

*Three's a Crowd?*

The Legal and Ethical Considerations of  
Mitochondrial Replacement Therapy

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# Contents

<i>Introduction.....</i>	<i>1</i>
<i>I Mitochondria, Mitochondrial Disease and Mitochondrial Replacement Therapy .....</i>	<i>2</i>
<i>A Mitochondria .....</i>	<i>2</i>
<i>I Mitochondria's function.....</i>	<i>3</i>
<i>B Mitochondrial DNA and Genetics.....</i>	<i>3</i>
<i>I Mitochondria's genetic structure .....</i>	<i>3</i>
<i>II Mutations in the mitochondria .....</i>	<i>5</i>
<i>III Mitochondrial inheritance .....</i>	<i>5</i>
<i>C Mitochondrial Disease .....</i>	<i>6</i>
<i>I Symptoms of mitochondrial diseases .....</i>	<i>7</i>
<i>III Current clinically available options for treatment .....</i>	<i>9</i>
<i>D Mitochondrial Replacement Therapy.....</i>	<i>10</i>
<i>I Pronuclear transfer.....</i>	<i>11</i>
<i>II Maternal spindle transfer .....</i>	<i>12</i>
<i>III Cytoplasmic transfer .....</i>	<i>13</i>
<i>II The New Zealand Legal Framework .....</i>	<i>14</i>
<i>A The Human Assisted Reproductive Technology Act 2004 .....</i>	<i>14</i>
<i>I Established procedures .....</i>	<i>16</i>
<i>II Assisted reproductive procedures .....</i>	<i>17</i>
<i>III Prohibited actions .....</i>	<i>18</i>
<i>B MRT and the Current New Zealand Legal Framework .....</i>	<i>19</i>
<i>I The Human Assisted Reproductive Technology Act 2004 .....</i>	<i>19</i>
<i>II Other relevant legislation.....</i>	<i>21</i>
<i>C The definition of “genetically modified” .....</i>	<i>24</i>
<i>I “Genetically modified” in other legislation .....</i>	<i>24</i>

II	Definition of genetically modified under the HART Act .....	27
III	Is MRT “genetic modification”? .....	32
III	The Ethics of Mitochondrial Replacement Therapy.....	33
A	HART Act Principles and MRT.....	35
I	The health and well-being of children.....	35
II	The health, safety and dignity of all present and future generations .....	39
III	The health and well-being of women .....	42
IV	Informed consent .....	43
V	Donor offspring are to be made aware of their genetic origins.....	43
VII	Other considerations under the ACART framework .....	45
B	Conclusion .....	49
IV	Lessons from the United Kingdom.....	51
A	The Human Fertilisation and Embryology Act (UK) 1990.....	51
I	Proposed regulations, consultation response and application in New Zealand.....	52
B	The Way Forward for New Zealand .....	58
	Bibliography.....	61

## *Introduction*

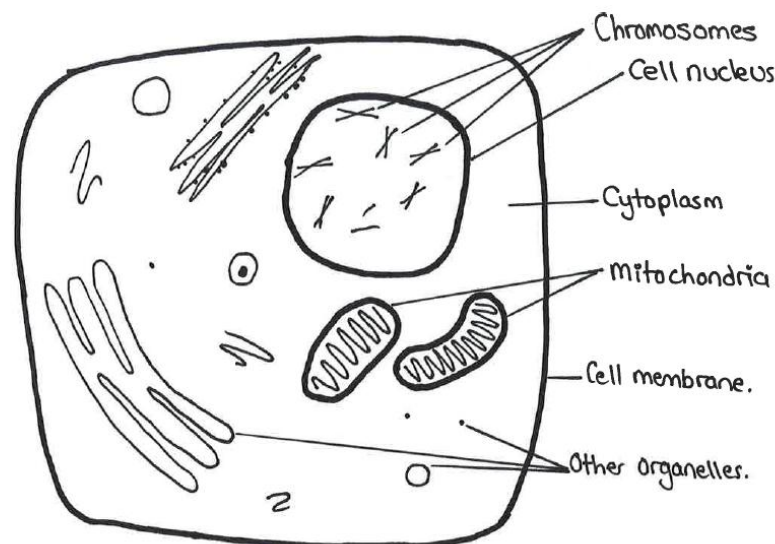
Mitochondrial diseases are a group of severe and debilitating diseases. They can be caused by mutations of the mitochondrial DNA. Researchers have developed mitochondrial replacement therapy as a means of preventing mitochondrial mutations being passed on to the offspring of those with mitochondrial disease, or people who are carriers of the mutations. The technique uses a donor embryo or egg as a source of healthy mitochondria, into which intending parents can have their own nuclear DNA inserted.

This dissertation first describes the science behind mitochondria, mitochondrial diseases and the technique itself, before examining the legal framework in New Zealand concerning assisted reproductive technologies such as mitochondrial replacement therapy. In particular, the meaning of “genetically modified” is considered. It then discusses the ethical issues of the technique before considering the current proposal in the United Kingdom to allow the technique. By way of conclusion, I will outline the legislative reforms I consider necessary to provide a regulatory environment in which mitochondrial replacement therapy can be provided to those who wish to use it.

# *I Mitochondria, Mitochondrial Disease and Mitochondrial Replacement Therapy*

## **A Mitochondria**

The majority of our body's energy is provided by Adenosine Triphosphate (ATP), a tiny molecule responsible for our ability to move, to grow and for our cells to communicate with each other and co-ordinate the diverse array of functions they perform. Most of this ATP is supplied by the mitochondria. Mitochondria are small organelles ("organelles"<sup>1</sup> are membrane-bound structures found within the cell) found in the cell's cytoplasm (the jelly-like substance that fills the cell and surrounds the cell nucleus). They are approximately 0.5-1 $\mu$ m in diameter and make up to 25% of the cell's total volume. Mitochondria are found in every cell of the body except the red blood cells. The number of mitochondria in an individual cell varies greatly depending on the cell's energy requirements; some cells contain a single mitochondrion, while others have several thousand.



**Figure 1: Schematic diagram of a typical human cell (not to scale)**

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<sup>1</sup> A term I am treating as including the nucleus itself, though it should be noted that this is a matter of scientific debate.

## *I Mitochondria's function*

The mitochondria's dominant role is the conversion of chemical energy into ATP. This is achieved by adding a phosphate group to an Adenosine Diphosphate (ADP) molecule. The ATP can then be used by the rest of the cell as an energy source, by cleaving the third phosphate group and releasing the stored energy. This leaves an ADP molecule that can then be recycled over and over by the mitochondria. Due to the cyclical nature of this energy production, the human body only contains about 25g of ATP at any one time, but uses the equivalent of a person's body weight each day of ATP. The proper functioning of mitochondria is therefore essential to the survival of the higher animals, such as mammals and other vertebrates. This is because the mitochondria are by far the most efficient way of producing energy and the only way we can obtain sufficient energy to function. From one glucose molecule, the mitochondria are able to make 30 molecules of ATP. This is compared to just two molecules of ATP produced by glycolysis (the other means of extracting energy from glucose).

In addition to energy production the mitochondria have a role in cell signalling, cell growth, cell differentiation, control of the cell cycle and cell death. The mitochondria also transiently store calcium which can be used to initiate calcium spikes (a precursor to nerve conduction activity).

## ***B Mitochondrial DNA and Genetics<sup>2</sup>***

### *I Mitochondria's genetic structure*

Mitochondria are unique within the human cell's organelles, in that they are the only organelles to have their own DNA (mtDNA).<sup>3</sup> All other DNA in a cell is held

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<sup>2</sup> For a more comprehensive description of the mitochondrial genome, see Tom Strachan and Andrew Read *Human Molecular Genetics* (4<sup>th</sup> Ed, Garland Science, New York, 2011) at ch 9.

within the nucleus (nDNA). While nDNA is organised into 23 pairs of chromosomes, the mtDNA genome is a single, circular genome. The human mitochondrial genome is approximately 16,000 base pairs long and contains 37 genes. In contrast, the total human genome is approximately 3.1 billion base pairs in size and contains at least 26,000 genes.<sup>4</sup> Therefore, the mitochondrial genome accounts for only 0.0005% of the total human genome in size, and for 0.14% of the total genes in a cell.

All the genes found in the mitochondria regulate the mitochondria itself. There are 24 genes that code for translation RNAs (molecules that “read” mtDNA and translate it into protein) and 13 genes that code for proteins that make up the machinery that produces ATP. However, over 3000 proteins are found in the mitochondria. These extra proteins are coded in the nDNA and transported into the mitochondria.

While there is one copy of the nDNA genome in a sperm or egg (the “gametes”) and two copies in almost all other cells (the mother and father of a person contribute one each), there are often two to eight copies of the mtDNA genome in a single mitochondrion, and up to several thousand mitochondria per cell. The notable exception to this is the egg cell (the “*oocyte*”) which can contain as many as 100,000 copies of the mitochondrial genome. Due to the number of copies, multiple variants of the genome can be found within a single cell (this is termed “*heteroplasmy*” with the term “*homoplasmy*” indicating that all of the mtDNA in the cell is the same). This phenomenon does not occur in the nDNA genome due to the low number of copies of the genome per cell. Mutations can arise in both the

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<sup>3</sup> In plant cells, the chloroplasts (the organelles responsible for photosynthesis) also have their own DNA.

<sup>4</sup> This is a constantly changing figure as a lot of the human genome is of unknown function.



nDNA and mtDNA during the life span of an organism, resulting in different cells having slightly different genomes. However, provided the mutations do not occur in the reproductive cells (the “*gametes*”) these mutations will not be passed on to any offspring.

## *II Mutations in the mitochondria*

Mutations in their simplest form are changes to the sequence of base pairs within DNA. They can be caused by a variety of mechanisms. The type of mutation and where it occurs will ultimately determine the mutation’s effect. A mutation in a non-coding region will often be less problematic than a mutation that occurred near the start of a gene. A mutation in a gene that is hugely important will have more of an effect on the body than a mutation in a less important gene (for instance, a mutation in a gene that controls cell division may lead to cancer, while a mutation in the gene that controls hair pigment may alter the colour of one’s hair but ultimately be less problematic for the body’s functioning).

As the mtDNA genome is far more gene-dense than the nDNA genome, any mutation is far more likely to be in a gene coding region in the mtDNA genome compared to the nDNA genome. Also, as some mtDNA genes overlap, a single mutation can affect multiple genes and therefore proteins. This means that mutations are far more likely to affect the functionality of proteins coded for in the mitochondria than in the nucleus, and a single mutation in the mtDNA is more likely to have consequences for the cell than a nDNA mutation.

## *III Mitochondrial inheritance*

Mitochondria are inherited solely along the maternal line through the oocyte. While sperm have their own mitochondria (which provide sperm with the energy required to move), these are located in the sperm’s tail and are actively degraded

by the cell following fertilisation. This means that both males and females will inherit their mitochondria from their mother, but only females will pass on their mitochondria to any offspring.<sup>5</sup> In contrast, the genes that regulate the mitochondria but are found in the nucleus are inherited half from the mother and half from the father of the embryo, along with all of the other nDNA.

At the developmental stage of the oocyte, only a small number of mitochondria are used by the cell to produce the resultant 100,000 mitochondria per cell. Due to the small number of initial mitochondria, a bottleneck effect can be observed. This can skew the mitochondrial genetics of the oocyte, with potentially a large portion of the mitochondria in the oocyte being affected by a mutation despite the mother having a relatively low percentage of mutated mitochondria in her body. This bottleneck effect can explain the differences that can be observed between generations, where a woman with no symptoms of a mitochondrial defect can have several children, all which develop severe mitochondrial disease caused by an inherited mutation of the mitochondria.

### *C Mitochondrial Disease*

Mitochondrial diseases are a group of around 150 diseases caused by the mitochondria malfunctioning. All ultimately result in the body (or parts of the body) failing to get the energy it requires. They are caused by a variety of mechanisms, including mutations arising in the mtDNA or nDNA, the inheritance of faulty mtDNA or nDNA, or being acquired due to exposure to an external environmental factor (such as exposure to certain drugs or an infection).

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<sup>5</sup> There has been one documented case of a person inheriting mitochondria along the paternal line, so while an extreme rarity, it is not impossible.

## *I Symptoms of mitochondrial diseases*

The ubiquity of mitochondria means that mitochondrial disease can affect almost every tissue in the body. Not all those who suffer a mitochondrial disease will exhibit the same symptoms. This is because mutations will not be spread evenly within a heteroplasmic person, and mutations can arise later in life. Different symptom patterns also arise due to the fact that when heteroplasmic cells divide they will not split the mitochondria evenly between the two resultant cells or with equal ratios of mutated to healthy mitochondria. During development of the foetus, this can result in a particular area of the body ending up with a higher ratio of mutated to healthy mitochondria than the rest of the body. This helps explain why different organs can be affected differently in different people with mitochondrial disease.

Symptoms of mitochondrial diseases include poor growth, muscle weakness and loss of muscle coordination, problems with vision and hearing, learning disabilities, disease of the heart, liver and kidneys, gastrointestinal issues, respiratory problems, neurological problems, autonomic dysfunction and dementia. However, these symptoms are not exclusive to mitochondrial diseases. While certain combinations of symptoms (for instance either type 1 or type 2 diabetes and deafness) are common in particular mitochondrial diseases, the fact that a mitochondrial disease is present (opposed to another condition) is often difficult to diagnose. A genetic diagnosis will often be necessary to determine that a mitochondrial disease is present and to establish how it is being caused (i.e. through a mitochondrial defect or a nuclear DNA mutation).

## *II Epidemiology of mitochondrial diseases*

While statistics for the prevalence of mitochondrial disease are not available for New Zealand, it is believed that one in 5,000 children in the United Kingdom is

born with a mutation that will cause a mitochondrial disease.<sup>6</sup> This accounts for disease caused by mutations of both the mtDNA and the nDNA. It is estimated that one in 200 children born will have a defect of the mtDNA, but not all these children will suffer from mitochondrial disease. Currently around one in 10,000 adults in the United Kingdom are severely affected by mitochondrial disease.<sup>7</sup> However, given that one study in a United Kingdom children's hospital estimated that 50-60% of children being treated for mitochondrial disease had not been genetically tested for genetic defects, it is difficult to ascertain the exact numbers of those carrying a mutation or what types of mutations are causing the disease and they are likely to be higher in reality.<sup>8</sup>

While specific mutations have been identified that cause specific mitochondrial diseases, there is by no means a definitive test to establish if a person has or carries a disease-causing mutation. Various mutations also require different percentages of mutated mitochondria to be present in a cell before the cell is affected and symptoms arise. This is known as the "*mutation load*" and is measured as the percentage of affected mitochondria per cell. The disease-causing mutation load is important for determining if a person carries a mutation at a clinically relevant level. However, a woman carrying a mutation that is not at sufficient levels to cross the disease threshold will nonetheless be able to pass the mutation on to her offspring, and due to the mitochondrial bottleneck discussed above, any offspring may have a mutation load capable of causing severe mitochondrial disease.

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<sup>6</sup> Geoff Watts and others *Novel techniques for the Prevention of Mitochondrial DNA Disorders: an Ethical Review* (Nuffield Bouncil on Bioethics, London, 2012) at 1.23.

<sup>7</sup> At 1.23.

<sup>8</sup> At 1.23.

### *III Current clinically available options for treatment*

For many mitochondrial diseases there are limited treatments. Treatments provide symptomatic relief rather than treat the cause of the disease or reverse its effects. Therapeutic treatments are also difficult to develop as they are very difficult to test clinically due to the variation exhibited by those with mitochondrial diseases and the rarity of patients.<sup>9</sup> It is also difficult to assess the efficacy of a proposed treatment, as there are few reliable ways to objectively measure if a treatment has improved the patient's condition. Recently, some vitamins and coenzymes, and in particular pyruvate (a key component of several of the mitochondria's energy producing pathways), have been suggested as potential treatment options, but their clinical value is yet to be adequately assessed.

Pre-implantation genetic diagnosis ("PGD") could potentially be used by intending mothers who suspect they carry a mitochondrial defect. This could allow for selection of embryos that do not carry a mutation-causing defect, or select an embryo with a mutation load under the threshold that will cause symptoms to arise. This option is complicated by the fact that various mitochondrial diseases have different threshold levels of when symptoms will occur, and clinicians would need to consider the most appropriate form of genetic counselling with regards to this issue. Further, not all mitochondrial diseases arising from DNA mutations can be adequately genetically diagnosed so are currently impossible to predict with PGD screening. The option of PGD would also only be possible for heteroplasmic women, as all the oocytes of a homoplasmic woman will carry the mutation. Depending on a heteroplasmic woman's individual mutation load, there is the possibility that some embryos will be suitable for transfer and not have the risk of causing the resultant offspring to

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<sup>9</sup> Due to the small population of patients, mitochondrial disease has been given orphan drug status in the United States of America as a way to incentivise research into the area by pharmaceutical companies.

develop a mitochondrial disease. However, if the offspring was a female, there is still a chance that she could pass a mutation on to future generations. As stated above, the mitochondrial bottleneck effect can hugely skew mitochondrial genetics between generations in unpredictable ways. There are many ethical issues concerning this approach that would need to be considered, but these are outside of the scope of this dissertation.<sup>10</sup>

The second option potentially available is prenatal testing of the foetus. This could occur by testing the placenta or amniotic fluid. Testing would occur between 11 and 15 weeks into a pregnancy, with the exact timing dependent on the technique used. Both these techniques are invasive, and if the foetus was found to carry a mitochondrial defect, would result in the parents having to decide if they wish to continue with the pregnancy or terminate it. Therefore this is not a treatment option as such; rather it provides the parents with information in order to make an informed choice as to whether continue with the pregnancy. As with PGD, there are a large number of ethical issues involved in these options that are outside the ambit of this dissertation.

#### ***D Mitochondrial Replacement Therapy***

Mitochondrial Replacement Therapy (MRT) or “three-way in vitro fertilisation”<sup>11</sup> is an assisted reproductive technology that would allow women who carry a mitochondrial mutation to have healthy children that are genetically related to them but do not carry the mitochondrial mutation. MRT can only be used to

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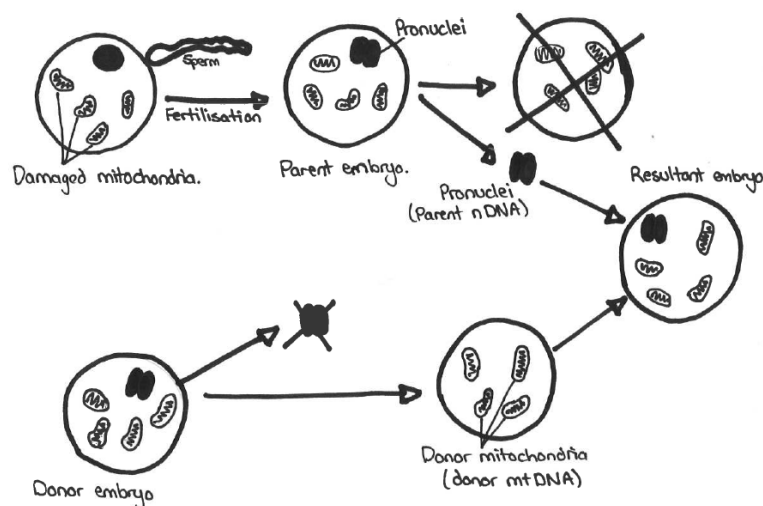
<sup>10</sup> Bredenoord and others “Preimplantation genetic diagnosis for mitochondrial DNA disorders: ethical guidance for clinical practice” (2009) 17 Eur J of Hum Genet 1550-1559 provides a comprehensive review of ethical issues of PGD testing for mitochondrial diseases.

<sup>11</sup> A term I am not using for the remainder of this dissertation as it over-states the genetic contribution made by the donor embryo or egg, but it should be noted the term is commonly used in the media to describe MRT.

prevent mitochondrial disease caused by an inherited defect in the mtDNA. It will not prevent mitochondrial disease caused by an inherited defect in the nDNA, a mutation that occurs after fertilisation in either the nDNA or mtDNA, or acquired mitochondrial diseases from environmental factors.

MRT can be performed in two ways. Both techniques require both the mother and a female donor to undergo a round of ovarian stimulation to retrieve the oocytes, and for the father to have his sperm collected. PGD would also ideally be used to ensure the neither the mother nor donor carried a mitochondrial mutation.

### *I Pronuclear transfer*



**Figure 2: Schematic diagram of pronuclear transfer (not to scale)**

Pronuclear transfer (“PNT”) involves transferring pronuclei from the parents’ embryo into an embryo from the donor. The donor embryo’s pronuclei have been removed prior to transfer. The technique uses zygotes, which are cells in the stage prior to becoming a true embryo. Zygotes contain pronuclei, the nuclei of the two parents prior to their fusion to form a single nucleus. The pronuclei are transferred to the donor zygote. This results in the nDNA from the biological mother and father of the zygote being transferred to the donor embryo, but leaves

behind the cell's cytoplasm, including the mother's mutation-carrying mitochondria. Instead, the second zygote's cytoplasm is used including the donor mtDNA but not the donor nDNA.

## II Maternal spindle transfer

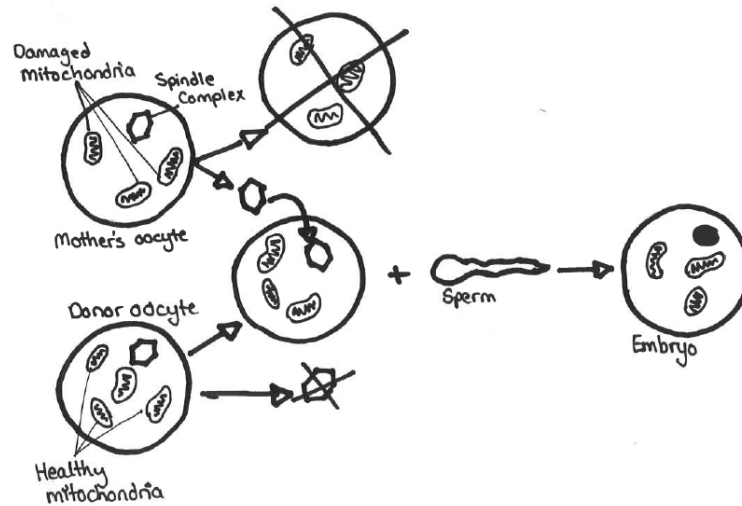


Figure 3: Schematic diagram of maternal spindle transfer (not to scale)

The second variation of the technique is maternal spindle transfer (“MST”) which is performed prior to an oocyte being fertilised. In an oocyte, all the chromosomes containing the nDNA are found at one end of the cell in a spindle-shaped group. The spindle group can be transferred from the mother’s oocyte into the donor’s oocyte, which will have had its nDNA removed. The oocyte can then be fertilised by the father’s sperm to create a zygote which contains the donor’s healthy mtDNA.

Once the zygote is produced by one of the above two methods, it will be allowed to develop into a blastocyst (a five to six day old embryo) before being implanted into the mother or a surrogate.



### *III Cytoplasmic transfer*

A related technique is cytoplasmic transfer (“CT”) which involves transfer of part of the cytoplasm of a donor egg into the intending mother’s egg. The cytoplasm transferred would include some of the donor’s mitochondria, resulting in a heteroplasmic cell. While this technique is not the focus of this dissertation, many of the legal and ethical issues raised by MRT are also issues for CT. It may be a more widely-used technique than MRT if it was allowed to be performed in New Zealand, as it would likely increase the chances of a more mature woman of conceiving.

While not used in New Zealand, CT is offered in various countries around the world. It was used for a period of time by a clinic in the United States where 17 live births occurred. There has been no medical follow up of these children.<sup>12</sup> The use of the technique was stopped after the US Food and Drug Administration required the clinic to seek regulatory approval to continue after two pregnancies were affected with Turner’s syndrome (where a female has one X-chromosome instead of two) and a child was diagnosed with an autism spectrum disorder. However, given that in total only 17 children were born, it is unclear if the technique itself was responsible for these conditions.

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<sup>12</sup> Steve Connor “Medical dilemma of three parent babies: Fertility clinic investigates health of teenagers it helped to be conceived through controversial IVF technique” (25 August 2014) The Independent <[www.independent.co.uk](http://www.independent.co.uk)>.

## II      *The New Zealand Legal Framework*

### A      *The Human Assisted Reproductive Technology Act 2004*

In New Zealand, all assisted reproductive technologies (“ART”) fall within the scope of the Human Assisted Reproductive Technology Act 2004 (“the HART Act”). An ART is defined as a procedure performed for the purpose of assisting human reproduction using any of the following techniques: *in vitro* creation of an embryo, the storage, manipulation or use of an *in vitro* human gamete or embryo, the use of cells derived from an *in vitro* human embryo, and the implantation into a human being of human gametes or human embryos.<sup>13</sup> The term *in vitro* is used to describe the fact that the embryo, foetus, gamete or cell is outside of a living organism.<sup>14</sup>

The HART Act is an amalgamation of two bills that were before Parliament in the early 2000s. The first was a member’s bill entitled the Human Assisted Reproductive Technology Bill (“the HART Bill”). This was submitted by Diane Yates MP of Labour in 1996. The Assisted Human Reproduction Bill (“the AHR Bill”) was introduced in 1998 by the then Minister of Health, Hon Bill English MP. The two Bills were before the Health Committee at the same time. The Select Committee recommended that the AHR Bill not be passed.<sup>15</sup> In 2003, the government amended the HART Bill by Supplementary Order Paper, updating the Bill and removing the licensing regime that was originally proposed.<sup>16</sup>

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<sup>13</sup> Human Assisted Reproductive Technology Act 2001, s 5.

<sup>14</sup> Section 5; the term literally means “in glass”, in contrast with *in vivo* meaning “within the living”.

<sup>15</sup> Assisted Human Reproduction Bill 1996 (227-1) (select committee report).

<sup>16</sup> Supplementary Order Paper 2003 (80) Human Assisted Reproductive Technology Bill 1998 (195-1).

The HART Act aims to *“secure the benefits of assisted reproductive procedures...for individuals and for society in general by taking appropriate measures for the protection and promotion of the health, safety, dignity and rights of all individuals, but particularly those of women and children, in the use of these procedures...”*<sup>17</sup> Further aims of the Act include prohibiting unacceptable procedures and certain commercial transactions, and to establish a regime to hold information concerning children born of donated embryos and cells.<sup>18</sup> In addition to regulating ARTs, the HART Act creates two committees to oversee and approve certain categories of ART procedures. These committees are the Advisory Committee on Assisted Reproductive Technology (“ACART”) and the Ethics Committee on Assisted Reproductive Technology (“ECART”). ACART was established under s 32 of the HART Act and is responsible for providing independent advice on ARTs to the Minister of Health and issuing guidelines for ECART to follow when approving certain procedures.<sup>19</sup> ECART was established under s 27 and has the power to consider individual applications for the use of certain ARTs, along with determining applications to operate fertility clinics and monitoring them.<sup>20</sup>

Alongside the HART Act’s purposes are several principles that all persons exercising powers or performing functions under the HART Act must be guided by, as much as the principles are relevant to the particular power or function.<sup>21</sup> Therefore these principles must be considered by ACART and ECART when considering any application made to them. The principles include the health and well-being of any child born as a result of an ART<sup>22</sup> and the health, safety and

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<sup>17</sup> Section 3.

<sup>18</sup> Section 5.

<sup>19</sup> Section 35.

<sup>20</sup> Section 28.

<sup>21</sup> Section 4.

<sup>22</sup> Section 4(a).

dignity of present and future generations.<sup>23</sup> It is stated that women are more directly and significantly affected by ARTs and therefore their health and well-being should be protected.<sup>24</sup> Informed consent must be given before any procedure is performed,<sup>25</sup> and all donor offspring should be made aware of their genetic origins and be able to access information about themselves.<sup>26</sup> Finally the needs, values and beliefs of Maori should be considered and treated with respect,<sup>27</sup> alongside the different ethical, spiritual and cultural perspectives of society.<sup>28</sup>

The Act divides ARTs into three categories, which are largely representative of the ethical acceptability of each specific procedure to society, and the frequency at which they are performed.

#### *I      Established procedures*

ACART are able to advise the Minister of Health on procedures and treatments that should be declared as established procedures.<sup>29</sup> Established procedures are not assisted reproductive procedures for the purposes of the HART Act, meaning that an established procedure can be performed without ECART approval, unlike all other assisted reproductive procedures.<sup>30</sup> On the recommendation of ACART, the Minister of Health must then recommend to the Governor-General that the procedure be declared to be an established procedure by an Order in Council.<sup>31</sup>

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<sup>23</sup> Section 4(b).

<sup>24</sup> Section 4(c).

<sup>25</sup> Section 4(d).

<sup>26</sup> Section 4(e).

<sup>27</sup> Section 4(f).

<sup>28</sup> Section 4(g).

<sup>29</sup> Section 6.

<sup>30</sup> Section 5(b).

<sup>31</sup> Section 6(1).

The Human Assisted Reproductive Technology Order 2005 (“the Order”) was made pursuant to this power.<sup>32</sup> Schedule 1 of the Order contains the list of procedures that are established procedures for the purposes of the Act. These are procedures that have been performed in New Zealand for a number of years, and while they may raise some ethical and safety issues, they are procedures that are widely considered to be acceptable. Current established procedures include artificial insemination, the collection of gametes for the purposes of donation, egg and embryo cryopreservation, and in-vitro fertilisation (“IVF”).<sup>33</sup> Under certain circumstances, PGD is also an established procedure<sup>34</sup>. There are also circumstances where listed established procedures are not to be treated as established procedures, such as the collection of eggs from a deceased person.<sup>35</sup>

## *II Assisted reproductive procedures*

The assisted reproductive procedures are all procedures that are not established procedures.<sup>36</sup> They include the prohibited actions, but these are discussed in the next section. Each assisted reproductive procedure must first be approved by ACART, which will give interested parties (including the general public) the opportunity to comment on the proposal to allow the procedure.<sup>37</sup> ACART then issues guidelines on the procedure to ECART (and online) who then approve each use of the procedure on a case-by-case basis.<sup>38</sup> Procedures that currently have

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<sup>32</sup> Human Assisted Reproductive Technologies Order 2005.

<sup>33</sup> At cl 5.

<sup>34</sup> For instance, where the testing is for diagnosis of chromosomal abnormalities in women of advanced age or following repeated miscarriages, or for the sex selection of the embryo in circumstances where there is a 25% risk or higher of a sex-linked disorder.

<sup>35</sup> At cl 5(2)(7).

<sup>36</sup> Human Assisted Reproductive Technology Act, s 5.

<sup>37</sup> Section 36(1).

<sup>38</sup> Section 28(1)(a).

ACART approval, and are therefore subject to ECART approval before they can be performed, include the use of PGD in conjunction with Human Leukocyte Antigen (HLA) tissue typing of an embryo (i.e. embryo screening to produce a “saviour sibling”), embryo donation (except within certain familial relationships which are treated as an established procedure), and clinical assisted surrogacy arrangements. There are also a range of other ARTs that could fall into this category if they were to be approved by ACART, but are currently not approved and therefore are unable to be performed in New Zealand (for instance, the performing PGD for a disease that has less than a 25% risk of affecting a pregnancy).<sup>39</sup>

### *III Prohibited actions*

The final category of ARTs under the Act is the prohibited actions. These are procedures and treatments that are never allowed to be performed in New Zealand. As stated by Hon Dr Paul Hutchison MP, the listed prohibited actions are procedures that are “unacceptable to mainstream society”.<sup>40</sup> They are listed in Schedule 1 of the HART Act and include the creation of a cloned embryo for reproductive purposes, and implantation of a cloned embryo, a human- non-human hybrid embryo, or an animal embryo into a human. It is an offence to take any action described in Schedule 1, and any person who commits such an offence is liable to a term of up to five years imprisonment and/or a fine of up to \$200,000.<sup>41</sup>

Within the Act, there are also several actions which are forbidden, but are not listed in Schedule 1. For instance, it is an offence to select a human embryo for

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<sup>39</sup> Human Assisted Reproductive Technology Order, sch 5, pt 2, cl 6.

<sup>40</sup> (6 October 2004) 620 NZPD 15900.

<sup>41</sup> Section 8(4).

implantation into a human being on the basis of the sex of the embryo or to perform any procedure to increase the probability that the embryo will be of a particular sex.<sup>42</sup> It is also an offence to give valuable consideration in exchange for a human embryo or gamete.<sup>43</sup> Compared to the scheduled prohibited actions, a breach of ss 11 or 13 carries the lesser penalty of up to one year imprisonment and/or a fine of up to \$100,000.<sup>44</sup>

ACART are also able to recommend to the Minister of Health that a moratorium be issued in relation to an ART procedure or human reproductive research.<sup>45</sup> This is for 18 months, with the ability to renew the moratorium for a further 18 months if necessary.<sup>46</sup> While a moratorium is in place, ECART is unable to consider any request for the procedure. No moratoriums are currently in force.

## ***B MRT and the Current New Zealand Legal Framework***

### ***I The Human Assisted Reproductive Technology Act 2004***

In New Zealand, the legal position for MRT is far from settled. While some aspects of the process are established procedures (for instance, the collection of eggs and sperm from the primary parents, and elements of the MRT procedure that are identical to conventional IVF therapy), other elements require ethical approval. In particular, the donation of an embryo requires ECART approval,<sup>47</sup> as does the donation of eggs between certain family members. The donation of eggs to a

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<sup>42</sup> Section 11(1).

<sup>43</sup> Section 13(1).

<sup>44</sup> Sections 11(2) and 13(1).

<sup>45</sup> Section 24(1).

<sup>46</sup> Section 24(2).

<sup>47</sup> ACART “Advisory Committee on Assisted Reproductive Technologies: Guidelines on Embryo Donation for Reproductive Purposes” (17 November 2008) <[www.ACART.health.govt.nz](http://www.ACART.health.govt.nz)>.

stranger does not require ECART approval. The legal position in relation to these aspects of the procedure is clear.

The contentious issue surrounding MRT is where within the regulatory framework the creation of the embryo or oocyte using MRT and the implantation of that embryo fits. It is neither an established procedure, nor has it been considered by ACART for approval. Therefore currently, it is not legal to perform the procedure and ECART is unable to approve an application made that wishes to perform it.

Under the HART Act Schedule, it is a prohibited action to “*implant into a human being a genetically modified gamete, human embryo, or hybrid embryo.*”<sup>48</sup> The HART Act does not define the term “*genetically modified*” nor has ACART issued any guidance on the term. There is at least a *prima facie* argument that MRT would create a genetically modified embryo as the embryo has had its genetics altered by artificial means. This would mean that any embryo created by MRT could not be implanted into a human for reproductive purposes. This is discussed in the next section of this chapter.

Further, an MRT embryo is not a hybrid embryo for the purposes of the HART Act. While it could be said that MRT is “fusing or compacting the cell of a human embryo with the cell of another human embryo”<sup>49</sup> this would be an awkward interpretation to adopt, given the transfer of a nucleus between human and non-human embryos is explicitly mentioned<sup>50</sup>, but not the transfer of a nucleus between human cells.

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<sup>48</sup> Schedule 1, clause 8.

<sup>49</sup> Section 5(c).

<sup>50</sup> Sections 5(d) and (e).



## *II Other relevant legislation*

The HART Act is currently the only regulatory framework that MRT falls comfortably within its scope. Other legislation, such as the Medicines Act 1981, the Human Tissue Act 2008, and the Hazardous Substances and New Organisms Act 1996 (“the HSNO Act”), exclude the procedure from their ambit. MRT also potentially engages issues concerning the status of the donor. The Status of Children Act 1969 clearly delineates this issue for the purposes of altruistic donation of eggs and embryos. The Care of Children Act 2004 will apply to any arrangement entered into if the woman who donated the donor egg or the couple who donated the donor embryo wish to be a part of the child’s life.

### *(a) Medicines Act 1981*

Mitochondrial replacement therapy is not a medicine for the purposes of the Medicines Act, because it is neither a substance, nor does it achieve its intended action by pharmacological, immunological or metabolic means.<sup>51</sup> It does not fall within the ambit of Part 7 of the Medicines Act as a related product because it is not a food, cosmetic or dental product. Finally, it is also not a specified biotechnical procedure under Part 7A of the Medicines Act, as MRT is not xenotransplantation.<sup>52</sup> However, MRT does meet the definition of “therapeutic purpose” that all medicines must meet. This is because it has the purpose of preventing, alleviating, curing, and/or compensating for a disease, ailment, defect or injury.<sup>53</sup>

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<sup>51</sup> Medicines Act 1981, s 3(1)(a)(ii).

<sup>52</sup> Section 96A; xenotransplantation requires animal biological material to be transplanted into a human, as occurs in pig heart valve transplants.

<sup>53</sup> Section 4(1).

As discussed later in this chapter, the HART Act repealed a provision of the Medicines Act that could have applied to MRT.<sup>54</sup> This was the legislative regime for specified biotechnical procedures, as created by the Medicines (Restricted Biotechnological Procedures) Act 2002. The provisions covered germ-line genetic procedures, including genetically modified embryos and oocytes. However, the repeal of these provisions shows a clear intention of Parliament to remove ARTs from the ambit of the Medicines Act.<sup>55</sup>

#### (b) Human Tissue Act 2008

All ARTs involving the use of gametes and embryos are not subject to the Human Tissue Act by virtue of s 7(2) of that Act, which states that “a human embryo or human gamete is not human tissue for the purposes of any provision of this Act”.<sup>56</sup> Of particular importance to MRT is that this exclusion prevents family members objecting to the donation and use of a relative’s egg or sperm for the purposes of an ART, or the donation of an embryo, as they would be able to if embryos and gametes were regulated by the Human Tissue Act.<sup>57</sup>

#### (c) Hazardous Substances and New Organisms Act 1996

The HSNO Act regulates the use and introduction into the environment of new and modified organisms and potentially hazardous substances. While MRT may arguably be creating a new organism if the embryo produced by the technique matured to a human being, the HSNO Act specifically defines “organism” as not including human beings, but including human cells.<sup>58</sup> Human cells include

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<sup>54</sup> Human Assisted Reproductive Technology Act, s 86.

<sup>55</sup> These provisions are discussed later in this chapter.

<sup>56</sup> Human Tissue Act 2008, s 7(2).

<sup>57</sup> Section 31; while not explicit in the statute, medical practitioners will refuse to use a donated organ if close family object to its use.

<sup>58</sup> Hazardous Substances and New Organisms Act 1996, s 2(1).

embryonic cells and gametes, but the HSNO Act only applies to cells that are “grown or maintained” outside the body.<sup>59</sup> As MRT does not involve growing or maintaining the embryo outside of the body (rather the embryo is produced, developed for 5-6 days then transferred into the womb), the MRT procedure does not fall within the ambit of the HSNO Act.

(d) Status of Children Act 1969 and Care of Children Act 2004

Under Part 2 of the Status of Children Act, a woman who falls pregnant following an “assisted human reproduction” (AHR) procedure will be the legal mother of that child, not the donor who supplied the egg.<sup>60</sup> For the purposes of the Status of Children Act, an AHR procedure includes a donor ovum or donor embryo implantation procedure, with a donor embryo being an embryo created with a donor ovum and a man’s sperm, whether or not the sperm is from the social father of the resultant child or a male donor.<sup>61</sup> While it is highly unlikely that at the time of enactment Parliament considered whether the definition of “embryo” in the Status of Children Act would apply to an embryo created by MRT, the wording of the provisions is clear, unambiguous and will therefore apply to an MRT embryo. Further, there would be a significant anomaly if embryos created by MRT were to be treated differently from more traditional donated embryos when considering the issue of legal parentage. Therefore Part 2 of the Status of Children Act should apply to embryos produced through MRT and any resultant children.

The Care of Children Act 2004 expands on the Status of Children Act. Under s 40 of the Act, there is encouragement for parents and donors to come to their own arrangements concerning the resultant child’s upbringing. However, while a

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<sup>59</sup> Section 2(1)(a).

<sup>60</sup> Status of Children Act 1969, s 17.

<sup>61</sup> Section 15(2).

Court can make an order that embodies the arrangement, the arrangement itself is not binding on the parties.<sup>62</sup>

### *C The definition of “genetically modified”*

Under the HART Act, it is a prohibited action to implant into a human a genetically modified human embryo or gamete.<sup>63</sup> The term genetically modified is not defined in the Act. It was also not defined in the two Bills that were the precursors to the HART Act. It is a contentious issue as to whether the MRT technique results in the production of a genetically modified embryo.

#### *I “Genetically modified” in other legislation*

The term “genetically modified”<sup>64</sup> is not used consistently in either law or within the scientific community. The term is used in the HSNO Act, the Australia New Zealand Food Standards Code (“ANZFSC”), and was defined in the Medicines Act until the HART Act repealed the provision. However, each use takes a different approach which demonstrates the range of definitions that can be attributed to the term.

##### (a) Hazardous Substances and New Organisms Act 1996

The HSNO Act defines a “genetically modified organism” as:<sup>65</sup>

*any organism in which any of the genes or other genetic material have been modified by in vitro techniques, or are inherited or otherwise derived, through any number of replications, from any genes or other genetic material which has been modified by in vitro techniques.*

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<sup>62</sup> Care of Children Act 2004, s 40(4).

<sup>63</sup> Schedule 1, cl 8.

<sup>64</sup> And similar terms.

<sup>65</sup> Section 2(1).

The term is further defined by the Hazardous Substances and New Organisms (Organisms Not Genetically Modified) Regulations 1998. The regulations list a multitude of ways in which genetically modified organisms can be created, but for the purpose of the HSNO Act should not be treated as such (and therefore do not require the safety analysis of a new organism under that Act).<sup>66</sup> It is unnecessary to fully describe the techniques contained within the regulation for the purpose of this dissertation, but the comprehensive list does demonstrate the large array of techniques which could be considered to be genetic modification if it were not for the regulation.

The HSNO regulations demonstrate that certain techniques will be acceptable in some circumstances and not others. For instance, the regulations state that the regeneration of a plant from organs, tissues or cell culture, including those produced through somaclonal variants is not to be considered to produce a genetically modified organism for the purpose of the HSNO Act.<sup>67</sup> However, if this technique were to be performed in humans, it would amount to cloning. Whether or not this technique results in a genetically modified embryo would therefore be irrelevant as cloning is an explicitly prohibited action if performed for reproductive purposes in humans.<sup>68</sup>

#### (b) The Australia New Zealand Food Standards Code

Standard 1.5.2 of the ANZFS Code defines a genetically modified food in a far more restrictive way. Genetically modified food is food (or a food's ingredient) which is

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<sup>66</sup> Regulation 3.

<sup>67</sup> Regulation 3(1)(b); somaclonal variants are produced in plants where cells from non-reproductive tissue demonstrate a favourable trait, and are used to produce a strain of plants (compared to inbred pollination techniques which continue breeding the original strain).

<sup>68</sup> Human Assisted Reproductive Technology Act 2004, Sch 1, cl 3.

produced using gene technology and which contains novel DNA and/or novel protein, or has altered characteristics. A gene technology means a recombinant DNA technique<sup>69</sup> that alters the heritable genetic material of living cells or organisms. Novel DNA is DNA which is different in chemical sequence or structure from the DNA or protein present in counterpart food which has not been produced using gene technology.

(c) The Medicines Act 1981

The Medicines Act was amended by the Medicines (Restricted Biotechnological Procedures) Act 2002, which provided temporary measures to control the use of germ-line genetic procedures in respect of humans.<sup>70</sup> The Amendment Act was passed in expectation of a “comprehensive legislative regime” being enacted, i.e. the HART Act.<sup>71</sup> The Amendment Act gave the Minister of Health the power to authorise a person or group of persons to conduct a specified biotechnical procedure.<sup>72</sup> Specified biotechnical procedures included a germ-cell genetic procedure, which was defined as including the insertion or injection into a human being of a genetically modified gamete or embryo.<sup>73</sup> The Amendment Act also defined a “*genetically modified embryo*” as a “*zygote or an embryo whose genetic structure has, as a result of artificial processes, been modified.*”<sup>74</sup> The reference to genetic structure may indicate that the term should be interpreted as being wider

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<sup>69</sup> A recombinant DNA technique is a laboratory technique that involves splicing DNA to break or remove a section, then inserting a new section of DNA into the disrupted section and re-joining the DNA together. The technique can be used to remove part of the organisms DNA so that a gene is no longer complete and will not be expressed, or to add DNA from another organism into the first organism’s DNA.

<sup>70</sup> Section 4.

<sup>71</sup> Section 4.

<sup>72</sup> Section 6.

<sup>73</sup> Section 6.

<sup>74</sup> Section 6.

than simply the nuclear genome and includes mitochondrial DNA. The HART Act repealed all of the above provisions,<sup>75</sup> but they are a helpful piece of legislation for interpretation purposes.

It is unclear what inference should be drawn from the repealing of the Medicines Act provision. While it is clear that Parliament intended to exclude ARTs from the Medicines Act's ambit, it is also possible that Parliament intended to repeal the definition of genetically modified embryo or gamete. This conclusion is supported by the fact that Parliament did not re-enact the definition in the HART Act. Unfortunately the Hansard record of the debate prior to the HART Act being passed into law contains no discussion of the term.

## *II Definition of genetically modified under the HART Act*

As demonstrated by the definitions above, genetically modified is a term that can be used in different ways. Potential definitions could be said to lie on a continuum. The widest definition possible would be to say that any organism that has had its genetic material altered in any way is genetically modified. However, this definition would encompass all living organisms currently in existence, as no species has their genetics completely unchanged by natural, sexual or artificial selection, random mutation, virus activity and other genetic events. In the context of the HART Act, this is obviously not the intended definition because these changes are *in vivo* alterations and the HART Act only applies to *in vitro* gametes and embryos

Alternatively, the narrowest meaning of genetically modified would be similar to the ANZFSC definition and require novel DNA to be inserted into an organism's genome using recombinant techniques to be considered genetic modification. In

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<sup>75</sup> Human Assisted Reproductive Technology Act 2004, s 86.

the context of human genetics, this would be too narrow a definition. It would allow clinics to move genes and sets of genes from one embryo to another as wished, provided the genes were not novel (i.e. provided the genes were human), and would also allow deletion of genes. In effect, it would allow “designer babies”.<sup>76</sup>

Between these two extremes lie definitions involving various combinations of the following factors: insertion, deletion or mutation of single genes by recombinant events; insertion deletion or mutation of a set of genes by recombinant events; insertion of genetic elements through the use of a pro-virus<sup>77</sup>; alteration of genetic structure; alteration of the nuclear DNA; transfer of chromosomes between cells; and transfer of an organelle genome between cells.

It is important to note that our scientific understanding of genetics and its related fields has expanded exponentially since the HART Act’s enactment in 2004. For instance, attention has turned from single gene mutations as a focus of disease research to multigene and multi-factorial diseases.<sup>78</sup> Likewise, our understanding of the genome itself has widened. In 2003, the Human Genome Project was declared to be complete. Since then, geneticists have been focussing their research

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<sup>76</sup> Designer babies are the result of genetic modification of an embryo. The genetic modification would involve the insertion of particular sets of DNA into the nuclear genome of the cell, thereby altering the nuclear DNA of the embryo and resulting in a child that exhibited particular traits. Designer babies are a distinct use of biotechnology and are ethically and scientifically distinct from using PGD for the avoidance of implanting an embryo with a high likelihood of developing a genetic disease.

<sup>77</sup> Pro-viruses reverse transcribe their genetic material, which can then be inserted into DNA- this is how the HIV virus functions.

<sup>78</sup> For instance, the development of the majority of cancers is now understood to involve the mutation of multiple genes in combination with environmental factors, while earlier predictions were that specific alleles in a single gene would be the main predictor or cause of cancer - as is the case with the BRCA 1 and 2 genes associated with particular types of breast and ovarian cancer.



not just on the human genome, but also the proteome, metabolome, microbiome and epigenome, and studying these in conjunction with environmental factors. This is not to suggest that the definition of “genetically modified” should encompass all of these associated fields of research, but to emphasise the point that the term may not be as clearly defined within the science community as the authors of the HART Act likely expected it to be, and may in turn become less definitive as science progresses.

The Interpretation Act 1999 requires the meaning of an enactment to be ascertained from its text and in light of its purpose.<sup>79</sup> Further, enactments apply to circumstances as they arise.<sup>80</sup> Therefore, “genetically modified” must be interpreted in accordance with the HART Act’s principles and purposes, and this definition can change as new techniques arise and public opinions change. Of particular importance are the purposes of promoting and protecting the health, safety, dignity and rights of all individuals, and the prohibition of unacceptable assisted reproductive procedures.<sup>81</sup> Within the section 4 principles are the important principles of promoting the health and well-being of children born as a result of the performance of an ART, the health, safety and dignity of present and future generations, and the need to respect the needs, values, and beliefs of Maori, and the different ethical, spiritual and cultural perspectives in society.<sup>82</sup>

As stated above, there are clear arguments against allowing “designer babies” under the HART Act. To do so would risk the health of the individual produced, and any of their offspring. At this stage we do not have the technology to do this

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<sup>79</sup> Interpretation Act 1999, s 5(1).

<sup>80</sup> Section 6.

<sup>81</sup> Human Assisted Reproductive Technology Act 2004, ss 3(a) and (b).

<sup>82</sup> Section 4.

safely. Such a procedure would also violate the child's inherent dignity.<sup>83</sup> A "made to order" child risks treating a child as a commodity, will likely violate the right to an open future for the child, and is generally considered unacceptable by the vast majority of the population of New Zealand. To produce a designer baby would be to treat a child as a means to an ends, whether the commissioning child's parents wished for a child with increased IQ or certain physical traits. Therefore, the definition of genetic modification needs to restrict any ability to select and insert specific genes or sets of genes for a child, or to delete "undesirable" genes.

It is more than likely that the prohibition on implanting a genetically modified embryo was targeted towards designer babies. This was a major concern amongst a large portion of the population when the HART Act was being enacted.<sup>84</sup> This assessment is supported by what types of pre-implantation genetic diagnosis (PGD) are able to be used for at present. PGD is only able to be used in a very restricted manner, and only for the avoidance of genetic defects that carry a significant risk of serious disease.<sup>85</sup> While we have or are near to having the technology to use PGD to detect alleles that confer particular characteristics (for instance eye colour, height or intelligence) PGD is not currently allowed for these purposes. This aligns with the social acceptability of selecting or designing a child that fulfils the wishes of its parents as to how their child will look or perform in sporting endeavours.

Similarly, the transplant of individual chromosomes would be an extension of this concept, as a chromosome can be considered to be a large group of genes. While not disrupting the nDNA, considerable safety concerns arise due to the interactions that we know occur between genes on different chromosomes.

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<sup>83</sup> Dignitarian law is considered in more depth in the next chapter.

<sup>84</sup> And remains a concern.

<sup>85</sup> Human Assisted Reproductive Technology Order 2005, sch 1, pt 2, cl6.

Further safety concerns would arise concerning the fact that a chromosome transplant would require the nuclear membrane to be pierced, which could potentially have unforeseen consequences. Similar safety concerns arise with the use of pro-viruses (used in a way similar to gene therapy) in that we have no way to predict where a gene will be inserted into the DNA, with potentially disastrous results.

In contrast, other forms of technology that could be defined as genetic modification do not violate the principles of the HART Act. I consider that organelle transplant between cells falls within this category. In particular, the use of genetic manipulation to prevent serious disease could be appropriate given that a purpose of the HART Act is to promote the health and safety of those born through ARTs and future generations. Further, the dignity of the resultant child, and humankind in general, would not be violated as the child is not being created as a means to an ends.

The distinction between the two categories of genetic techniques is whether or not a discrete genome is disrupted. If the nDNA or mtDNA is altered, through deletion, insertion, rearrangement or mutation of genes, this should be considered genetic modification under the HART Act. In contrast, to take the nDNA or mtDNA genome in its entirety and transplant it into another cell does not raise the same concerns about violation of the HART Act principles and purposes, and should therefore not be considered genetic modification.

Finally, as Associate Professor Peter Dearden has recently argued (albeit in the context of the HSNO Act provisions), defining genetic modification by the

technique used rather than the outcome achieved can be problematic.<sup>86</sup> I would support this comment, especially in light of the rate that the science of ARTs develops compared to how fast the law is able to regulate ARTs. There is a need to define the term “genetically modified” in a way that clearly delineates what is genetic modification and what is not. This protects the intent of the legislation from those seeking to avoid it by circumventing the statute. This statement is supported by problems that arose in the 1990s in the United Kingdom, following the cloning of Dolly the sheep. As the case *R (Quintavalle) v Secretary of State for Health*<sup>87</sup> serves to demonstrate, too prescriptive an approach in this area can result in parties wishing to circumvent the legislative restrictions by performing ARTs in inventive ways. As such, the clear delineation of genetic modification as stated above is appropriate and unambiguous.

### III Is MRT “genetic modification”?

If the above definition of genetic modification is applied, MRT is not genetic modification as the technique involves the transfer of entire mitochondria and keeps the individual mitochondrial genomes intact. This conclusion is supported by the British Government, who has stated that MRT is not genetic modification.<sup>88</sup> This conclusion allows ACART to consider if MRT ought to be performed in New Zealand and to issue guidelines to ECART for them to approve applications for the procedure.

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<sup>86</sup> Peter Dearden “Defining Genetic Modification” (5 August 2014) Sciblogs <[www.sciblogs.co.nz/southern-genes](http://www.sciblogs.co.nz/southern-genes)>.

<sup>87</sup> [2003] 2 AC 687 (HL).

<sup>88</sup> Public Health Directorate *Mitochondrial Donation: Government responses to the consultation on draft regulations to permit the use of new treatment techniques to prevent the transmission of a serious mitochondrial disease from mother to child* (Department of Health (UK), July 2014) at 15; however, this statement has been criticised by several scientists.

### *III The Ethics of Mitochondrial Replacement Therapy*

In this chapter I will consider MRT through the lens of the ethical framework that ACART uses to guide deliberations when considering applications under s 36 of the HART Act. This analysis is therefore an assessment of whether ACART ought to allow MRT to be performed in New Zealand, rather than a comprehensive analysis of all the ethical issues concerned with MRT. The analysis also includes several wider ethical issues that need to be considered before MRT is performed, such as the level of disclosure to any child born from MRT. While I am using the framework as a template for this chapter, the major ethical objections to MRT are also covered in this chapter.<sup>89</sup>

ACART has issued an ethical framework<sup>90</sup> that it uses as a guide to navigate the ethical matters that arise around ARTs (and human reproductive research). However, the framework is just a framework; ACART is not bound by the document and can consider any wider implications of ARTs. ACART stresses that the document is not intended to be a “recipe, a checklist or a set of decision criteria.”<sup>91</sup> It is also important to note that ACART’s role is defined by statute. It has the mandate to consider specific technologies, and to monitor international developments in relation to ARTs.<sup>92</sup> As such, it is not an “ethical think tank”<sup>93</sup> and does not engage in the wider ethical debate surrounding ARTs. Instead it should

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<sup>89</sup> For an expanded discussion of MRT, see the Nuffield Council on Bioethics Report, above at n 6.

<sup>90</sup> Gareth Jones and Maja Whitaker “Ethical Framework for ACART” (17 November 2008) <[www.ACART.health.govt.nz](http://www.ACART.health.govt.nz)>.

<sup>91</sup> At 2.

<sup>92</sup> Human Assisted Reproductive Technology Act 2004, s 35.

<sup>93</sup> At 2; the New Zealand Bioethics Council which would perform this role was disestablished in 2009.

be viewed as a policy making body, with such policy being guided by wider legislation and general policy considerations.

In considering an application to approve an ART, ACART's powers are limited by the HART Act. As established in the previous chapter, it cannot approve any of the prohibited actions contained within Schedule 1 of the Act, or any of the other procedures prohibited by specific sections of the HART Act. Therefore ACART only has the ability to consider allowing MRT to be performed in New Zealand if it considers MRT not to be genetic modification.

ACART must also consider the purposes and principles of the HART Act,<sup>94</sup> and must call for and consider public submissions before issuing guidelines.<sup>95</sup> Not all the purposes and principles will be able to be accommodated for every ART application. ACART acknowledges that in particular the requirement to take into account public opinion can be challenging.<sup>96</sup> There is no guarantee that any public consultation will reflect the general public's opinion, and often submitters have very strong feelings towards ARTs in general rather than the ART being considered. While public submissions are important, especially in light of the HART Act principle that "the different ethical, spiritual, and cultural perspectives in society should be considered and treated with respect",<sup>97</sup> such perspectives are never determinative of a matter. The pluralistic nature of New Zealand (with regard to religious, cultural, ethnic and ethical groups) means it will be near impossible to reconcile all perspectives. ACART has stated that it will adopt "an approach of cautious liberalism",<sup>98</sup> while ensuring that all of the HART Act's principles (and in particular the principle that secures the benefits of ARTs for all in society) are adhered to as far as possible.

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<sup>94</sup> Sections 3 and 4.

<sup>95</sup> Section 39(1).

<sup>96</sup> Above at n 90, at 1.

<sup>97</sup> Section 4(g).

<sup>98</sup> Above at n 90, at 2.

## **A     *HART Act Principles and MRT***

### *I       The health and well-being of children*

The first principle of the HART Act is that the “health and well-being of children born as a result of...an ART...should be an important consideration in all decisions about that procedure.”<sup>99</sup> Firstly, it should be noted that while the health and safety of the child is an important consideration, it is not a consideration of paramount importance.<sup>100</sup> The interests of the child must be balanced against the interests of other parties. ACART has stated that this can mean that a small degree of risk to a resulting child can be acceptable in some circumstances, if, when balanced against other interests, this can be justified.

#### **(a) Safety considerations**

In relation to MRT, safety considerations are of particular concern. There is still a degree of uncertainty surrounding the safety of the technique, but the only way to fully establish its safety is to allow it to be performed. Bioethicists in the United Kingdom have raised concerns about potentially adverse reactions between the mother’s nDNA and the donor mtDNA, and have also questioned the potential for epigenetic reprogramming of the embryo.

A recent scientific review update issued by the Human Fertilisation and Embryology Authority (“HFEA”) in the United Kingdom has recommended a set of experiments be performed before the technique is attempted in humans, though it should be stressed that the HFEA does not consider the two MRT techniques to

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<sup>99</sup> Section 4(a).

<sup>100</sup> Cf Care of Children Act 2004, s 4.

be unsafe.<sup>101</sup> For instance, the HFEA has recommended that experiments be conducted assessing the level of mutant mitochondrial transfer (mitochondria that are inadvertently transferred alongside the nucleus during MRT), and further analysis of any epigenetic effects of the technique.<sup>102</sup> This type of research is necessary to answer important questions raised about MRT. From an ethical standpoint, it is imperative that we know as much as possible about the effects and risks associated with MRT prior to implementing the technique in humans for reproductive purposes.

Once we are able to more accurately predict any harms associated with MRT, it is important to balance this harm against any potential harm in not performing the technique. If the child's mother is homoplasmic for a mitochondrial disease, MRT is the only option that ensures both a genetic relationship between the mother and the child and the chance of a healthy child. Compared to the certainty of the child also being affected by the mitochondrial defect, there is a strong argument that a statistically significant risk to the child from MRT is acceptable. Further, different groups of society will assess and prioritise risks differently. It therefore accords with principles of reproductive liberty<sup>103</sup> that once a procedure has been assessed as sufficiently safe to allow its use, the decision concerning exactly how much risk is acceptable to specific parents should be left to those parents.<sup>104</sup> The parents should be able make this decision for themselves in conjunction with counselling as to the available options (which include MRT, egg or embryo donation and adoption). The ACART framework recognises that parental views generally

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<sup>101</sup> Andrew Greenfield and others *Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 update* (Human Fertilisation and Embryology Authority (UK), June 2014) at 4.

<sup>102</sup> At 4.10.

<sup>103</sup> As discussed below.

<sup>104</sup> But subject to ECART approval.



prevail in judging what is in the best interests of their children, even when the children themselves are not yet in existence.<sup>105</sup>

#### (b) Wider well-being considerations

Further, ACART recognises that “well-being” is far wider than a child’s physical health. It can include social, emotional, psychological and cognitive aspects of a child’s welfare.<sup>106</sup> Therefore in considering MRT, the question is far wider than simply “is this technique safe?” Instead, ACART needs to take a more holistic approach in considering the general well-being of the child. For instance, is there merit in allowing this technique if it is the only way for the child to have a genetic link with their mother?<sup>107</sup>

#### (c) Identity

These considerations can also extend to the notion of identity. The Nuffield Bioethics Council has discussed these issues at length, and noted that “identity” is a highly elastic term.<sup>108</sup> Identity can include genetic identity, encompassing the characteristics we get through our genetic make-up and how we perceive ourselves (or self-concept identity). Also relevant is qualitative identity, which includes the total sum of our physical traits along with our more holistic features such as social and spiritual identity. Finally, quantitative identity recognises that no two people are alike, and as such, each person is a distinct and separate individual.

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<sup>105</sup> Above at n 88, at 6.

<sup>106</sup> At 7.

<sup>107</sup> This is perhaps not an ethical issue. The legislation clearly favours allowing women to have their own genetically related child, given that procedures such as PGD and IVF are allowed and no consideration is given to the issue of whether adoption has been contemplated.

<sup>108</sup> Above at n 6, at 52.

While MRT is likely to alter the identity of a child in regard to several of these aspects of identity, this is unlikely to adversely affect the child's wellbeing. The Nuffield Bioethics Council was sceptical about placing an ethical distinction on any concept of identity, but did note that having a mitochondrial disease would likely affect a person's identity as much as not having one.<sup>109</sup> What a person considers their identity to be is a highly flexible, individual and largely unpredictable concept, and is influenced by far more factors than simply the nature of one's conception and the genetic relationship to one's parents.<sup>110</sup>

The use of MRT will ultimately change what individual comes into being. This causes the non-identity paradox to arise. It can be argued that, because MRT is used, another person was not born (i.e. the person that would have been produced by using only the parents' or the donor's embryo) and that person could be said to be harmed by not being born. The paradox exists because if the only harm is to that potential person and not a person that was ever in existence, no harm is actually caused.<sup>111</sup> No ethicist has adequately rebutted the non-identity paradox, but it is worth noting in passing that it exists. However, given that the paradox also arises whenever PGD is used and we allow PGD to be performed, it would be an unjustified inconsistency to consider it a major ethical problem for MRT but not PGD.

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<sup>109</sup> At 57.

<sup>110</sup> For instance, when and how information relating to a person's genetic origins is a hugely influential factor on how they process the information psychologically and if they go on to accept this information.

<sup>111</sup> For discussion of the non-identity paradox, see Parfit *Reasons and Persons* (Clarendon Press, Oxford, 1987).

## *II The health, safety and dignity of all present and future generations*

### *(a) Germ-line therapy*

The factors above need to be considered in conjunction with “the human health, safety, and dignity of present and future generations”.<sup>112</sup> Of particular importance to this principle is the fact that MRT is a germ-line therapy. This means that the therapy will affect not only the child produced by the technique, but also any subsequent generations along the maternal line. Because mitochondria are only inherited along the maternal line, there has been suggestion that sex-selection techniques be used to select for only male offspring for the first generation of MRT babies, to ensure subsequent generations are not adversely affected if unforeseen side effects arise. Several ethicists have argued strongly against such an approach.<sup>113</sup> In particular, they object to a class of male children being created as a generation of “experimental offspring”.<sup>114</sup> It was also noted that there is at present no evidence to suggest that within the first generation there would be any medical distinction between the male and female children produced by MRT and it is therefore unjustified to allocate all the risk of implementing the procedure in humans to males. I would suggest that if there were sufficient safety concerns to warrant such a course of action, the procedure should not be performed at all for now.

A second safety concern is that it is unclear what effects the technique will have on subsequent generations of offspring born to those produced by MRT. Like the concerns for the first generation, there is no failsafe way to establish safety in this regard. However, there should be further research using non-inbred laboratory

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<sup>112</sup> Human Assisted Reproductive Technology Act 2004, s 3(b).

<sup>113</sup> Above at n 6, at 80.

<sup>114</sup> Above at n 6, at 80.

animals to show the procedure is safe for subsequent generations to the greatest extent possible.<sup>115</sup>

#### (b) Dignity

ACART has not expanded on what it considers “dignity” to mean other than to say the HART Act is concerned with the “inherent dignity” of present and future generations. Dignitarianism is a relatively recently developed area of law and bioethics encompassing both philosophy and international law. It is a far from clearly defined discipline, and applies to far more areas than only ARTs.

In the international legal sphere, the UNESCO Universal Declaration on the Human Genome and Human Rights specifically states that there is inherent dignity in the human genome, and that discrimination based on genetic characteristics is a violation of this inherent dignity.<sup>116</sup> The Declaration cites the example of cloning as against the inherent dignity of all humans and states that it ought not be performed. However, the term “dignity” is not defined and MRT-like procedures are not mentioned. It is clear however that dignitarian concerns apply at both the individual and community levels as well as to the whole of mankind.

MRT has been criticised as being eugenic and therefore an affront to human dignity and a violation of the UNESCO Declaration.<sup>117</sup> However, allegations that MRT is eugenic are unlikely to be sustained. MRT’s aim is not to prevent those

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<sup>115</sup> Research to this end is being conducted in relation to monkeys currently.

<sup>116</sup> UNESCO Universal Declaration on the Human Genome and Human Rights (11 November 1997), Articles 1 and 6.

<sup>117</sup> John Appleby and others “Is mitochondrial replacement therapy eugenic and incompatible with human dignity?” (2 December 2013) Bionews <[www.bionews.org.uk](http://www.bionews.org.uk)>.

with “undesirable” genetics from reproducing. Rather its aim is the prevention of significant suffering by preventing mitochondrial diseases.

A second common criticism of MRT is that allowing MRT will eventually lead to designer babies being acceptable, and this is a violation of human dignity. This is a slippery slope argument and is of dubious accuracy. There are currently legal restrictions in the HART Act that prevent designer babies being born, so legislative reform would be required before this concern has any validity.

The United States President’s Council on Bioethics has observed that a child is not made, but “begotten”<sup>118</sup> and it has been posited that the more “manufacturing” that occurs, the greater the violation to the child’s inherent dignity. In this vein, it is important to note that the only genetics affected by MRT is the mitochondrial DNA, and this selected for its normalcy. The technique itself is not aimed at creating offspring with superior mitochondria.<sup>119</sup> Obviously the IVF nature and *in vitro* treatment of the embryo is far from natural, but the same could be said about all ARTs and none of the ARTs currently performed are widely criticised for violating the inherent dignity of humankind. With MRT, the natural process of sexual reproduction (with half of the child’s DNA being selected at random from each of the parent’s total nDNA) is still present, and this is the vital distinction between MRT and morally objectionable technologies such as cloning and designer babies that are contrary to human dignity.

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<sup>118</sup> Daniel Sulmasy “Dignity and Bioethics: History, Theory, and Selected Applications” in President’s Council on Bioethics *Human Dignity and Bioethics: Essays Commissioned by the President’s Council on Bioethics* (2008) <<https://bioethicsarchive.georgetown.edu/pcbe/>> at 494.

<sup>119</sup> If this is even a possibility, a debatable proposition in itself.

Foster has traversed current bioethical opinion as to the content of dignitarian values in his book *Human Dignity in Bioethics and Law*.<sup>120</sup> While there is a lack of consensus on the issue, “dignity” can be interpreted to include freedom from being used as a means to an end, autonomy, freedom from discrimination, notions of justice and equality, and the valuing of human life. With these factors in mind, MRT could be said to be promoting human dignity. By allowing a child to be born free from a debilitating illness, they are able to have a more open future than had they been born without MRT being performed. It would also likely increase the autonomy of the child, as free from disability they would have the opportunity to pursue opportunities available to them. Further, as mitochondrial diseases can affect the brain processes, a child born through MRT may be more competent to make their own decisions and thus be more autonomous. They are also more likely to have equality in the opportunities available to them, and to live longer and have significantly more quality of life. This is not to say that those with disabilities in any way lack dignity. Rather, we should be attempting to maximise as many of these dignitarian values as possible.

### *III The health and well-being of women*

The HART Act acknowledges that the health and well-being of women in particular is to be afforded protection, due to the fact that women will most often be more affected by ARTs than men.<sup>121</sup> While many aspects of the MRT process are particularly onerous on women (for instance, the hormone therapy performed to stimulate ovulation in order to collect a woman’s eggs), women are also particularly affected by mitochondrial disease. For mitochondrial disease caused by defective mitochondria<sup>122</sup> the woman is the sole contributor of these genetics.

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<sup>120</sup> Charles Foster *Human Dignity in Bioethics and Law* (Hart Publishing, Oxford, 2011).

<sup>121</sup> Section 3(c).

<sup>122</sup> In contrast to nDNA mutations or acquired mitochondrial disease.

There will be a significant psychological burden on a mother knowing that their genetics caused their child's illness. This is a burden that can be avoided by MRT.

#### *IV Informed consent*

Principle (d) requires informed consent to be given before any ART is performed. This is in accordance with both medical best practice and Right 7 of the Code of Health and Disability Services Consumers' Rights. Informed consent is required not only from the parents but also the egg or embryo donor. Currently ECART reviews all decisions to donate embryos, but the donation of an oocyte is an established procedure so does not require approval. ACART has published guidance on what should be considered by ECART when approving an embryo donation.<sup>123</sup>

MRT raises the issue of how much information needs to be given to the donor of an embryo or gamete in relation to the use the embryo or gamete will be put to. Clause 2(a)(vii) of ACART's guidance requires ECART to consider if there is consensus between the parties as to the use of the embryos. For MRT this should extend to the donor agreeing for only the mitochondria of the embryo being used by the recipients. Legal advice must also be obtained, which should include explanations of any anonymity granted to the donor or what contact information could be provided to a child born.

#### *V Donor offspring are to be made aware of their genetic origins*

The HART Act requires a database to be kept containing information relating to donors. This is in accordance with principle (e) that all donor offspring should be made aware of their genetic origins and be able to access this information.

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<sup>123</sup> Above at n 47.

However, the HART Act only requires parents to be counselled on the importance of imparting that information to the children and there is no duty for the parents to do so. Given this is the status quo for children born using donated embryos and gametes, it would be unreasonable to require disclosure of a donor that provided far less than 1% of a child's genetic material. This is further supported by the fact that a benefit of disclosing genetic origins is providing offspring with knowledge of any genetic risk they may have received from their donor in relation to medical conditions. This is not such a concern with the mitochondria as genetic disorders of the mitochondria almost always present in the first decade of life, so the donor's risk in relation to mitochondrial disorders will be relatively low.

*VI Other parties interests to be considered and treated with respect*

Finally, the ethical, spiritual and cultural beliefs in society, and in particular the needs, values and beliefs of Māori, should be considered and treated with respect.<sup>124</sup> Such beliefs are very rarely, if ever, universal and ACART has adopted the position that most often a view of "cautious liberalism" is appropriate to allow all opinions to be adequately considered, while not allowing non-shared beliefs to dominate the outcome. For relatively newly developed technologies such as MRT, there will inevitably be some resistance to adopting them. This can be due to a lack of understanding of the safety of the procedure, or about what the procedure is trying to achieve. For MRT, there is also a general lack of understanding of mitochondrial diseases within the general population. ACART does not have a mandate to educate the public on such issues, so there is potential for a negative public opinion of MRT to persist. At present, there is no way to gauge public opinion of the technique, but if New Zealand were to regulate to allow the technique, public opinion is a factor that would need to be considered.

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<sup>124</sup> Sections 4(f) and (g).



## VII *Other considerations under the ACART framework*

Alongside the seven HART Act principles, ACART takes into account several wider considerations in its assessment of ARTs.<sup>125</sup> These are welfare (expressed as non-maleficence and beneficence), autonomy, altruism, social trust and responsibility, the status of the embryo, and justice and equality. Many of these have already been covered within the above discussion

### (a) Welfare

The welfare of the child and future generations has already been covered under principles (a) and (b) respectively. The welfare of women is covered under principle (c). Welfare also includes principles of non-maleficence and beneficence. Non-maleficence is the obligation to avoid harm, while beneficence is the obligation to provide benefit. The terms are often adopted in the medical profession as core values. While the terms have not been explicitly used in the above discussion, many of the considerations discussed have encompassed non-maleficence and beneficence in some capacity. For instance, the discussion concerning the level of harm caused by performing or not performing MRT is a consideration of beneficence and non-maleficence.

### (b) Autonomy

Autonomy encompasses several considerations including informed consent, privacy and confidentiality, access to information and reproductive liberty. Informed consent was considered under principle (d) and access to information in principle (e). Privacy and confidentiality may be a relevant concern for the donor if they were required to be on a register. However, as discussed above, this may

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<sup>125</sup> Above at n 90, at 16.

be inappropriate in the case of a mitochondrial donor. Also relevant is the privacy of the children produced by MRT. As there are a small but significant number of safety concerns around MRT, it is appropriate that any child produced by the technique be monitored to detect any potential medical issues. However, this register of children should be only available to the appropriate authorities and, like the current ART register, not available to the public. Once the children are old enough to give informed consent they ought to be able to withdraw from any medical monitoring if they wish to do so.

ACART considers autonomy to also include the right of reproductive liberty, encompassing the right to seek or avoid reproducing or becoming a parent and the right to seek to have a healthy child. This is appropriate where parents' actions will not unreasonably impact or threaten others, or cause unjustified harm to any child.<sup>126</sup> Further, for some groups, cultural values will have an impact here (for instance, many Māori consider communitarian values to be just as important as individual rights) but this is not a sufficient justification to generally prevent MRT being performed. Having MRT as an option therefore accords with reproductive liberty (and more widely autonomy) provided that it is offered as an option and there is no presumption that the technique will be used (as is currently the case for almost all medical procedures).

### (c) Altruism

Altruism is a value considered by ACART due to the fact commercial surrogacy and gamete donation is prohibited.<sup>127</sup> For MRT this means the donor egg or embryo used must not be paid for or obtained in exchange for valuable

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<sup>126</sup> Above at n 90, at 12.

<sup>127</sup> Human Assisted Reproductive Technology Act, ss 15 and 17.

consideration and that if a surrogate is used this again must not be a commercial transaction.<sup>128</sup>

(d) Social trust and responsibility

Social trust and responsibility includes consideration of all the beliefs and values of the community, as discussed above in relation to principles (f) and (g). Also important in this regard are disability rights. ACART states that “on occasions the common good may outweigh individual interests, but such occasions are likely to be exceptional”.<sup>129</sup> There are several interest groups in New Zealand that campaign for disability rights. In particular, the Down syndrome and deaf communities, and increasingly the parents of children with autistic spectrum disorders, strongly advocate for the protection of their communities fearing that those living with the condition will be marginalised if we allow abortion or discrimination on the basis of the condition.

In relation to MRT, this is important as both deafness and autistic spectrum disorders can be mitochondrial diseases (though they also have other causes). If MRT were to be performed there may be concerns from these communities that they are being marginalised. However, it is only in a minority of cases within these communities that the condition is caused by a mitochondrial defect. MRT is targeted at preventing the more debilitating mitochondrial diseases, rather than specifically preventing autistic-spectrum disorders or deafness. Due to the seriousness of the conditions targeted by MRT, there is a strong case for allowing the procedure despite these concerns. The harm being prevented would be far greater than any harm caused to the deaf or autistic communities. This is

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<sup>128</sup> ACART has recently recommended a law change that would allow egg and embryo donors to be paid. If this were to go ahead, this poses no specific ethical issues for MRT.

<sup>129</sup> Above at n 90, at 13.

especially the case in light of how few people within the communities actually have a mitochondrial disorder.

(e) Status of the embryo

ACART also considers the status of the embryo in relation to ARTs. It notes that the HART Act makes no explicit comment on its status but recognises that a number of HART Act provisions, along with other legislation such as the Crimes Act 1961, implicitly indicate that an embryo is not to be afforded the same status as human beings, especially during the early stages of development. It has noted that there are a range of views as to what status should be given to the embryo, ranging from the belief that an embryo is human and should therefore be given the same rights, through to those who believe an embryo has no moral status. There is simply no way to accommodate all these strongly held beliefs.

If PNT is used one embryo will be destroyed for the purposes of creating the implanted embryo. MST does not have this result. However, given that embryos are able to be destroyed for research purposes and at the end of an IVF cycle, it would be an anomaly to prevent embryos being destroyed for reproductive purposes. Therefore, whatever the status afforded to the embryo by ACART and society more widely, there is insufficient reason to prohibit MRT (in either form) on the basis that embryos are being unethically treated.

(f) Justice and equality

In the past, justice and equality have mainly been considered in relation to any discriminatory grounds prohibiting groups of persons from accessing ARTs (for instance, based on marital status or sexual orientation). These are not considered to be sufficient grounds to prevent a person accessing an ART (and would also be a breach of the Human Rights Act 1993).

ACART also considers that resource allocation would be a relevant ethical consideration under this heading, but issues of resource allocation are beyond its jurisdiction.<sup>130</sup> The cost of MRT will be a significant barrier to many if the procedure was not publically funded, with estimates from the United Kingdom expecting MRT to cost on average around £80,000 per child born from the technique.<sup>131</sup> In New Zealand some parts of the procedure would be publically funded (for instance up to two IVF cycles are funded for women or couples who meet strict eligibility criteria), while other aspects (including the actual transfer procedure) are currently not funded. Given the cost to the public healthcare system of mitochondrial diseases, it would be justified for the public health sector to reconsider funding arrangements for MRT. However, even if this was not done, it is unlikely that the harm caused by inequality of access to MRT would be greater than the harm of not allowing the technique.

## **B Conclusion**

Following consideration of the ethics of MRT and guided by ACART's ethical framework, I do not consider there to be a sufficiently weighty reason to absolutely prohibit MRT being performed in New Zealand. This is on the assumption that the scientific evidence produced by any future research does not raise any significant safety concerns. This is also based on the assumption that there is not wide-spread, strong objection to the procedure from the vast majority of the New Zealand public (a factor I cannot predict at this point in time).

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<sup>130</sup> Above at n 90, at 16.

<sup>131</sup> Health Science and Bioethics Division *Mitochondrial Donation: A consultation on draft regulations to prevent the transmission of a serious mitochondrial disease from mother to child* (Department of Health (UK), February 2014) at 38.

This conclusion is also on the basis that, depending on the individual circumstances, it may be more appropriate to adopt a different approach in regard to other available ARTs. The division between ACART and ECART is extremely valuable in this respect. It allows ACART to approve or prohibit a technique based on the scientific risk and the broader ethical objections, while relying on ECART to assess each individual application on a case-by-case basis, ensuring that the interests of the individual child in question are promoted.

#### *IV Lessons from the United Kingdom*

In March 2013, the HFEA in the United Kingdom formally advised the British Government (“the Government”) that it believed there was sufficient public support and assurances of safety to justify allowing MRT to be performed in the United Kingdom. The HFEA report led to the Government announcing it would be regulating to allow MRT in June 2013 and releasing draft regulations which would amend the Human Fertilisation and Embryology Act 1990 (UK) (“the HFE Act”) in February 2014. The initial consultation ran until May 2014, with the Government response being published by the Department of Health in July 2014. If the regulations are implemented, the United Kingdom would be the first country to allow MRT to be performed.

As the HFE Act and New Zealand’s HART Act are of similar structure and create similar powers,<sup>132</sup> the draft regulations provide a potential template for New Zealand could base any amendment to the HART Act. In this chapter I will examine the proposed regulations, then consider any amendments that would be required to the HART Act to implement them in New Zealand. I will, by way of conclusion, describe the course of action I believe to be the best way forward for New Zealand.

##### *A The Human Fertilisation and Embryology Act (UK) 1990*

Unlike the HART Act, which sets out ARTs as established procedures, prohibited actions, and the ACART/ECART approval process for assisted reproductive procedures, the HFE Act refers to “permitted”<sup>133</sup> eggs, sperm and embryos. These

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<sup>132</sup> There are differences, with the HFEA having the role of ACART and ECART combined, and the HFE Act providing a licensing regime that is not present in New Zealand.

<sup>133</sup> Human Fertilisation and Embryology Act 2008 (UK), s 3(5).

are the only gametes and embryos that are able to be used for reproductive purposes. The definition of permitted gametes and embryos includes the requirement that “no nuclear or mitochondrial DNA has been altered”.<sup>134</sup> Subsection 3ZA(5) of the HFE Act creates one exception to this restriction. It allows regulations to provide that an egg or embryo is a permitted egg or embryo “even though the egg or embryo has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease.”<sup>135</sup> The draft regulations would use this power of regulation to allow MRT-created embryos to be treated as permitted embryos.

*I Proposed regulations, consultation response and application in New Zealand*

The draft regulations, as proposed by the Government and published by the Department of Health, were made available for comment early in 2014. The Department of Health has since published a consultation response document that detailed the responses that were submitted to the above draft regulations and the Government’s response to the submissions. In total, 1857 responses were received, but the Department of Health noted that almost 80% of submissions were simply comments on the acceptability of the procedure, which was not within the scope of the consultation. In total, 700 generally supported the regulations, 1,152 disagreed with the regulations and the remainder did not express a view either way.<sup>136</sup> While many responses were in people’s personal capacity, several influential medical and bioethics groups also submitted, including the British Medical Association, British Fertility Society, Medical Research Council, the

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<sup>134</sup> Section 3(5).

<sup>135</sup> Section 3(5).

<sup>136</sup> This should not be taken as the level of public support for MRT in the United Kingdom, as typically only those with strongly held views will submit during consultation periods so this will not be representative.



Nuffield Council on Bioethics and the Wellcome Trust, along with a diverse range of religious groups.

(a) Permitted eggs and embryos

The major effect of the regulations is to allow eggs and embryos that have been modified by MRT to be treated as permitted eggs and embryos. The regulations allow both MST and PNT to be performed in creating these eggs and embryos, but the regulations would require amendment if a third procedure was developed to achieve MRT. The regulations as drafted would not allow cytoplasmic transfer to be performed.

Any MRT procedure must transfer the entire nuclear genome into a cell that has had its entire nucleus removed. This prevents the resultant offspring having nDNA from more than two sources (i.e. any offspring will have DNA from their mother and father, but not the donor). Nuclear DNA is defined as including “material that is necessarily removed or inserted along with that DNA, and may include any associated organelles”.<sup>137</sup> Despite criticism in the consultation period that this may allow mitochondria to be transferred alongside the nucleus and that the definition is in fact describing nuclear transfer rather than mitochondrial donation, the Government considers the definition adequate.<sup>138</sup>

In my opinion, this is the only poorly drafted clause in the regulations. All others, both in policy and form, are suitable for their purpose. However, by defining nuclear DNA as including any “necessarily transferred” organelles, the regulations are creating an unnecessary test: “Are as few organelles as possible brought with the nucleus?” For the purpose of the nuclear DNA transfer, this is

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<sup>137</sup> Above at n 131, at 30.

<sup>138</sup> Above at n 131, at 19.

irrelevant. As the only organelles to possess their own DNA are the mitochondria, any organelles transferred across with the nucleus will not affect the end result. They will be destroyed within several cell cycles of the cell replicating. If such a transfer were to cause any issue, this would likely have been found when testing the technique in cells and non-human animals. From a scientific perspective, organelles other than the mitochondria and nuclei do not have the capacity to convert themselves back into DNA. Such a reversion would be needed for the organelle to replicate independently of nDNA. In regard to mitochondria being inadvertently transferred, this factor has already been considered by the HFEA, which recommended more research into how a mixture of two peoples' mitochondria will react following MRT.<sup>139</sup> Therefore the definition as drafted is superfluous and one I would recommend New Zealand not adopt.

(b) Performance of MRT

The regulations would only allow MRT to be used to avoid the transmission of a serious mitochondrial disease. The HFEA must be satisfied in each instance that there is a particular risk that the egg or embryo carries a mitochondrial abnormality, and that there is a significant risk that a person with that abnormality will have or develop a serious physical or mental disability, illness or medical condition.<sup>140</sup> While many submissions questioned the appropriateness of HFEA's continued involvement in approving MRT once the technique's safety has been assessed, the Government considers there to be no viable alternative to this case-by-case approval process.<sup>141</sup>

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<sup>139</sup> Above at n 101, at 38-39.

<sup>140</sup> Above at n 131, at 30-31.

<sup>141</sup> Above at n 131, at 24.

While in New Zealand ACART, rather than Parliament, would be the regulator issuing the guidelines on when MRT is able to be performed, the requirement for serious mitochondrial disease is an appropriate one to implement here. The wording is consistent with the restrictions we place on the use of other ARTs such as PGD. However, ACART should be mindful that the unique characteristics of mitochondrial disease<sup>142</sup> mean that imposing a percentage of likelihood of a disease occurring may be an unrealistic requirement.

Clinics wishing to offer MRT would need to be licensed by the HFEA to perform the procedure, and each use of the procedure would also need to be individually licensed.<sup>143</sup> The regulations leave what procedure to use when assessing such an application to the HFEA's discretion. Currently in New Zealand, clinics are not required to be licensed, and each use of MRT would need to be approved by ECART.

(c) Status of the donor

The regulations would reflect the fact that a mitochondrial donor does not have the same status as a gamete or embryo donor due to the tiny amount of DNA that is actually contributed. For traditional gamete and embryo donors, they would be treated as the legal parents but for the regulations which state they are not to be treated as such. The proposed regulations for MRT would clearly state that a mitochondrial donor would never have been treated as a parent in the first place.<sup>144</sup> The regulations also prevent a mitochondrial donor from obtaining a parenting order for a child born through a surrogacy arrangement.<sup>145</sup>

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<sup>142</sup> Such as the way mitochondria replicate and the complicating factor of mutation loads.

<sup>143</sup> Above at 131, at 31.

<sup>144</sup> Above at 131, at 33.

<sup>145</sup> Above at 131, 33-34.

These provisions were the provisions that received the widest variety of feedback.<sup>146</sup> While some considered mitochondria donation similar to bone marrow donation, others believed that the mitochondrial donor was genetically and ethically a parent and therefore should also be considered a legal parent. The Government noted that all of those that adopted the view that the donor was a parent were of the opinion that MRT ought not to be performed to begin with. While accepting that MRT was a germ-line therapy and therefore different to organ donation, the Government has decided that they are not sufficiently different to justify a different approach to donor anonymity and responsibility.

Due to the tiny percentage of DNA contributed by the mitochondria, I consider it acceptable to treat a mitochondrial donor differently from a gamete or embryo donor. However, the proposed law seems unnecessary given that the net result for a donor would be the same whether the law was enacted or not and the situation could never arise naturally. In New Zealand, given the Status of Children Act provisions already in force this specific regulation would be of no particular value.<sup>147</sup>

#### (d) Identification of donor and offspring

Also reflecting the donor's more limited role in contributing DNA with MRT, only non-identifying information about the donor will be available to any offspring. Such information includes any screening prior to donation and any other information the donor wishes to make known to the recipient of their mitochondria. The fact that a person is a result of MRT would be available at 16 years of age and the non-identifying information about the mitochondrial donor

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<sup>146</sup> Above at n 88, at 27.

<sup>147</sup> As discussed above in Chapter II.

available at 18. Both pieces of information would be available on application to the HFEA.

While some consultation submissions questioned whether the HFEA was the right body to hold such information, or whether the information should be made available prior to turning 16 or 18, the Government decided that the regulation is sufficient. In particular, they noted that for most cases the child will know about their mitochondrial origins far earlier than the prescribed 16 years, and this is simply a failsafe to ensure those who were not told can find out the information. The level of information available was also a contentious issue, with some submitting that to withhold identifying information breached basic human rights (without expanding on what human right was being infringed).<sup>148</sup>

Similarly a donor would be prevented from being informed of any identifying information about the offspring produced from their gametes or embryo. They will be able to be told that a live birth has occurred as a result of their donation, and the sex and year of birth of the child. The Government has noted that these regulations do not prevent voluntary arrangements being made between the parents and donor as to how much information they will tell the offspring and any contact they will have with the donor.

Given the small amount of DNA contributed by the donor, the level of anonymity given to a donor and donor offspring is appropriate. If this approach was adopted in New Zealand the HART Act would need to be amended as Part 3 of the HART Act gives those who hold donor information the discretion to refuse to disclose it only where they believe that a person would be endangered by the release of the information.

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<sup>148</sup> Above a n 88, at 32.

(e) Monitoring of offspring

Finally, the regulations do not require that parents agree to a child born through MRT being monitored by medical professionals before MRT is carried out. The Government does not consider such a requirement to be within the scope of the regulating power. However, they do recommend that parents are counselled on the potential risks of MRT and the fact that it has yet to be established as completely safe in humans. The Government also consider that, for the sake of future generations, it is important that follow-up monitoring is facilitated where at all possible and that the HFEA monitor this process.

Under the New Zealand framework, ECART should be considering whether parents have been counselled and/or agree to medical monitoring of any child produced through MRT. As a principle of the HART Act is “taking appropriate measures for the protection and promotion of human health”, such an approach is appropriate. As discussed previously in Chapter III, the child should be able to withdraw from such monitoring if they wish when they have capacity to do so.

***B The Way Forward for New Zealand***

The HART Act (unlike the HFE Act) does not contain any power to make a regulation that would effectively amend the primary Act. Therefore, if ACART considers MRT to amount to genetic modification, it would take a legislative change to amend the HART Act and allow the procedure in New Zealand. Alternatively, if they consider it not to be genetic modification, then ACART is able to issue guidelines and ECART could approve use of the technique. The following amendments would create a regulatory environment that more clearly permits ACART to approve of, and issue guidelines relating to, the performance of MRT.

While the analysis of whether MRT is genetic modification under the HART Act is clearly an interpretive exercise (and one I consider that leads to the conclusion that MRT is not genetic modification as discussed in Chapter II), I propose that the HART Act be amended to include a definition of “genetic modification” that more clearly excludes MRT from its ambit.

This definition should read:

*“Genetic modification is the deliberate alteration, by insertion, deletion or mutation, of a gene or the genes of any of the nuclear or mitochondrial DNA of a gamete or embryo. For the avoidance of doubt, the transplantation of organelle (including the organelle’s complete genome) is not genetic modification.”*

This is the most appropriate approach for several reasons. Firstly, to simply repeal clause 8 of Schedule 1 of the HART Act would be a politically polarising approach. With a significant portion of society opposed to genetic modification,<sup>149</sup> it is a course of action that few politicians are likely to adopt. If clause 8 is to continue in force, the only way to clarify the provision would be to define genetic modification. Further, the current prohibition is an appropriate one. Genetic modification (on the narrow interpretation advocated for) is neither safe nor ethical at the present time, is generally opposed to by the vast majority most of society and ought not to be performed.

The second justification for this approach is that by amending the legislation, ACART are protected from potential judicial review on the grounds that MRT

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<sup>149</sup> The Royal Commission on Genetic Modification (2001) found that 30% of submissions made to the Commission were either strongly against or tends to be against genetic modification. I propose the number would be higher if asked about genetic modification in humans or animals.

does constitute genetic modification and therefore any action taken by ACART in allowing the procedure was ultra vires.<sup>150</sup> Finally, the above definition would leave to ACART's discretion the circumstances for which the technique is able to be used, as is the case with other ARTs currently. This is appropriate as ACART has the expertise and mandate to adequately assess the technique and to consider the limits placed on its use.

Section 47 of the HART Act would also require amendment, in recognition of the limited genetic contribution of a mitochondrial donor to the child. Section 47 currently requires certain information to be kept by the provider of an ART about the donor of an embryo or gamete. The section should be amended to not require a donor to have such records kept, but allow them to do so if they wish.

Finally, section 59 allows offspring aged over 18 to consent to an ART provider providing identifying details to their donor. Given this provision does not require identifying details of either party to be disclosed to the other without their consent, it is justifiable for this provision to remain available for any offspring. This will afford the donor sufficient protection if they wish to remain anonymous, while allowing any child to contact them (or make their wish of contact known to the donor) if they so desire.

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<sup>150</sup> This is a practical consideration whether or not, in reality, there are interest groups in New Zealand that would take steps to litigate the matter.



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