).¹²⁵⁴ The inductive reasoning approach I

¹²⁵³ For more about fuzzy logic and judicial decision-making see Beverly Blair Cook, "Fuzzy Logic and Judicial Decision Making" (2001) 85 *Judicature* 70.

¹²⁵⁴ For more about the use of logical forms such as inductive and reductive approaches in legal reasoning, see Scott Brewer, "Exemplary Reasoning: Semantics, Pragmatics, and the Rational Force of Legal Argument by Analogy" (1996) 109:5 *Harv L Rev* 942-944.

propose has a more modest, but attainable goal – developing a new legal test using a list of categories to identify as many interventions that could be regarded as genetic enhancements. This inductive approach enables bypassing the great challenges with the deductive approach of the therapy/enhancement distinction by creating an indication-based legal mechanism to designate genetic enhancements as disallowed. The new legal test offers a new way forward in addressing these significant legal line-drawing problems by not only articulating which genetic interventions are allowed but for the first time designating which genetic interventions are disallowed.

The Open List of Non-Pathologic, Disallowed Genetic Interventions

I propose a new mechanism that would require regulators to create an open list of non-pathological, disallowed genetic interventions. To be included on this list, the genetic trait or characteristic needs to be non-pathologic and be either: a) cosmetic characteristic; b) athletic ability, c) behavioural characteristic or d) above-median intelligence or cognitive capabilities.¹²⁵⁵ For instance, genetic interventions, to select, delete or insert genes via genetic modification associated with above-median IQ would fall under the cognitive category. A genetic intervention to have a child with tall stature or blue eyes would fall under the cosmetic category. In addition, I propose a fifth, blanket clause to capture the remainder of non-pathologic, disallowed conditions that do not fit neatly in the other categories, such as non-medical sex selection or the use of artificial gene synthesis technology to endow future children with traits that humans do not naturally possess. Together, the four above-mentioned categories and the broad blanket clause would cover many of the non-pathologic, socially motivated or enhancing genetic interventions.¹²⁵⁶

¹²⁵⁵ The four above mentioned categories were chosen based on an extensive review of the literature. The literature tends to classify types of non-pathological and enhancing interventions and divide them into broad categories. Hank Greely lists the four above mentioned categories (cosmetic, physiological, behavioural and cognitive genetic interventions) and discusses why such interventions raise ethical, societal and regulatory issues. See Henry T Greely, "Regulating Human Biological Enhancements: Questionable Justifications and International Complications" (2005) 7 UTS L Rev at 90-91.

¹²⁵⁶ While this legal test has been developed to set legal limits for genetic intervention technology, it could be equally useful in parallel contexts such as the regulation of bionic or neuroprosthetic implants, which could be used for the purpose of human

A general definition of impermissible, non-pathological interventions would aid in guiding interpretations, but is not necessary for operationalizing this mechanism.¹²⁵⁷ Experience already shows that lawmakers, ethics commissions and regulators were able to specifically identify a host of non-pathologic, disallowed genetic interventions. Regulators, lawmakers and the courts have already explicitly named eye colour, skin colour, height and intelligence as impermissible traits for genetic intervention. For instance, in a rare case of relevant litigation¹²⁵⁸ - *R v HFEA*, the House of Lords has explicitly stated that licensing of genetic diagnosis to select “eye or hair colour as well as more sinister eugenic practices“ would be contrary to the legislative intent of the HFE Act.¹²⁵⁹ The UK Department of Health has specifically named genetic interventions to enhance a child’s intelligence or musical ability as genetic interventions that should be disallowed under the HFE Act.¹²⁶⁰ These institutions did not need a legal definition of non-pathological, disallowed traits to classify certain genetic interventions as impermissible. What is needed is a mechanism, such as the one presented here, to classify traits that are regarded as impermissible, officially and with a binding status.

A Review Mechanism to Ensure the List of Disallowed, Non-Pathologic Genetic Interventions is as Comprehensive as Possible

To ensure the list is an effective governance tool, I would recommend amending the governing acts to

enhancement. Another particularly useful application of the new legal test is to regulate somatic gene therapy, which could also be used for genetic enhancement purposes, such as athletes using the technology for gene doping.

¹²⁵⁷ The Belgian and Portuguese acts contain general prohibitions of genetic diagnosis against non-pathological traits, however, they leave clinicians and parents to interpret what does not pathological means. These laws do not offer any regulatory mechanism to designate any particular non-pathological interventions as disallowed. See Loi du 11 mai 2003 Relative à la Recherche sur les Embryons in vitro, Moniteur Belge, 28 mai 2003. See also Law n. 32/2006, of the 26th of July, concerning Medically Assisted Reproduction.

¹²⁵⁸ Overall, there has been very little litigation relating to genetic intervention provisions of the HFE act.

¹²⁵⁹ *R (Quintavalle) v Human Fertilisation and Embryology Authority* [2005] supra note 468 at para 25.

¹²⁶⁰ United Kingdom, Department of Health, Review of the Human Fertilisation and Embryology Act Proposals for revised legislation (including establishment of the Regulatory Authority for Tissue and Embryos) Presented to Parliament by the Secretary of State for Health by Command of Her Majesty December 2006 14. online: http://www.hfea.gov.uk/docs/Review_HFEA_Act_White_Paper_DH.pdf

legally require regulators to publish a comprehensive and complete list of the disallowed, non-pathologic genetic interventions based on the five above categories. I would further recommend a periodic review by the responsible ministry and the parliament in order to scrutinize the list to ensure that it is comprehensive and includes as many as possible, non-pathologic disallowed genetic interventions. Moreover, I would recommend that the list of disallowed, non-pathologic interventions would be published to enable members of the public to provide additional oversight to ensure that the list is as comprehensive as possible. A comprehensive list of disallowed, non-pathologic genetic interventions would help to establish clear and predictable norms to finally determine which genetic interventions are disallowed. A comprehensive list would move towards establishing clearer, predictable industry norms against the eugenic practice of human genetic enhancement by utilizing the expressive function of the law,¹²⁶¹ and the deterrence associated with the respective acts' criminal and administrative sanctions.

The Ultimate Success of the List of Disallowed, Non-Pathologic Genetic Interventions Depends on its Implementation

The new legal test can contribute to better lines demarcation, yet its ultimate success greatly depends on its actual implementation by regulators. For this new test to draw clearer lines, regulators would have to make sure that the list remains comprehensive and up to date (and include new technological developments, such as the use of artificially synthesized genes to create novel traits that do not exist in nature).¹²⁶² In particular, regulators would need to resist pressures from industry and consumer lobbies to remove traits from the list and open the door to various forms of human genetic enhancement. The sociological theory of legal change and the evidence I reviewed indicate that regulators are likely to face mounting pressure to eventually allow genetic enhancements because certain industry groups, consumers and political actors could view such

¹²⁶¹ Cass R Sunstein, "On the Expressive Function of Law" (1996) 144:5 U Pa L Rev 2021-2053.

¹²⁶² Supra note 205 and 206.

genomic alterations as beneficial in promoting certain personal, institutional or financial interests. The pressure on regulators to approve genetic enhancements would make this important task of demarcating better lines between therapy and enhancement particularly challenging. In sum, the above described legal test offers a new mechanism to draw clearer lines between permissible and impermissible genetic interventions, but the degree of this legal test's success depends on its implementation by regulators. If this legal test is implemented properly, it could considerably reduce the likelihood that regulators would approve certain forms of genetic enhancement. However, this legal test, like laws in general, cannot create a stable and durable distinction between the subjective constructs of therapy and enhancement.¹²⁶³ The law's inability to effectively distinguish between genetic therapy and enhancement warrants careful reconsideration of the legislative policy regarding inheritable genetic modification.

An Inconvenient Truth: The Need to Recognize that the Regulation would not be able to Effectively Distinguish between Therapeutic from Enhancing Genetic Modifications

The legal and policy communities would benefit from a sober and more realistic perspective that recognizes that laws cannot create a stable and durable distinction between the highly subjective constructs of therapy and enhancement. A more realistic viewpoint is required in light of this thesis's analysis that shows that contrary to recent assumptions,¹²⁶⁴ the regulation of inheritable genetic modification would face considerable, if not insurmountable challenges in distinguishing genetic therapy from enhancement. I would recommend that the legal and policy communities take note and reflect on the potential ramifications of the two new loopholes flagged in this thesis. These two loopholes have a high abuse potential as indicated by the sociological theory of legal change and the social science evidence that there is a market demand for the

¹²⁶³ The regulation of human genetic modification is prone to ever-greater challenges relating to the therapy/enhancement distinction than other contexts, because genetic modifications that are simultaneously both therapeutic and enhancing further blur the lines between these two nebulous constructs.

¹²⁶⁴ Supra note 49.

genetic enhancement of children's appearance, physiological and mental capabilities.¹²⁶⁵ While the new legal test I have described above would reduce the risk of misusing genetic modification for enhancement purposes, realistically, there is no entirely effective way to completely close the two loopholes. Closing the two loopholes would essentially require developing a legal test to clearly and effectively distinguish between therapy from enhancement, a nearly insurmountable task. The inability to deal with the loopholes and disallow human genetic enhancement would mean that the laws could ultimately be unsuccessful in performing their key task – preventing inheritable genetic modification's eugenic misuse.

Policy Recommendation: Reconsider Reversing the Ban on Inheritable Genetic Modification in Light of the Potential Inability to Set Effective Legal Limits

The legal and policy communities should carefully reevaluate recent proposals to reverse the ban on human inheritable genetic modification in light of this thesis's findings and analysis that regulators are likely to struggle with setting effective legal limits. An inability to effectively legally govern these already contentious technologies further tilts the balance in favour of maintaining the ban on inheritable genetic modification. The US National Academy report on Human Genome Editing concluded that if it was not possible to "prevent extension to uses other than preventing a serious disease", in the Committee's view "germline genome editing would not be permissible".¹²⁶⁶ In particular, human germline genetic modification would be further viewed as impermissible because of a host of potential long-term ethical, societal and political ramifications of the failure to effectively regulate this high-impact technology. These potential ramifications include the potential approval of editing of genes with a questionable ratio between their medical benefits and risks, ineffectiveness in accomplishing the key legislative objective, the associated ethical and human

¹²⁶⁵ See the discussion in chapter 7.

¹²⁶⁶ National Academy of Sciences and National Academies of Sciences, Engineering, and Medicine, "Summary of Principles and Recommendations" Human Genome Editing: Science, Ethics, and Governance (Washington D.C.: National Academies Press, 2017).

rights risks, and the growing risk of future state involvement in these markets.¹²⁶⁷ Moreover, I have explained that inheritable genetic modification to endow people with enhanced, superior, and ultimately -- transcend the human species' biological limits,¹²⁶⁸ raises a host of entirely novel, incalculable long-term ramifications for individuals, families and society.¹²⁶⁹ This sheer difficulty in setting effective legal limits warrants a careful rethinking of the legislative policy to ensure safe and responsible governance of these transformative technologies. Adopting a precautionary principle¹²⁷⁰ or approach could be justified in light of the various risks inheritable genetic modification entails, particularly the significant and potentially irreversible risks to health and safety, its questionable clinical value given safer alternatives and the profound challenges in setting effective legal limits. A careful, sober approach to the legal governance of genetic modification technologies is required to effectively manage their novel risks and avoid critical pitfalls.

Policy Alternative: Maintain the Bright-Line Rule - the Distinction between Somatic and Germline Genetic Modification

If lawmakers wish to draw clearer legal lines, they need not look any further than the lines already found in the law - the distinction between modifying the genome of consenting persons (somatic modification) and modifying the genome of the unborn and their future lineage (germline modification).¹²⁷¹

¹²⁶⁷ See the analysis in chapters 2, 3 and 8.

¹²⁶⁸ UNESCO IBC supra note 907, See also Roberto Andorno supra note 917. Explanatory Report to The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4.IV.1997, Section 89.

¹²⁶⁹ For more about the long-term, incalculable risks of attempting to transcend the species' biological limits, See Nicholas Agar, *Humanity's End: Why We Should Reject Radical Enhancement* (Cambridge, MA: MIT Press, 2010).

¹²⁷⁰ UNSECO IBC has adopted a precautionary approach in regards to inheritable genetic modification See UNESCO International Bioethics Committee (IBC) supra note 907 at para 81. For more about the precautionary principle and approach see Roberto Andorno, "The Precautionary Principle: A New Legal Standard for A Technological Age" (2004) 1:1 J International Biotech Law 11. See also Andrew Jordan & Timothy O'Riordan, "The Precautionary Principle: A Legal and Policy History" in Martuzzi M, Tickner JA, eds. *The Precautionary Principle: Protecting Public Health, The Environment and The Future of Our Children* (Rome: World Health Organization, 2004) 31-48.

¹²⁷¹ HFE Act, Schedule 2, Paragraph (1) (4), 2008 ; Code Civil, art. 16-4 (Inséré par la Loi No 94-653 du 29 juillet 1994 art. 1 1, II, art. 3 J Officiel du 30 juillet 1994 ; Loi no 2004-800 du 6 août 2004 art. 21 J Officiel du 7 août 2004) ; Loi no 2004-800 du 6 août 2004 relative à la bioéthique, J.O. 6 Août 2004.

This distinction is a central pillar in the legal governance of biotechnologies precisely because somatic therapy of consenting persons is widely regarded as a safer, ethically preferable alternative to the modification of future generations' germline genome. This is since the alteration of the germline genome entails multi-generational health risks, unpredictable and potentially irreversible outcomes as well as risks of eugenic abuse.¹²⁷² On top of those flagged risks, this thesis's findings that regulators would struggle to set limits to the technique provide another significant reason to preserve the germline/somatic distinction's bright-line rule. The distinction between germline and somatic modification establishes a bright-line rule precisely because the line is based on basic facts of human biology, the difference between the somatic cells (the body cells of an existing person) and the germline cells (the reproductive genomic material, which is inherited by the offspring). Legal scholar Tony McGleenan writes about the distinction between somatic and germline genetic modification that "Science and nature rarely provide us with such clear, non-arbitrary points at which to draw a bright-line."¹²⁷³ Doug Walton, an expert on slippery slopes, argues that the somatic/germline bright-line distinction can prevent a slide down the slope precisely because it sets particularly clear limits, which leave no grey area for judges and adjudicators to misconstrue. The somatic/germline bright-line rule sets a strong safeguard against attempts to technologically "improve" human hereditary traits of future generations.¹²⁷⁴ Legal decision-makers would do well to recognize that the task of preventing the misuse of transformative biotechnologies requires effective legal limits that can stand the test of time.

¹²⁷² Geneticist Francis Collins, the Director of the National Institutes of Health, stated unequivocally that germline manipulation "has been viewed almost universally as a line that should not be crossed." See Francis Collins, "The NIH Director: Statement on NIH Funding of Researching Using Gene-editing Technologies in Human Embryos" National Institutes of Health (April 28, 2015) online: <https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos>. United States, Department of Health and Human Services, "Recombinant DNA Research: Actions under the Guidelines," (1995) 60:80 Federal Register 20726–20737.

The Danish Council on Ethics, "Statement from the Danish Council on Ethics on Genetic Modification of Future Human genetic modification of future humans in Response to Advances in the CRISPR Technology" (2016) at 12; Etisk-Raad online: <http://www.etiskraad.dk/~media/Etisk-Raad/en/Publications/Statement-on-genetic-modification-of-future-humans-2016.pdf>

¹²⁷³ Tony McGleenan, "Human Gene Therapy and Slippery Slope Arguments" (1995) 21:6 J Med Ethics 354.

¹²⁷⁴ Douglas Walton *supra* note 54.

Conclusion

This chapter has offered operative solutions to the now documented problem of overextensive legal change in the form of a blueprint for reform. The reform is specifically tailored to address these profound technology governance challenges with more effective tools. The proposed reform aims to offer a new avenue to advance towards the key policy goal of preventing the misuse of genetic intervention technologies by strengthening its governance. The foundations for the reform are based on two general lessons regarding the qualities that genetic intervention laws require in order to set more durable and effective legal limits. First, to improve on the conceptual design of existing rules, lawmakers need to identify clearer normative and clinical distinctions capable of better determining which genetic interventions are permissible and impermissible. Second, the legislative drafting process needs to place greater attention on making careful language choices that express the laws' underlying conceptual distinctions with clarity, reduced subjectivity, and an explicitly delimited scope. The chapter then translated these two general lessons on drawing more durable legal limits into practical advice specifically designed to address the issues leading to overextensive legal change. To do so, the law reform blueprint includes suggestions for specific legislative amendments, clearer conceptual distinctions and newly developed legal tests. These general lessons and the reform blueprint can inform various countries across the globe that lack a comprehensive system of clear legal limits to genetic interventions or face challenges in governing these novel technologies. The law has a critical role to play in ensuring that these highly-transformative reproductive biotechnologies are governed in a manner that is safe and socially responsible.

With new insights into the problem and with legal solutions at hand, the remaining question is which steps will governments take to govern this technological revolution? Will legislatures and regulators take the necessary steps to overhaul genetic intervention laws to set effective limits to these game-changing biotechnologies? Will we let laws direct technology, or will we let technology direct the law?

Chapter Ten – Conclusion

Setting Lasting Legal Safeguards in the Wake of a Brave New World

This thesis's goal is to offer insights about the critical shortcomings of genetic intervention laws in order to find effective solutions to what is dubbed as one of tomorrow's greatest problems.¹²⁷⁵ The thesis has demonstrated a pattern of continuous legal changes in the regulation of genetic interventions and provided insights into its potential drivers in order to develop more effective regulatory and legislative solutions. This chapter offers concluding thoughts by explaining how this thesis' various lines of inquiry are all tied to the greater goal of strengthening the governance of genetic intervention technologies. This chapter provides a number of practical lessons, which can assist academics, policy and legal decision-makers in addressing the growing issues with the governance of genetic intervention technologies. The task of finding effective legal governance solutions for the growing problem of the misuse of biotechnologies is likely to play a critical role in the wake of a brave new world.

The Thesis' Objectives and Contributions

For over 50 years, the slippery slope to eugenics has been a central problem in bioethics and perhaps, the key problem in the governance of genetic intervention technologies.¹²⁷⁶ Nevertheless, over the course of the past five decades, the literature has not produced any accounts to either prove or disprove a slippery slope to eugenics is occurring. Aside from the task of factually demonstrating a slippery slope, the literature has

¹²⁷⁵ See Nicholas Agar *supra* note 1269. Bryan Lufkin, "10 Grand Challenges We Will face by 2050" (July 12, 2020) BBC Future online <https://www.bbc.com/future/article/20170713-what-will-the-challenges-of-2050-be>; Carmen Rienke, "Morgan Stanley Says These 10 Geopolitical Risks Are Looming Over Markets in 2020 — And Keeping Its Strategists Up at Night" Business Insider (December 30, 2019) online: <https://markets.businessinsider.com/news/stocks/biggest-geopolitical-risks-for-markets-2020-stocks-morgan-stanley-2020-2019-12-1028788174>

¹²⁷⁶ For instance, Canadian philosopher Will Kymlicka argues that the slippery slope to eugenics is the key ethical issue in the governance of reproductive biotechnologies. See Will Kymlicka, "Moral Philosophy and Public Policy: The Case of NRTs" (1993) 7:1 Bioethics 16.

identified the need to explain the potential causes of the slippery slope and propose solutions.¹²⁷⁷ However, the literature has yet to offer such solutions, theoretical explanations or factual accounts to prove or disprove that a slippery slope to eugenics is occurring. Since slippery slope arguments are prone to several theoretical and methodological challenges, relying on these arguments might not be the most effective way forward in studying developments in genetic intervention technologies, especially in the legal context. Hence, this thesis suggests focusing on an alternative: the comprehensive study of the legal change of genetic intervention laws.¹²⁷⁸ This comprehensive study revealed key patterns and trends in which the regulation of this field has been transformed over the years.

The objectives of this thesis were to contribute to the discussion by addressing four key gaps in the literature through an analysis of genetic intervention laws' legal change from various perspectives. First, this thesis argued that the legal change pattern raises a number of significant issues and challenges such as ineffectiveness in accomplishing the key legislative goal, the associated ethical and human rights risks and the risk of future state involvement in neo-eugenic markets. Understanding the nature and potential ramifications of this governance problem is an essential motivation to study the legal change patterns, critically re-evaluate the performance of the laws and consider a law reform to ameliorate legal and regulatory flaws. Second, the thesis provided a comprehensive study of the legal change of genetic intervention laws since their inception in the 1980s to the present day. The thesis has shown that genetic intervention laws in the UK and France exhibit a pattern of continuous legal change over the past several years to include a broadening range of previously prohibited genetic interventions. Third, the thesis employed a theoretical framework together with social science evidence to offer insights into the potential drivers of the overextensive legal change problem.

¹²⁷⁷ See for example Petersen *supra* note 85.

¹²⁷⁸ For a lengthier discussion about empirical methodologies for studying legal change, see Ibbetson *supra* note 64.

Fourth, based on the analysis of the potential drivers of the overextensive legal change problem, chapter 9 proposed legislative and policy solutions to strengthen the governance of genetic intervention technologies.

Figure: Overview of the Thesis' Objectives and Contributions

<i>Objectives</i>	<i>Highlights</i>	<i>Applications</i>
 1) Issues and challenges with overextensive legal change	+ A key legislative objective is preventing a slippery slope to eugenics + Tension with ethical and human rights norms + Risk of state involvement in market-driven neo-eugenics + Public concerns about the slippery slope, policy and public discourse shortcomings	+ Better understanding why overextensive legal change is problematic + Reasons to reform genetic intervention laws
 2) Analysis of long-term legal change trends	+ Legal change concerning treatable conditions + Legal change concerning susceptibilities that have low and remote chance of manifesting + Legal change concerning mild conditions + Loopholes could allow for inheritable genetic modification for enhancement purposes	+ A comprehensive chronology of the legal change trend + Analysis of the regulatory shortcomings
 3) Insights into the potential drivers of the legal changes	+ A Socio-legal theoretical framework + A multi-disciplinary analysis to examine the potential drivers of the complicated problem of overextensive legal change	+ Theory and evidence-based insights into the potential drivers of the rapid legal change + Theoretical and Factual Foundations for a reform
 4) A blueprint for a law reform	+ General lessons on how to strengthen the legal governance + A review of international legislation + Legislative amendments proposals + A new legal test to disallow human genetic enhancements	+ A reform blueprint to strengthen genetic interventions' legal governance + Legal and regulatory solutions for Canada and other nations

I) The Potential Ramifications of Genetic Intervention Laws Shortcomings in Setting Limits

This thesis identified and examined four key issues and potential ramifications arising from the diminishing ability of the genetic interventions' legal governance to set meaningful, clear, and effective limits. First, the current rules, as interpreted and applied, are ineffective in accomplishing the key legislative goal of preventing a pattern in which the legal boundaries would become gradually laxer and lead to a mission creep. Second, as reproductive technologies become increasingly capable of pre-selecting, altering and enhancing children's genetic traits, the regulatory system comes closer to *prima facie* inconsistency with national and international norms that view certain genetic interventions as potentially derogating from liberty, human dignity and freedom from discrimination. Third, the legal change gradually erodes the safeguards that could prevent nations in the future from intervening on the markets in child genetics and promote the birth of future citizens with physical and mental characteristics deemed beneficial to the "public good". Fourth, decision-makers and the public are largely unaware of the significant shortcomings of the law in setting effective limits. This unfounded belief that the regulations are robust could hinder a law reform to rectify the growing problem of overextensive legal change. Without a law reform, the combination of overly malleable legal limits and rapidly advancing technologies threaten to exceed the pace of democratic debate, while increasingly setting the course for how these transformative biotechnologies continue to evolve and affect the future of human society.

II) A Comprehensive Chronicle and an Analysis of the Legal Change Patterns

This thesis has shown in detail how laws in the UK and France exhibit a pattern of continuous legal changes over the years to include a broadening range of previously prohibited genetic interventions. The great extent of the legal changes becomes apparent when analyzing the patterns of how the application and interpretation of genetic intervention laws have considerably changed since its inception to the present day. The application and the interpretation of the regulatory requirements have substantially moved away from

the original focus on single-gene caused, lethal congenital malformations. In chapters 4-7, I have examined in detail the process of legal change to four key rules of genetic intervention laws to show a considerable change and weakening of the rules in setting meaningful limits. Genetic intervention laws in the UK and France exhibit a pattern of continuous legal changes over the past several years to permit a broadening range of interventions previously prohibited. This pattern is characterized by the regulatory licensing of genetic interventions specific rules sought to prohibit: screening against conditions that are mild, treatable and not predominantly determined by genes. Furthermore, chapter 7 identified and described two new two loopholes in the proposed regulatory model for inheritable genetic modification. The analysis shows how the broad remit of intervention on “serious” conditions and for a “therapeutic” purpose can enable the very same outcomes sought to be prohibited – human genetic enhancement.

The Significance of the Findings about the Legal Change Pattern

This study’s finding of a legal change pattern are important for several reasons. First, the findings of this study are important as they provide some of the first comprehensive accounts of a distinct pattern of legal change to permit a broadening range of genetic interventions previously prohibited. While this thesis does not seek to produce proof that the slippery slope to eugenics is occurring, the continuous legal change pattern described here bears a certain similarity to demonstrating an “empirical slippery slope”.¹²⁷⁹ Second, this thesis’s finding of an overextensive legal change pattern demonstrates that the prevalent narrative that the regulatory regime is robust and has successfully prevented the notorious slippery slope to eugenics is unfounded. Third, the thesis has corrected this illusory, and potentially misleading narrative. I have shown that quite to the contrary, the regulation suffers from significant weaknesses in setting limits that ended up manifesting in the overextensive legal change pattern. This thesis has shown how the process of legal change of the main rules (lack of treatment, onset, risk and seriousness) has left the regulatory requirements with

¹²⁷⁹ For more about the empirical slippery slope, see Wibren Van der Burg *supra* note 54.

very little ability to perform a meaningful limit-setting function. Fourth, the concerning findings of systematic regulatory shortcomings in setting meaningful limits demonstrate the need for a law reform to establish effective governance of genetic intervention technologies.

Suggestions for Future Research about Legal Change Patterns

This study opens the door for additional research to further examine the fascinating phenomenon of rapidly changing legal governance of genetic intervention technologies. This fast-paced, highly dynamic field will surely require much follow-up research to continue to study and analyze future legal change patterns. I have shown in chapter 2 that the landscape of reproductive biotechnology itself is ever-changing, moving further away from the focus on the prevention of congenital malformations to developing novel methods to preselect and genetically enhance human physical and intellectual capabilities. Genetic interventions' rapid technological evolution finds laws and policies unprepared to address the various and novel challenges it creates. Laws are currently silent on a number of controversial emerging technologies to enhance human capabilities such as creating artificial gametes and embryos¹²⁸⁰ and artificial gene synthesis. For instance, modifying the offspring genome by inserting artificial genes created using synthetic biology techniques could confer traits that do not exist in nature, such as making humans resistant to radiation and able to metabolize inorganic materials.¹²⁸¹ The long-term societal ramifications of biotechnological methods to radically "re-engineer" human biology and tweak individuals' physical and mental characteristics are incalculable. In an era of rapid and relentless changes, future research will need to evaluate major patterns and assess the soundness of the legal governance of human reproductive biotechnology. I have aimed to aid future researchers in the field to assess, evaluate and study change patterns by suggesting we move away from the slippery slope problem, and instead focus on the concrete, context-specific study of legal change.

¹²⁸⁰ Tetsuya Ishii & Mitinori Saitou *supra* note 162.

¹²⁸¹ *Supra* note 205.

III) Insights into the Potential Drivers of the Legal Change Phenomenon

This thesis provides some of the first insights into the potential drivers of the overextensive legal change problem. The analysis primarily relies on the theoretical framework developed by Eugen Ehrlich, one of the founding fathers of the sociology of law and a pioneer of the study of legal change. Ehrlich's theory holds that legal change is a constant process in which legal institutions and rules are re-aligning with society's ever-changing common practices and power relations.¹²⁸² The law, as a living and a dynamic institution, is forced to readapt to the constantly changing cultural, technological, and economic circumstances, many times having to do so within the confines of pre-established and older legal texts.¹²⁸³ The open texture of legal language provides an opportunity for evolving practices and norms to reshape the law.¹²⁸⁴

This thesis explained that genetic intervention laws' legal change largely stems from mounting pressures from the industry, prospective parents and government entities on vague, subjective and overbroad constructs such as "serious condition" and "therapeutic" to be interpreted more expansively and permissively. This thesis has examined in detail the considerable changes in the interpretation and application of genetic intervention's rules over the years. Under the more permissive interpretations, newly approved conditions exhibited a pattern of diverging from the rationale of having a profound impact on the child's health to those that would barely even affect it, but are nevertheless, regarded as abnormal. This inquiry has delved deeper by conducting an analysis of the legal change patterns using social science evidence to examine key players' and institutions' motivations behind pushing for a more permissive approach of approving previously prohibited genetic interventions. This analysis has revealed a host of potential factors affecting regulatees and regulators in pushing for a more permissive approach to genetic interventions. This thesis has examined a variety of influencing factors such as an interest in reducing expenditures on treatment and accommodations,

¹²⁸² Ehrlich *supra* note 109 at 433, 439, and 341–45.

¹²⁸³ *Ibid* at 400-401.

¹²⁸⁴ Antonov *supra* note 115.

clinics' financial interests, how new biotechnologies encourage genetic perfectionist and reductionist views, and parental wishes to have children with less "abnormal" and more desirable traits. A better understanding of the legal linguistic and societal drivers of the overextensive legal change phenomenon aids in addressing this growing problem effectively.

IV) Examining Genetic Interventions Laws' Past and Current Problems to Provide Solutions for the Future

The Need for a Better Informed Discourse about Genetic Intervention Laws' Critical Shortcomings

If political, legal and public discourse comes to confront the current flaws in drawing and holding effective lines to govern genetic intervention technologies, a soberer and more effective policy can emerge. Better informed policy choices about the regulation of genetic intervention technologies are essential if Western democracies wish to take effective steps to prevent the emergence of neo-eugenic practices in the biotechnology era. In order to make responsible choices, the public and policy discourses need to be first better informed about the various critical shortcomings of genetic intervention laws in setting and holding legal limits. This thesis endeavours to pave the way to a better informed, more accurate discourse by correcting a common misconception that dominates the current discourse in the field – that the regulation of genetic intervention successfully prevented the slippery slope to eugenics. It has shown in detail how the overextensive legal change process gradually eroded the regulatory requirements' ability to set meaningful limits, which resulted in a pattern of approval of genetic interventions sought to be disallowed. With greater awareness of genetic intervention laws' various weaknesses, public and political discourse would be able to meaningfully reflect on this growing problem and consider reform.

A Blueprint for Legal Reform to Address the Overextensive Legal Change Problem

Chapter 9 offers a blueprint for a reform that aims to better achieve the key legislative goals of setting effective legal limits and prevent the misuse of reproductive biotechnologies. The proposed reform is based

on two general lessons regarding the qualities genetic intervention laws require to be able to set more effective and durable limits. In order to set more durable boundaries, genetic intervention laws must have two general qualities. First, to improve on the conceptual design of existing rules, lawmakers need to identify clearer normative and clinical distinctions capable of better determining which genetic interventions are permissible and impermissible. Second, the legislative drafting process should place greater attention on making careful language choices that express the laws' underlying conceptual distinctions with clarity, reduced subjectivity, and an explicitly delimited scope. To illustrate these points, chapter 9 provided suggestions for specific legislative amendments, clearer conceptual distinctions and newly developed legal tests. The chapter describes a newly developed legal test that uses a system of categories to designate interventions that would genetically enhance a future child's behavioural, physiological and cosmetic traits as prohibited. The lessons and proposals provided in this thesis are general in nature and can support various ethical viewpoints and policies. These lessons can serve many jurisdictions that lack a comprehensive system of clear legal boundaries to genetic interventions, including Canadian jurisdictions.¹²⁸⁵ I would recommend more work to be done by academics, governments and civil society to identify the laws' challenges in setting limits to rapidly evolving technologies and develop clearer, more effective legal distinctions, tests and boundaries. With strong and durable boundaries, technological progress and humanistic values can coexist in the world of tomorrow.

Recommendations for Canada

Canada can become a leader in adopting truly robust legislation to keep the misuse of genetic interventions at bay. Canadian policy documents acknowledged the paramount importance of properly regulating genetic interventions. One of the key risks identified was a slippery slope to eugenic uses and

¹²⁸⁵ For more about Canada's lack of comprehensive legal regime regarding genetic intervention technologies see François Baylis *supra* note 1188.

human genetic enhancement.¹²⁸⁶ Without such proper regulation, neo-eugenic practices may emerge and jeopardize key human rights to dignity, equality and freedom from discrimination.¹²⁸⁷ Attempts to create “designer babies” and improve the gene pools create novel risks for future generations and the species as a whole.¹²⁸⁸ Official Canadian documents warned that “the very essence of humankind [is at] stake.”¹²⁸⁹ and another states that “Canada must respond decisively and comprehensively to control development and use of [reproductive] technologies” because not intervening “would amount to an abdication of social responsibility and a failure of political will.”¹²⁹⁰ It is only appropriate that Canada would give effect to these concerns it identified with the proper legal response. Canada can become a world leader in the governance of genetic interventions by adopting a legislative scheme that supports innovation while safeguarding the rights of present and future generations.

The timing is right for Canada to consider a reform to its genetic intervention laws. In 2016, the Federal government has announced it is considering changes to the *Assisted Human Reproduction Act*, 2004.¹²⁹¹ The 2010 Supreme Court Decision in *Reference re Assisted Reproduction Act*¹²⁹² can be viewed as an opportunity for the provinces and the federal government to work collaboratively and come up with

¹²⁸⁶ See Canada, House of Commons Standing Committee on Health, *Assisted Human Reproduction: Building Families* (Ottawa: Standing Committee on Health, 2001), online: www.parl.gc.ca/InfoComDoc/37/1/HEAL/ See also House of Commons Science & Technology Committee, *Human Reproduction and the Law 5th Report of Session 2004-05 Vol. I*, (London: TSO, 2005) at 58, 125; Canada, Canadian Biotechnology Secretariat, *Brave New World: Where Biotechnology and Human Rights Intersect* (Ottawa: Government of Canada, 2005) at 3-26.

¹²⁸⁷ Canada, Royal Commission on New Reproductive Technologies, *Proceed with Care: Final Report of the Royal Commission on New Reproductive Technologies: Summary & Highlights* (Ottawa: Canadian Government Publishing, 1993).

¹²⁸⁸ Health Canada, “Guide to The Proposals for Legislation Governing Assisted Human Reproduction” (Ottawa: Health Canada, 2001:3); Health Canada, “Issues Related to the Regulation of Pre-Implantation Genetic Diagnosis under the Assisted Human Reproduction Act” (Ottawa: Assisted Human Reproduction Office, 2005) at 11-13. See also House of Commons Standing Committee on Health *supra* 1286.

¹²⁸⁹ Government of Canada, “Government Notices Department of Health - Assisted Human Reproduction Act Canada Gazette” - Vol. 150, No. 40 — October 1, 2016 online: <http://www.gazette.gc.ca/rp-pr/p1/2016/2016-10-01/html/notice-avis-eng.html>

¹²⁹⁰ Law Reform Commission of Canada, *Human Dignity and Genetic Heritage* (Study Paper) (Ottawa: Law Reform Commission of Canada, 1991), at 1. Royal Commission on New Reproductive Technologies *supra* note 1287 at 10.

¹²⁹¹ Health Canada (2005) *supra* note 1288 at 11.

¹²⁹² *Reference re Assisted Human Reproduction Act, 2010* [2010] SCC 61, 3 SCR 457.

solutions to regulate genetic interventions for the benefit of society. The Federal and provincial governments would need to address one of the greatest challenges with the regulation of genetic interventions – the overextensive legal change problem. This thesis offers decision-makers a toolkit developed to enable Canada and other nations to address this uniquely complicated problem of overextensive legal change and promote responsible governance of genetic technologies.

Shaping Today Tomorrow's History

At this critical juncture, decision-makers should ask themselves one important question - can the current laws truly handle the great responsibility of setting effective limits to potent biotechnological interventions to influence the genetic characteristics and traits of future generations? Beyond the immediate benefits and harms, genetic interventions require careful reflection about the long-term ramifications of this unprecedented technological revolution. In particular, decision-makers should consider what will be the long-term ramifications if the pattern of overextensive legal change demonstrated in this thesis continues towards the gradual “liberalization” of the emerging genetic supermarket. Do the citizens of the future want to live in a society in which children’s traits such as looks, intelligence and behavioural characteristics are a commodity that is selected and bought on the market? What would be the socio-economic ramifications of people in higher stratas genetically enhancing their children and giving them advantages over the lower classes and the global poor? Would the emergence of an elite class of people endowed with superior genetic traits bring back the darker side of the eugenic culture, that of hate, discrimination and judgment of people based on their biology?¹²⁹³ If genetic modification unlocks the door to directing the course of human evolution, as many eminent life scientists claim,¹²⁹⁴ do governments truly have the ability or the necessary legal mechanisms to responsibly govern how such biotechnologies might shape future human evolution? Future decision-makers

¹²⁹³ See for instance, Roberto Andorno et al., "Geneva Statement on Heritable Human Genome Editing: The Need for Course Correction" (2020) 34:8 Trends in Biotechnology 352-353.

¹²⁹⁴ Campbell et al. supra note 45. See also Jennifer A. Doudna, & Samuel H Sternberg, *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution* (Boston: Houghton Mifflin Harcourt, 2017).

might have to deal with these novel and profoundly perplexing problems if the legal limits remain overly malleable and ever transitory in the face of ever-evolving technologies. Critical choices regarding effective legal governance are essential to finally address the looming, novel challenges and problems arising from technologically preselecting and altering the human biological traits and characteristics. Missteps with such transformative technologies to select, modify, and “improve” human biological characteristics could change the fabric of future society. The critical choices made now regarding the governance of these transformative technologies are bound to affect generations to come.

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