Fetal Gene Therapy: Balancing ethical theory, scientific progress and the rights of others

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Thesis Abstract

This thesis examines the relationship between rights and duties in the field of fetal gene therapy and assesses if the current regulatory position within England and Wales is compatible with the intergenerational aspects of scientific progress within fetal gene therapy (FGT). Within the field of genomics, the fetal junction has become a site where gene therapists are developing a range of medical techniques, such as fetal gene therapy and in utero stem cell therapy. Utilising such techniques raises questions about the intergenerational aspects of scientific progress and how intergenerational rights can reshape regulation. The thesis focuses upon these key questions: Are the intergenerational issues of FGT taken into account by both direct and indirect stakeholders? Can intergenerational issues override the reproductive rights of the mother? Have intergenerational issues impacted upon the clinical applications implicit and manifest in this work? Addressing such questions is important because the conflict between the rights of the mother, fetus, clinical researchers and society have the potential to delay progress in FGT.

In addressing these questions the thesis utilised thematic analysis of relevant regulatory institutional documents, from international declarations to regulatory guidelines; and semi structured interviews of identified FGT practitioners to identify areas of potential conflict. Following the data collection and analysis, the field data identified five key areas of potential conflict, which were then assessed using the Principle of Generic Consistency (PGC) as proposed by Alan Gewirth (1978) and later altered by Beyleveld and Brownsword (2001). The thesis will argue that the field data shows that established regulatory principles such as human dignity are of limited value in relation to FGT. In other areas such as informed choice, autonomy and intergenerational equity the PGC is applied to define and partially resolve the outstanding areas necessary for consistent ethical and regulatory guidance in FGT.

Acknowledgements

After three years, an unquantifiable amount of money (well I like to think it is, but clearly it is not!), sweat and tears (none of these so far, but who knows!), the thesis has been written. It has been a long innings, with its up, downs and side to sides, but I could not have got to the end without the help and support of so many people; all of which need to be acknowledged and thanked.

Firstly, a huge thanks to my supervisors Dr Ian Welsh and Prof Ruth Chadwick. I could not have finished the thesis without their help, patience and support. Could I ever truly appreciate the stress and strain I must have put them both through? If I ever have a student that writes a sentence that is so dense that it bends light and assumes its own gravity, then it may be a possibility! Until that day, I will have to just imagine it (but I won't as that sounds like torture!).

Another massive, but obvious, thank you must go to the interviewees. Without them the thesis would not have the impact and real life evidence that it needs. Work should be fun and the interviews were surely that. All of the interviews gave illuminating narratives about their work and I would have no hesitation in doing it again. Hopefully, they would say the same? In fact, I'm going to assume that they would as I don't hear any screams of 'no' from anyone. So thanks must go to each and every one of them.

Thanks must also go to my parents (Mike and Dolly Childs), brothers (Sean, Navid and Seriashe), newest family members (Sarah and little Otis) and all my friends. I am not entirely sure if transmitting stress down the phone is a crime, but it probably should be. Perhaps a claim may arise under psychological damage in a torts claim? If so, then my parents would no doubt have a prima facie case on their hands. However, their encouragement and support has been invaluable. In addition thanks go to my athletics coaches Ed Thompson and Gwyn Williams. For three years (in Ed's case far longer than that) they have had to endure the journey of a thesis. It has been a journey, but it has been well worth it. I've picked up some friends along the

way and now that it is over, I can look back with pride at the work that I have achieved.

Finally, thanks must also go to the Economic and Social Research Council, Cesagen and Cardiff University for their financial and resource support over the last four years which made the PhD possible.

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List of Acronyms

ASA – Argument for Sufficient Agency
DOH – Department of Health
EC – European Community
ECHR – European Convention on Human Rights
ECtHR – European Court of Human Rights
ECJ – European Court of Justice
EMA – European Medicines Agency
EU – European Union
FGT – Fetal Gene Therapy
GFA – Generic Features of Agency
GMC – General Medical Council
GMO – Genetically Modified Organism
GTAC – Gene Therapy Advisory Committee
HRA – Human Rights Act
HSE – Health and Safety Executive
ICCPR – International Covenant on Civil and Political Rights
ICESCR – International Covenant on Economic, Social and Cultural Rights
IE – Interviewee
RC – Richardo Childs (interviewer)
MHRA – Medicines and Healthcare products Regulatory Agency
MRC – Medical Research Council
PGC – Principle of Generic Consistency
UK – United Kingdom
UN – United Nations
UNESCO – United Nations Educational, Scientific, and Cultural Organization
USA – United States of America
WMA – World Medical Association

1 Introduction
1.1 Introduction

Since the rise of gene therapy during the 1960s and early 1970s, the idea of correcting dysfunctional genes has been a pursuit of many scientists. However, additional information about the genome was needed to develop gene therapy and this was the inspiration for the Human Genome Project (HGP). The HGP started in 1990 and sought to sequence the whole human genome. It was completed in 2003 and promoted increased research activity in genomics by expanding the current knowledge of genetics and diseases, which in turn has opened the door for interventions such as somatic gene therapy (Hernandez 1999).[1] However, despite the prospect of gene therapy leading to cures for many genetic diseases, gene therapy has encountered scientific challenges which have slowed down its development. The most significant challenges to the development of gene therapy, and stem cell transplantation, has been the immune response of the patient to the genetic intervention causing the intervention to be rejected (Santore, Roybal et al. 2009). Therefore, gene therapy has sought to exploit many properties that the fetus possesses in order to overcome these difficulties. These properties include: an immature immune system and the unique healing property within the fetus which increases the chance of therapeutic vectors attaching to the cells; and early prevention of clinical manifestation of disease (Turner and Fauza 2009: 477). As a result, Fetal Gene Therapy (FGT)[2] has developed in order to overcome the technical difficulties of postnatal interventions.

Nevertheless, utilising FGT raises questions about the intergenerational aspects of scientific progress and the way that scientific progress can reshape how rights and duties can be regulated. For example, in utero choices are intergenerational as they engage directly with the next generation through the fetus, which is the 'fulcrum' or 'pivotal point' between generations. Therefore, questions regarding rights and duties

[1] Somatic cells are any body cells that compose the tissues, organs, and parts of that individual other than their germ cells (National Institute of Health 2011b).
[2] There is more than one spelling of fetus that is commonly used: that of fetus and foetus. However, fetus will be used as this is more commonplace within the literature of FGT.

towards the next generation and beyond are explicit within FGT. The rights and duties of future people through medical criteria such as 'the fetus as a patient' challenges the extent that autonomy can be exercised in relation to the maternal fetal conflict (chapter 4) (Savulescu 2007). In researching possible intergenerational issues within FGT several key elements could be explored, including conflicting rights and duties, access to such technologies and further institutional effects of FGT such as in the realm of sport. However, the thesis will focus upon rights and duties within FGT, how these rights and duties are perceived or established as well as how scientific progress impacts upon them. Other important aspects, amongst many, include how maternal rights are viewed in relation to the fetus and whether researchers have to take into consideration anything other than obtaining results. Current regulation and practice needs to be examined to ascertain whether they are sufficient to cope with FGT as it develops.

The thesis will argue that within the data collected, established regulatory principles such as human dignity are of limited value in relation to FGT. The thesis will highlight that the current regulatory and practical application of FGT cannot sufficiently take into account some of the key issues within FGT. Despite the majority of regulation coping with the potential pitfalls of FGT it is clear that certain regulatory restrictions and/or positions do not provide adequate consideration to particular prevailing issues, such as the regulation of germ line technologies[3] and the interplay between abortion and the practice of FGT.

The international development of FGT is also important given the globalised nature of science (Glasner and Rothman 2001). The majority of fetal therapy innovations and legislative changes emanate from the USA. Within the United States a father, for example, may have a legitimate right to consent or object to treatment.[4] The state of Michigan has moved towards prosecuting excessive drug use by pregnant women and enforcing certain duties upon mothers within pregnancy. Also the American

[3] Germ cells are those cells involved in reproduction such as an oocyte, sperm cell or one of their antecedent cells (Debyser 2003, National Institute of Health 2011b).
[4] Code of Federal Regulations: Title 45 - Public Welfare, Part 46, Protection of Human Subjects, s.46.203.

Academy of Pediatrics has issued guidance to clinicians about how to deal with refusal of treatment by mothers for their fetus. The guidance results in mothers being forced to change their consultant if they go against the consultant's treatment suggestion (American Academy of Pediatrics Committee on Bioethics 1999). These changes clearly indicate the impact that rapid scientific progress in the field of in utero knowledge has had upon law, ethics and society. The same may be said for FGT as Table 1 clearly indicates the rapid ascent of FGT from initial confirmation to potential clinical trials. Therefore, as FGT progresses towards clinical practice what rights and duties are taken into account becomes important because the way that FGT is framed will influence whether any legislative or regulative change is needed, as has been seen within the USA. In assessing that change understanding what issues FGT potentially possesses becomes important because regulation may not cover all areas that FGT could impact upon. This factor can lead to reactive regulation such as was clearly seen with the prohibition of reproductive cloning.

Table 1. Selective timeline of fetal gene therapy

Year	Event	Implications
1990	The first to use an in utero approach in applying a replication-incompetent retrovirus vector to fetal rats in utero (Hatzoglou et al 1990).	A large number of successful in utero gene experiments now conducted.
1997	Fetal interventions now viable due to development of diagnostic and genetic testing.	Fetal intervention for therapeutic basis becoming technically viable within humans.
1999	Phase 0 FGT proposal by Dr French Anderson within the USA due to gene therapy and fetal technique developments. GTAC issues guidance.	Potential ethical and legal issues being highlighted by significantly quick progress of FGT.
2003	First successful therapeutic application of gene transfer in utero within rats performed (Seppen, van der Rijt et al. 2003).	FGT can now progress towards human clinical trials.
2011	High level of transgene expression in cardiac and skeletal muscles (Mattar et al., 2011).	Human clinical trials now a real possibility.
2012-14	First FGT clinical trial in UK to be sent for ethical approval.	Potentially first human application of FGT in the world.

It should be noted that the law of England and Wales must be placed in its European context despite the room left to Member States (the margin of appreciation) to regulate fetal rights. However before outlining the regulatory position, section 1.2 of this chapter will give definitions of some of the terminology used within the thesis. Defining words such as rights and duties will clarify the remit of these terms and avoid confusion later in the thesis. Section 1.2.3 then outlines how the author wrestled with some of the concepts within the thesis and section 1.3 investigates the way that the progress of FGT is challenging the current regulatory position before concluding in section 1.4. However, before the definitional issues are addressed an important brief note is needed about FGT.

1.1.1 A note about fetal gene therapy

It should be noted that FGT is a practice that is not aimed at germ line interventions either advertently or inadvertently. However, germ line interventions will be referred to in order to produce a progressive and more complete thesis that could be used if FGT does ever choose to utilise germ line interventions in the distant future. Therefore, the reader should be reassured and not jump to the conclusion that FGT is a practice that currently seeks to actively alter a patient's germ line, or that it might do so in the future.

1.2 Definitional issues

1.2.1 Defining fetal gene therapy

Although FGT appears to be a relatively straightforward concept, it still needs defining. 'Fetal' can refer to an unborn or unhatched vertebrate, especially after attaining the basic structural plan of its kind (National Institute of Health 2012). Major leaps in human FGT such as developments in surgical interventions and techniques in human fetuses, especially fetuses with congenital diaphragmatic hernias, have been a direct result of animal experimentation, with lambs being considered a suitable model for fetal surgery (Jancelewicz and Harrison 2009). However, 'fetal' within FGT refers to an unborn human that is past the 56^{th} day of gestation (Soanes 2001: 330) and therefore FGT should preclude embryology from the remit of the thesis. However, there are issues that are relevant to pregnancy in general and so embryology cannot be completely ignored within the debate about

FGT. It should also be noted that terms such as 'in utero' and 'prenatal' are used which encompass both embryonic and fetal stages of development.

The terms fetal surgery, fetal therapy and FGT can be misleading because any fetal intervention also involves the pregnant woman. For example, maternal-fetal surgery has been used to describe the same procedures that are covered by 'fetal surgery' to show the relevance of the mother within any fetal intervention (Wu and Ball 2009). However, the term fetal surgery does not exclude the mother from the debate and therefore the same can be said for 'FGT.' Defining gene therapy will also be important.

Gene therapy is a medical technique that seeks to deliver genetic material to a cell in order to generate a therapeutic effect by correcting an existing abnormality within the host cell (David and Peebles 2008: 204). Gene therapy utilises gene transfer, which is the introduction of genetic material into cells that can be of a different origin (Debyser 2003) and would be used to treat those conditions that may not be amenable to stem cell transplantation (Roybal, Santore et al. 2009). These conditions are essentially (but not exclusively) non hematopoietic (blood) disorders, such as cystic fibrosis, muscular dystrophy and central nervous system disorders (Wagner et al 2009). Gene therapy can be performed either ex vivo or in vitro, but is essentially accomplished through delivering the wanted genes through viral vectors such as retroviruses and adenoviruses (Senut and Gage 1999). More recently, HIV has been used as a viral vector but there has also been a shift towards using non viral vectors (Santore et al 2009). Therefore, it can be said that FGT is the use of gene therapy in order to benefit a fetus. The term 'benefit' indicates that the fetus does not have to be the direct recipient of the gene therapy, because in certain circumstances the recipient of the gene therapy will be the pregnant woman for the benefit of her fetus. She in turn benefits in that she will then, hopefully, have a child with a less serious debilitating condition or none at all.

1.2.2 Clarifying rights, duties and interests

It is clear that rights and duties will be a major element within the thesis. Elaboration of the difference between rights and duties as well as the difference

between competing and conflicting rights will serve to provide a background to the thesis. Firstly, the differences and relationship between rights and duties must be identified as this will help identify and resolve tensions between agents later within the thesis. Within this thesis rights emerge as an important factor. Rights can be either positive or negative. A 'positive' right is the right to do something or have an action facilitated by someone, but there are also negative rights (Carter 2007). A 'negative' right is the right not to be interfered with, or the right to omit doing something (See Carter 2007). Therefore, a positive right in this instance is the right to have medical treatment. However, positive rights are not absolute as they can be overridden by another agents competing or conflicting right, as well as other enforceable duties. An example of this is the conscientious objector within the scope of the Abortion Act 1967,[5] where a female's right to abortion cannot compel a doctor to treat her if the case falls within the conscience objector category.

Duties must also be defined and addressed. Duties arise from both positive and negative rights. These duties are known as correlative duties and have been referred to as negative and positive duties (Gewirth 1978, Rawls 1971). Generally, duties are seen as the duty to refrain (negative) and the duty to provide active assistance (positive) (Gewirth 1996). In certain circumstances this distinction makes little difference, but positive rights and their correlating duties pose a further question: when is it justifiable to coerce or infringe an agent's right in order to fulfil another agent's right?

As mentioned above, both competing and conflicting rights could be relevant within the thesis and therefore also need defining. Competing rights are where two or more agents are claiming the same right but against each other. Therefore, the right of agent A can only be satisfied by the same right of agent B not being satisfied (Beyleveld and Brownsword 2006). The classic medico-legal case is seen in that of the conjoined twins in *Re A*[6] whereby part of the many conflicting dimensions of the

[5] Abortion Act 1967 s.4.
[6] *Re A (Children)(Conjoined Twins: Surgical Separation)* [2001] Fam 147.

case was the competing aspect of Mary and Jodie's right to life.[7] Resolving competing rights entails a balancing act between the agents.

Conflicting rights, on the other hand, is where two or more agents are asserting different rights to the same issue. The conflict between the reporting of medical information under Article 10 and Naomi Campbell's right to private life under Article 8 in *Campbell v MGN Ltd*[8] is a classic example of conflicting rights whereby a balance between rights is needed rather than a balance between agents.

Within the thesis 'interests' are also important because there is a debate surrounding what an interest is and who has a relevant or sufficient interest. Within public law this is known as locus standi.[9] An interest can take many forms. For example, the Oxford dictionary has five definitions of an interest ranging from the feeling of wanting to know or learn about something or someone to a group or organization having a common concern (*Oxford Dictionaries Online* 2012). It can also be a right over land (Martin 2001) or those who are the primary, direct beneficiaries such as society as a whole or specific populations or entities who are unable to carry out research on their own behalf (Butcher 2000: 12). These wide definitions encapsulate many groups of people, such as public interest groups, the media, the government, or anybody who just likes science. An interest can be a powerful tool which can result in a successful defence against privacy actions[10] or require government bodies to consult or inform certain citizens or groups of citizens.[11] However, within the thesis an agent has an interest where another being has a duty towards them (Pattinson 2002: 2). Therefore, an interest can arise out of rights and can be in competition or conflict. An agent in this context refers to a being with agency, with agency referring to the ability or the capacity to conduct themselves within the world. How an agent is established is discussed in section 5.7.

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[7] See the leading judgement of Lord Justice Ward in *Re A (Children)(Conjoined Twins: Surgical Separation)* [2001] Fam147.
[8] *Campbell v MGN Ltd* [2004] UKHL 22.
[9] Senior Courts Act 1981 s.31(3) (formally called the Supreme Court Act 1981 but now cited as the Senior Courts Act 1981 by virtue of the Constitutional Reform Act 2005).
[10] Data Protection Act 1998 s.32(1).
[11] *Coughlan & Ors, R (on the application of) v North & East Devon Health Authority* [1999] EWCA Civ 1871.

1.2.3 Wrestling with terminology

There are some concepts which will also be subject to debate, such as the distinction between therapy and enhancement. It should be noted that the thesis makes a distinction between therapy and enhancement. Despite some academics suggesting that the distinction between therapy and enhancement is blurred (For example, see Colleton 2008, Kamm 2005, Schwatz 2005) the thesis is dealing with therapeutically aimed technologies as defined by those scientists involved in the research. Nonetheless, engaging with a definitional and ethical debate surrounding the distinction of 'therapy' and 'enhancement' creates a debate outside the remit of the thesis. The distinction between germ line and somatic interventions helps focus the intergenerational aspect of the intervention because somatic interventions affect only the next generation, whereas germ line interventions affect all future generations. The distinction between germ line and somatic interventions casts doubt over the limits of parental autonomy and creates an avenue for limited autonomy in favour of social ethics or justice (Buchanan et al. 2000).

It became apparent while working with the data that several terms were causing problems for various reasons. These terms were: mother, individual, patient, and agent. They all intersected at some point, therefore causing significant imprecision and ambiguity within the thesis. It became clear that the term 'mother' was being used when other terms such as 'pregnant woman', 'expectant mother', 'mother (as in future mother)', 'agent' and 'individual' could be used interchangeably. The following examples will demonstrate the complexity in using such terms within an emotionally charged area.

The Abortion Act 1967 uses the term pregnant woman, yet the leading American case *Roe v Wade*[12] refers to the harm to a mother. Fetal matter is considered maternal tissue regardless of whether that fetus has been born (Human Fertilisation and Embryology Authority 2009). However, the media appears to use the terms 'mother' and 'pregnant woman' interchangeably to describe pregnant women. For

[12] *Roe v Wade* 410 U.S. 113 (1973).

example, one Telegraph article is titled ‘Abortion 'doesn't harm mothers' mental health'’ (Adams 2011), but then the title of another article is 'Pregnant women have asked for terminations because they did not want their holidays spoilt' (Dalrymple 2012). The two articles are referring to the same point of pregnancy, but seemingly change terminology in order to emphasise their point within the articles. The media are not the only source of the interchangeable use of terms. Medicine refers to tissue collected from pregnant women as ‘maternal tissue’, yet ‘maternal’ is clearly a term derived from motherhood. Academics use terms such as maternal fetal surgery (Wu and Ball 2009), fetal surgery (Farmer 2003, Harrison 1993) or fetal therapy (Nicolaides and Chitty 2011) to refer to the same procedure. Therefore, it is important to be consistent within the thesis, because the meaning behind each of these terms could lead to criticism of the author’s ethical position even though the use of any of these terms within the thesis is ethically neutral.

Other terms were also problematic. The term ‘individual’ became problematic because identifying who is an individual (or patient) was not ethically or practically certain. The term fetus is a classic manifestation of such a dilemma. The work of Chervenak and McCullough (1994, 2008, 2009, 2011) shows that the term ‘patient’ can refer to a fetus as well as a mother. Recent media reporting of sex selective abortions once again highlights the interchangeable use of the term fetus and baby (Adams 2011) which has implications on who is termed an individual. Therefore, consistency in the use of such terms is needed.

The resolution of these issues was not a simple or straightforward task and involved many conversations with supervisors and interviewees. It should be noted that within the thesis the use of the term mother or fetus does not reflect the ethical position of the author or indeed the ethical position of the being in question. When referring to an ethical principle the term agent will be used instead of the term individual. However, the term individual will be used when referring to any agent, possible or not, within a clinical setting. The term mother will be used instead of pregnant woman or individual to reflect the literature, but also in the majority of cases birth is still a realistic proposition, which the term mother reflects. When

considering issues that could affect the fetus if it was deemed a patient then the term patient will be used.

Given the multidisciplinary nature of FGT, it was clear that using the specialist words of every practitioner involved, or even using generic terms such as researcher or clinician, did not serve to be inclusive enough or truly reflect the multidisciplinary nature of the work conducted within FGT. Therefore, the term FGT practitioner is used. A FGT practitioner is someone who works at any stage of the development of FGT. Therefore, the term is inclusive of those who are solely laboratory based right across to those who are clinically based and those who are in both settings. However, the terms researcher and clinician will be used when a distinction is needed between the two disciplines.

Other definitions which are needed to contextualise the thesis are intergenerational, next generation and future generation. Intergenerational refers to an issue that has a possible or proven implication between two or more generations; next generation refers to the immediate genetic offspring of an individual including those in gestation; future generation refers to any generation of genetic offspring. It should also be noted that the term therapy within the context of clinical trials is experimental treatment rather than certified therapy. However, the term therapy is not an indictment upon whether the treatment will work or not, but refers to the therapeutic aim of the work/research being conducted. For the readers reference these definitions can be found in Appendix G. Having identified these issues, the thesis aims to follow the same consistency.

1.3 Thesis structure and research questions

In chapter 2, the historical development of FGT is outlined. The development of FGT is contextualised relative to current fetal surgery and gene therapy, but also identifies the future direction of FGT. As Table 1 clearly indicates, the emergence of FGT as another treatment option within pregnancy raises possible theoretical issues because of its rapid ascent from its initial use to potentially clinically trials. Issues such as how to control technology (Ellul 1964, Winner 1978) and potential practical issues within future FGT place pressure onto regulatory and ethical thinking.

Therefore, when the Department of Health (DOH) in 2007 states that: 'No human clinical trials of in utero gene therapy have ever taken place in the UK, nor is this considered to be feasible in the next few years (BBC News 2007);' does not mean that these issues must not be addressed. Such statements quickly become redundant, thus forcing regulators to engage with rapidly progressing technologies such as FGT before they reach the clinical trial stage. Therefore, chapter 2 provides a foundation to the thesis in order to explore and discover the practice and regulation of FGT and whether FGT is adequately regulated.

What emanates out of these issues is that within FGT intergenerational issues are relevant to: those who create in utero practices involving stem cell and gene technologies; the regulation of fetal therapy; the thoughts of those who provide, access and are affected both directly and indirectly by the treatment of future generations. Therefore, the overriding research questions are:

- Are the intergenerational issues of FGT taken into account by both direct and indirect stakeholders?
- Can intergenerational issues override the reproductive rights of the mother?
- Have intergenerational issues impacted upon the clinical applications implicit and manifest in this work?

Having identified that intergenerational issues are relevant then the key players that emanate from FGT are regulators, FGT practitioners, patients, indirect communities and society in general. However, given the breadth of the stakeholders that the intergenerational issue affects the reproductive rights and duties can be viewed through that of the legislator/regulators,[13] FGT practitioners, patient and patient groups.[14] Despite the views of patients being relevant within reproductive rights, patient explicit views are not the contention of this thesis. It is how patients' rights are manifested and controlled through institutions such as the legislator, judiciary and supranational bodies that are of interest. Therefore, the focus of the thesis will be within the spheres of regulators, institutions and FGT practitioners.

[13] It is not the contention of this thesis to address the issue of whether a government reflects the will of the people.
[14] If such groups exist beyond those for specific *in utero* conditions, such as spina bifida.

Exploring an area of emergent science presents its own methodological problems because it challenges traditional methods of social science such as sampling and whether one data collection tool is adequate to provide enough data to explore fully (Hesse-Biber 2011). Therefore, a multidisciplinary approach will be used to mediate such fears. Chapter 3 indicates that documentary analysis and semi structured interviewing of FGT practitioners are the most appropriate research methods at this current time. Once FGT progresses from the laboratory to the clinic, it would then be appropriate to approach patients about their experiences. In order to provide an informed approach to the interviewing the documentary analysis was conducted before the interviews were scheduled. The documentary analysis includes an exploration of current positions within medicine and law towards fetal rights, establishing a founding principle within regulation and an exploration of FGT regulation. The chapter will also discuss ethical and access issues. Importantly, it will show that the thematic approach to analysing the data through Nvivo is an appropriate method in the given circumstances.

Chapter 4 then explores whether within FGT there is a divide between the mother and fetus, which is categorized as the maternal fetal divide. The maternal fetal divide is seen through the biological difference between mother and fetus, but also embraces the 'fetus as a patient' concept. The maternal fetal divide is important as it outlines current medical and legal views towards pregnancy, thus establishing whether future FGT will impact on the current maternal fetal position. The 'fetus as a patient' concept emanates from the viability of the fetus and the acknowledgement of the mother to continue a pre-viable fetus to term (See Chervenak and McCullough 2007). The term 'fetus as a patient' is based on the pre-viable fetus but acknowledges the future child which, given the lack of legal status afforded to a fetus, creates uncertainty regarding the rights and duties of not just a mother but of both prospective parents. Even if FGT does not challenge the legal status of a fetus, *per se* the intergenerational effect of such practices must be considered. FGT is seen as a potential 'cure' for debilitating conditions because of the above mentioned problems with postnatal interventions, thereby making the fetal junction the best opportunity to cure a condition. Therefore, if the 'fetus as a patient' concept is valid, in choosing not to correct a condition parents could be seen as breaching their duty

towards the fetus, and more importantly the future child. Therefore, issues regarding the prevention of harm within pregnancy become relevant, for example case law and the debate regarding the accountability of mothers' actions within pregnancy.

Within England and Wales the fetus has no legal rights[15] and fetal material is considered as maternal tissues (Human Tissue Authority 2009). A mother's refusal of treatment emanates from the concept of autonomy and cannot be challenged unless that person is deemed incompetent under the Mental Capacity Act 2005. It is clear that pregnancy *per se* does not automatically render a woman incompetent.[16] Therefore, the choice to refuse fetal treatment is treated as the right to refuse treatment upon her own body and cannot be held responsible for the outcome upon the fetus.[17] Where an individual is incompetent the 'best interest' test is used in order to identify if the procedure can be done without consent.[18] The maternal fetal divide is important because by identifying the current practices dealing with pregnancy one can evaluate if the future progress and regulation of FGT can be sustained within that model.

Due to the prospective nature of the thesis chapter 5 seeks to identify what, if any, ethical principle underlies FGT. The thesis identifies that human dignity is one such dominant underlying ethical principle. In trying to elaborate upon the definition of human dignity, it becomes evident that an ethical theory or principle is needed. Through the analysis of ethical theories associated with human dignity, it emerges that the Principle of Generic Consistency (PGC) as proposed by Gewirth (1978) and later amended by others (Beyleveld 2012, Beyleveld and Brownsword 1998, Beyleveld and Brownsword 2001) would be an appropriate ethical framework to critique the issues discovered within the data.

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[15] *Paton v United Kingdom* [1980] 3 EHRR 408.
[16] *Re MB (Caesarean Section)* [1997] 2 FLR 426.
[17] The exception to this is that while driving a motor vehicle a pregnant woman owes a fetus the same duty of care as other road users. See Congenital Disabilities (Civil Liability) Act 1976 s.2.
[18] Mental Capacity Act 2005.

Chapters 6 and 7 conclude the documentary analysis and chapters 8 and 9 present the results of the interviews conducted with FGT practitioners. It is clear that within the documents human dignity is used both explicitly and implicitly. However, human dignity appears to lack an explicit definition and is reliant upon implicit recognition through concepts such as autonomy. The consequence upon the maternal fetal divide is that within the clinic the mother is paramount. In other words the fetus has no rights, only interests, which despite the ray of light indicated within 6.6, the mother's autonomy is paramount. Nevertheless, those interests can act as a restraint upon the remit of research and ultimately restrict maternal choice within the clinic, thus exercised within a paternalistic bubble. However, these restrictions appear to emanate not just from safety concerns, but also from fears about the impact upon human dignity. When these restrictions are expanded upon, it appears that the possible reason why there is an apparent affront to human dignity by certain techniques, but not others, is that the restrictions are not consistently applied. For example, uncertainty and foreseeability of research appear as possible reasons to prohibit germ line activities despite these concerns being equally applicable to somatic interventions. However, technologies utilising somatic interventions are still permitted. Despite such contradictions, the data misses out key issues such as barriers to progress and confidentiality, which are explored within the interviews.

In order to make the comparison between the two data sources easier the interview data structure followed the documentary data. The interview data does confirm the documentary analysis by confirming that the mother is paramount within FGT. However, through chapters 8 and 9, it is evident that the term human dignity is not explicitly used by FGT practitioners. The lack of explicit definition was alluded to within the documentary analysis, with the interviewees establishing that they did not use human dignity explicitly. It confirmed the documentary analysis that human dignity is manifested and protected through the use of other concepts such as autonomy and informed consent. The interview data also highlights further issues that cannot be seen within the documentary data, such as the interplay of abortion with FGT treatments. The interplay between the two highlights the fragility of scientific progression and the way that FGT is also dependent upon public perception. The data also indicates how to implement regulatory principles with the

consequence of the inherent uncertainty of FGT being mediated by a convincing argument. Consequently, the comparison of the interview and documentary data lead to the following issues being identified:

1. Human dignity is not a useful concept within the practice of fetal gene therapy despite appearing to be so within regulation.
2. Is the paternalistic bubble that maternal choice is situated within, ethically correct according to the PGC?
3. Can a mother's autonomy be overridden by fetal interests given that the point of intervention is the only viable point of correction?
4. Are the current regulatory restrictions upon FGT practitioners justified?
5. Does the inherent uncertainty within fetal gene therapy meet the criteria for informed consent or render it ineffectual given that the nature of that uncertainty will affect future generations and their future autonomy?

Therefore, within chapter 10 the PGC is applied to the differing relationships in order to uncover possible conflicts and resolutions within each identified issue. By doing so it will apply the resolution of those relationships to the five key issues identified. What emerges is that the majority of regulation and practice is ethically permissible. However, the term 'human dignity' does not significantly add to the FGT debate and should not be used beyond reference within preambles. Issues concerning abortion and germ line technologies must be readdressed, as well as the way that regulators apply principles such as uncertainty and foreseeability within the clinic.

Chapter 11, the concluding chapter of the thesis focuses on several key issues, reaching the conclusion that specific issues such as long term follow-up and abortion need regulative changes in order to maintain an ethically consistent practice. These changes should be in line with the PGC, and include:

1. The removal of 'human dignity' from regulation, including its indirect application;
2. Make the prohibition upon germ line technologies conditional, therefore allowing FGT practitioners to conduct germ line research within animals once knowledge deficits have been satisfied;
3. Further investigate how abortion, informed consent, long term follow-up and confidentiality can be maintained and regulated ethically.
4. Reconsider how far bodily integrity can be respected where abortion is no longer an option and treatment is only available within pregnancy;

5. Review of research funding in relation to long term studies of fetal gene therapy.

1.4 Conclusion

FGT has the potential to revolutionise how therapy is conducted and to provide cures to previously incurable conditions. The aim of thesis is to highlight and address key issues that the current regulatory system has either failed to address or consider because of the rapid progress of FGT. By utilising the fetus as a site of intervention it raises intergenerational questions regarding aspects of scientific progress and how it can reshape the way that rights and duties can be regulated. Documentary analysis of the relevant regulatory institutions and the qualitative interviewing of practitioners will be analysed through the ethical framework proposed by Alan Gewirth. From this it will be concluded that the currently imposed rights and duties do adequately take into account ethics, scientific progress and the rights of others. The thesis will conclude by providing resolution to the problems identified above, as well as suggesting areas where further research should be conducted. Although the thesis sets an ambitious task which seeks to explore difficult methodological and theoretical territory, given the current stage of FGT such an approach is needed in order to keep FGT practitioners, regulators and other parties up to date and informed because of the rapid scientific progress of FGT. Therefore, the findings of this thesis will help those stakeholders in their efforts to move FGT from the laboratory into the clinic.

2 The Emergence and Current Practice of Fetal Gene Therapy

2.1 Introduction

Given some of the challenges that gene therapy has encountered, for example its inability to stop the manifestation of some conditions such as cystic fibrosis, FGT has the potential to overcome these challenges and fulfil the promises of gene therapy. FGT is a unique area where a large number of medical professions come together in aid of a fetus. A team may consist of paediatric surgeons, neurosurgeons, obstetricians, fetal medicine specialists, ultrasonographers, radiologists (with regard to vector delivery), MRI specialists, neonatologists, anaesthesiologists, geneticists, biochemists, assistants (nurses) and other personnel (Demirkan and Cevik-Demirkan 2004). For each intervention, the impact of FGT upon medical staff is therefore widespread and encompasses many different skills and expertise. Combining the multi-disciplinary nature of fetal surgery with gene therapy is where science fiction becomes a reality (Demirkan and Cevik-Demirkan 2004). FGT is rapidly becoming a discipline in need of review particularly because the advances that are being made re presenting specific ethical and legal challenges. FGT must therefore be explored to see whether the current regulatory systems are adequate to meet these challenges.

This chapter will consider four themes relevant to the development of FGT for the purposes of this thesis: the historical development of FGT; the techniques and medical knowledge associated with FGT; current regulation; and finally prospective aspects of FGT. These are important for the thesis as they outline the development and potential progress of FGT and establish that FGT is a fledgling practice that raises many questions that the thesis can address and why the multidisciplinary approach will be needed.

Firstly, the need for FGT will be established in order to confirm FGT as an important tool for resolving specific technical issues. These first two issues are central to the thesis as they establish a remit for the practice of FGT and to confirm the current and

future importance of FGT. Once these fundamental issues have been addressed, then the short, but progressive development of FGT will be introduced. It will be shown how FGT has evolved from a relatively unknown experimental practice into the emergent international practice nearing clinical trials.

After outlining the historical development of FGT, some basic medicine around the development of an embryo, inheritance and vectorology is given. Understanding inheritance will provide a basic background to the importance of genetic testing and explains the differences between the tissues that are targeted by therapy. Vectorology is an important technical area to understand as it is the method of administering genes within gene therapy. Therefore, vectorology and inheritance will be outlined (although it should be noted that although inheritance is important, genetic defects can also occur due to genetic mutation). After this, the current developments within FGT will be presented as well as the current regulatory framework that governs FGT outside the clinic (Outside the clinic in this context refers to the rules governing the technical aspects of FGT).

Finally, as FGT progresses into the clinic the future mechanics of FGT, as well as issues surrounding the progress of FGT must be examined because as technologies develop there is a danger of technology controlling regulation rather than regulations controlling technology. In highlighting these issues the need for a prospective methodology is identified and this provides the link to the next chapter where the methodology for the thesis will be established.

2.2 Why use gene therapy upon a fetus?

Postnatal gene therapy has encountered technical hurdles within the human body. The biggest of these hurdles is host vs. graft competition. However, using gene therapy upon a fetus has its advantages because:

- Induction of graft tolerance can occur in a fetus due to its relative immunologic immaturity.
- A fetus's unique wound healing properties.
- FGT results in the early prevention of clinical manifestation of a disease (Turner and Fauza 2009: 477).

The most important of these relates to the normal development of the immunological system, which creates a window of opportunity where engraftment of a transgene[19] is theoretically possible (Surbek et al 2008). The 'window of opportunity' which Surbek et al (2008) refer to, makes genetic inventions through FGT a distinct possibility because within the window of opportunity the fetus's immune system has not fully developed, thereby in theory eradicating the problems that patients post birth suffer due to having developed immune systems (Surbek, Schoeberlein et al. 2008). Long term tolerance of the engrafted transgene can also be induced prenatally (Wagner, Schoeberlein et al. 2008).

It should be noted here that within animal studies significant progress has been made in the last decade which show promising signs in relation to haemophilia disorders, cystic fibrosis, muscular dystrophy and central nervous system disorders in humans (Santore, Roybal et al. 2009). However, one has to recognise that the results of animal studies cannot definitively identify the outcome of FGT within humans. Therefore for progress to be maintained research must be conducted upon human subjects.

However, as FGT progresses nearer to clinical trials, concerns have been raised over the use of FGT. These concerns include mutagenesis,[20] germ line transmissions and disruption of normal development. The most pertinent is mutagenesis due to the viral vectors used within FGT to secure engraftment (Wagner et al 2009). There is also the concern over the use of germ line gene therapy. Even if the gene intervention is not specifically targeted at the germ line, which develops and is compartmentalised by week seven of gestation, the germ line could potentially be affected (David and Peebles 2008). If normal development is disrupted then this creates issues around postnatal litigation and treatment, if the fetus comes to term. However, before those issues can be addressed within the clinic, FGT must develop into a practice that is capable of being used as a legitimate therapy. It is the

[19] A gene that is taken from the genome of one organism and introduced into the genome of another organism by artificial techniques (National Institute of Health 2011b).
[20] The occurrence or induction of mutation (National Institute of Health 2011b).

development of FGT to the point of clinical trials that currently makes it an emerging technology with huge potential.

2.3 The development of fetal gene therapy

FGT is an amalgamation of the techniques used in fetal surgery, fetal therapy and gene therapy. Therefore, the development of FGT has been possible because of the advances in fetal surgery and gene therapy, consequently the development of FGT must also be contextualised within the developments in those fields. Fetal medicine can be traced back to Greek and Roman scholars who conceived the idea of a miniature man inside the mother's womb (Han and Hwang 2001). The father of medicine Hippocrates concluded that the fetus urinated in utero and that the uterus must therefore be full of fetal urine (Han and Hwang 2001). However, fetal intervention was not possible then and it would be some time before that was so.

According to the pioneers of modern day fetal surgery, Dr Michael Harrison and Dr Tim Jancelewicz, the origins of fetal surgery started out as an experimental timeline in the 19th Century with experimental animal preparations which were used to make observations on living mammalian fetus (Jancelewicz and Harrison 2009). The experiments and studies were conducted mainly on guinea pigs, with the first successful fetal surgery in 1925 on a guinea pig fetus (Han and Hwang 2001).

In the 1960s (Albert) William Liley emerged as the 'father' of fetal therapy. His pioneering intrauterine transfusion for Rh disease in fetuses in 1961[21] was later perfected successfully in humans in 1963 (Casper 1998, Nicolaides and Chitty 2011).[22] It was out of the discouraging results of hydrops fetalis,[23] that lead Liley to

[21] Rhesus (Rh) condition is a condition where there is a difference between the mother and fetus concerning the Rh antigen. Blood can be Rh positive or Rh negative. If your blood lacks the Rh antigen, it is Rh negative; if it has the antigen, it is Rh positive. Problems can arise when the baby's blood has the Rh antigen and the mother's does not as the mothers antibodies filter across the placenta, the mother's body may make *antibodies* that attack the baby's blood which can cause the baby to have anaemia, jaundice, erythroblastosis fetalis (a blood disease) and ultimately fetal death (Casper 1998; American College of American Congress of Obstetricans and Gynecologists 2009).

[22] The work of Liley cannot be underestimated, as his work on the fetus has been used and cited by the Supreme Court of Justice in the USA landmark case on the right to abortion: *Roe v Wade* 410 U.S. 113 (1973).

consider and attempt intra-abdominal transfusion of the fetus (Liley 1963). The procedure enabled relatively safe and efficient maternal-fetal transfusions, making Rh conditions within pregnancy less threatening and resulted in a decrease in the fetal mortality rate when the procedure was utilised (Casper 1994). Later in the same year, Freda and Adamsons at Columbia University, New York, carried out a similar procedure through an open exchange to transfuse an in utero fetus (Freda and Adamsons 1964). In 1964 Adamsons, Freda and Liley convened at Columbia University for a full year to continue the work together. The collaboration lead to ideas and innovations, such as the prospect of open uterus surgery, that would shape fetal surgery (Casper 1998). It was this ground-breaking research and techniques that were developed for the diagnosis of genetic and physical abnormalities that lead to the development of techniques such as open fetal surgery; fetendo fetal surgery; and fetal image-guided surgery[24] were developed.

Accurate diagnosis of a fetal anomaly allows appropriate counselling and transfer to a tertiary unit, planned delivery, and specialised neonatal therapy (Kumar and O'Brien 2004). This was primarily through the development of real time ultrasound imagery, which in the 1970s reported the first in utero diagnosis of the above congenital anomalies (Han and Hwang 2001). However, the evolution of genomics has introduced prenatal testing, and pre-implantation genetic diagnosis techniques which have both lead to conditions being diagnosed earlier and easier than before. For example, since the advent of Pre Natal Diagnosis (PND), diagnostic techniques, such as amniocentesis[25] and chorionic villus sampling,[26] with more recent non invasive techniques such as cell free fetal DNA, technologies are being used as more than 90% of structural and chromosomal abnormalities arise in pregnancies without

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[23] Hydrops fetalis is a serious condition, where abnormal amounts of fluid build up in two or more body areas of a fetus or newborn and is a complicated form of Rh Disease (Rauch 2006).

[24] For a full description and videos of these techniques in operation see The Fetal Treatment Center (2009a).

[25] In amniocentesis, a sample of the amniotic fluid is removed and analysed. It is the most common invasive prenatal diagnostic procedure undertaken in the United Kingdom. Most amniocenteses are performed to obtain amniotic fluid for karyotyping and the majority are undertaken from 15 completed weeks (15+0) onwards (Royal College of Obstetricians and Gynaecologists 2005).

[26] Chorionic villus sampling (CVS) is usually performed between 10 and 13 weeks of gestation and involves aspiration of placental tissue rather than amniotic fluid. CVS can be performed using either percutaneous transabdominal or the transcervical approach. Transabdominal CVS can be performed at gestations greater than 13 weeks (Royal College of Obstetricians and Gynaecologists 2005).

any obvious risk factors (Kumar and O'Brien 2004: 328). Therefore, genetic testing is creating more accurate and earlier diagnosis of conditions which may occur, depending on the condition. It should be noted that the development of PND means that genetic analysis can occur within the first trimester of pregnancy and the advent of non invasive genetic tests could result in positive tests leading to an increase in genetic related abortions. In addition PND coupled with increasing PGD and adult genetic testing could lead to FGT being redundant in relation to serious genetic conditions. However, 'therapy' would seemingly still have a place despite these developments.

Prior to 1997, fetal surgery was considered exclusively for fetuses with life-threatening anomalies (Pierro 2003: 195), but with the increase in accurate diagnostic equipment, the criteria for fetal surgery was now no longer restricted to that of life threatening anomalies but included progressive anomalies such as spina bifida (Jancelewicz and Harrison 2009). It was the advance into correcting relatively common birth defects that has raised the possibility of fetal surgery for a much greater number of patients (Chervenak and McCullough 2007). Fetal surgery was no longer focused within a few highly specialised areas but became relevant to a wider patient base. The consequence for FGT has meant that FGT can be targeted at congenital abnormalities as well as those that could affect the fetus.

There were early signs that FGT could be successful where adult gene therapy could not. In 1990, Maria Hatzoglou *et al* (1990) were the first to use an in utero approach in applying a replication-incompetent retrovirus vector to fetal rats in utero. Their work showed that it mediated expression of human growth factor, which was significantly more effective than the application of the same vector within an adult animal model. The success of Hatzolglou's *et al* (1990) work lead to a large number of successful in utero gene experiments, which demonstrated gene delivery to virtually all fetal tissues (See David, Themis et al. 2003). It was not until 1997 that a curative gene therapy protocol for cystic fibrosis by prenatal injection of an adenovirus into the amniotic fluid in mice was identified (Larson, Morrow et al. 1997). However, the research of Larson et al was substantially criticized in the literature at the time and later research has indicated that cystic fibrosis cannot be

replicated in the circumstance that Larson et al concluded (Buckley, Waddington et al. 2008).

Meanwhile, in the USA Dr French Anderson with his team of experts had gone one stage further by performing gene therapy in a four year old with Severe Combined Immunodeficiency secondary to a genetic defect in the purine catabolic enzyme Adenosine DeAminase [ADA-SCID] (Blaese, Culver et al. 1995).[27] The key to this advance was the advent of useful retroviral vectors that permitted relatively high efficiency gene transfer and stable integration (Blaese, Culver et al. 1995). After conducting their first human gene therapy trial in 1990 (Blaese, Culver et al. 1995) the group started to consider the possibility of using such therapy within the fetus due to perceived immunological advantages. Delivering a foreign protein or therapy to the fetus can take advantage of immune tolerance which is induced during fetal life. This was not a new concept and was first proposed nearly 60 years ago (Billingham *et al*., 1953, 1956). However nobody had ever tried it. Dr French Anderson therefore forwarded a clinical phase 0 proposal to the National Institute of Health Office of Recombinant DNA Advisory Committee (Office of Recombinant DNA Activities 1999).

At the same time, against the background of the human genome project,[28] within the United Kingdom (UK) the Gene Therapy Advisory Committee (GTAC) conducted its own review of the potential of prenatal (fetal) gene therapy. Under its New and Emerging Technologies (NETS) sub group it utilised the core principles that were used by the Clothier Committee, which sought to look into the issues and ethics in gene therapy in general (Clothier 1993). These core principles were:

a) gene therapy is research and not innovative treatment;
b) only somatic therapy should be considered;
c) in view of safety and ethical difficulties germ line interventions are off limits at present;

[27] ADA-SCID is a condition whereby the enzyme which catalyzes the conversion of adenosine to inosine is deficient; therefore, causing a form of severe combined immunodeficiency disease as a result of the accumulation of toxic metabolites which inhibit DNA synthesis (National Institute of Health 2011b).

[28] The Human Genome Project has been described by the Nobel Prize-winning molecular biologist Walter Gilbert as ‘a vision of the grail’ (Gilbert 1991:83).

d) gene therapy should be restricted to life threatening disorders where no current alternative effective treatments are available;
e) patients should take part in gene therapy research trials only after a full explanation of the procedures, risks and benefits and after they have given their informed consent, if they are capable of doing so; and
f) recognising that some people, including young children, may not be able to give such consent, therapeutic research involving such patients must not put them at disproportionate risk (Gene Therapy Advisory Committee 1998: 3).

Using these core principles in conjunction with recommendations from the Clothier Committee report they considered that no new ethical issues were raised by in utero gene therapy or stem cell interventions.

The first use of FGT was recorded in 1999 (See Zanjani and Anderson 1999), but the first widely accepted confirmation of FGT was provided by the correction of several different disease phenotypes in relevant animal models (Coutelle, Themis et al. 2005). It was not until 2003 that the first successful therapeutic application of gene transfer in utero was performed by direct injection of a lentiviral vector (Seppen, van der Rijt et al. 2003). Later FGT then progressed to show long-term expression of proteins at therapeutic levels and induction of immune tolerance (Waddington *et al*., 2007) in both small (Waddington *et al*., 2004), and large animals (Tran *et al*., 2001) and cured congenital disease in some animal models (Mehta, Abi Nader et al. 2011).

Table 2. Timeline of recent fetal gene therapy developments

Organ targeted	Animal model	Vector and transgene	Delivery route	Outcome	Year
Gut	Mouse, rat	Adenovirus, retrovirus, AAV	IA	Low level transduction of the intestine (Holzinger *et al.* , 1995; Douar *et al.* , 1997; Boyle *et al.* , 2001; Garrett *et al.* , 2003)	1995
Lung, gut	S489X cftr knockout mousea	Adenovirus encoding h-*cftr*	IA	One study reported improved survival but not replicated by two further studies (Larson *et al.* , 1997; Buckley *et al.* , 2008; Davies *et al.* , 2008)	1997
Liver	Guinea pig	Adenovirus encoding β-galactosidase	UV	High level liver transduction (Senoo et al., 2000)	2000
Liver	Late-gestation macaque	Adenovirus, lentivirus and retrovirus	IP, intrahepatic	High level liver transduction (Tarantal *et al.* , 2001b; Lai *et al.* , 2002; Lee *et al.* , 2005; Tarantal 2006)	2001
Lung	Mouse	AAV1 or AAV2 encoding eGFP	IP	Short-term expression of luciferase evaluated by bioluminescence and ex vivo luminometry of tissue homogenates (Lipshutz et al., 2001)	2001
Lung	Rabbit	AAV2 encoding luciferase	IA	Luciferase expression in amniotic membranes, trachea and pulmonary epithelium (Boyle et al., 2001)	2001
Liver	MPS type I dog	Retrovirus encoding canine α-L-iduronidase	Yolk sac and peritoneal cavity	Detection of enzyme activity at birth (Meertens et al., 2002)	2002
Liver	Crigler-Najjar type 1 syndrome rat	Lentivirus encoding bilirubin UDP-glucuronyl-transferase	IP and intrahepatic injection	45% reduction in bilirubin levels for up to 1 year (Seppen et al., 2003)	2003
Liver	Early-gestation sheep	Adenovirus	IP, intrahepatic	High level transduction of the liver after IP compared with intrahepatic injection (David *et al.* , 2003a,b)	2003
Lung	Early-gestation sheep	Adenovirus encoding β-galactosidase	IA by USS	β-galactosidase expression in skin, placenta, membranes and airways (David et al., 2003a)	2003
Lung	Late-gestation macaque	AAV2 encoding eGFP	IA	Low level eGFP expression scattered throughout airways for over 1 year (Garrett et al., 2003)	2003
Skin	Early-gestation sheep	Adenovirus	IA	Expression in superficial epidermis (David et al., 2003a)	2003
Liver	Haemophilia B mousea	Lentivirus encoding hFIX	Vitelline vessel	Permanent cure of haemophilia with immune tolerance to exogenous hFIX (Waddington et al., 2004)	2004
Lung	Mid-gestation sheep	Adenovirus encoding β-galactosidase	Tracheal injection by USS	Widespread, strong transgene expression in fetal trachea and bronchial tree (Peebles et al., 2004)	2004
Muscle	GSD type II (Pompe disease) mouse	AAV1 encoding acid α-glucosidase	IP	Strong transgenic protein expression in diaphragm muscle, restoration of contractile function (Rucker et al., 2004)	2004
Muscle	Mouse	EIAV encoding β-galactosidase, AAV vectors encoding β-galactosidase	Vitelline vessel injection, IM and IP injection	Yolk-sac vessel delivery targeted the liver and heart, IM transduced skeletal muscle and IP transduced the diaphragm; expression was observed for over 15 months (Gregory et al., 2004)	2004
Brain	Mucopolysaccharide type VII mousea	Adenovirus encoding β-glucuronidase	Injection of lateral ventricles	Prevented pathological lysosomal storage in neurons and glia for up to 4 months (Shen et al., 2004)	2004
Eye	Leber congenital amaurosis mousea	AAV1/2 encoding RPE65 gene	Transscleral transchoroidal subretinal injection	Restoration of visual function (Dejneka *et al.* , 2004; Williams *et al.* , 2006)	2004
Skin	Mouse	Adenovirus, lentivirus	IA	Expression in superficial epidermis and lung (Buckley, 2005); lentivirus conferred transgenic protein expression in basal epidermal stem cells into adulthood (Endo *et al.* , 2008)	2005
Heart	Mid-gestation Rhesus monkey	Self-inactivating lentivirus encoding eGFP	Intramyocardial injection by USS	Long-term and strong eGFP expression in myocardium and pericardium (Tarantal et al., 2005)	2005
Skin	Herlitz junctional EB mouse	Adenovirus and AAV encoding laminin-5 protein	IA	Laminin-5 expression but no effect on lifespan of mouse (Muhle et al., 2006)	2006
Eye	Leber congenital amaurosis chicken	Lentivirus encoding GUCY1* B gene	Injection of ventricle of neural tube	Restoration of visual function (Williams et al., 2006)	2006
Gut	Early-gestation sheep	Adenovirus encoding β-galactosidase	Intragastric injection by USS	Widespread transduction of intestine and gut (David et al., 2006a)	2006
Liver and HSCs	Mouse	Lentivirus encoding h-α-globin	Vitelline vessel	α-globin expression in liver, spleen and blood peaked at 4 months, but then declined (Han et al., 2007)	2007
Blood	Mouse	AAV1 and AAV2	Human FIX	Sustained hRX expression in the absense of an immune response for haemohpilia b (Sabantino 2007)	2007
Lung	Rat	Adenovirus and lentivirus encoding eGFP	Lung parenchyma injection by USS	eGFP expression only in interstitial cells (Henriques-Coelho, 2007)	2007
Muscle	Duchenne muscular dystrophy mousea	Adenovirus encoding murine dystrophin	IM	Regeneration of muscle fibres, prevention of muscle damage (Reay et al., 2008)	2008
Uterine artery	Mid-gestation sheep	Adenovirus encoding VEGF/β-galactosidase	Uterine artery injection	Efficient transduction of the uterine arteries, increased uterine artery blood flow (David et al., 2008)	2008
Blood	Mouse	Lentivirus	vitelline vein injection	Sustained transgene expression and correction of prothrombotic phenotypes in congenital thrombotic thromnocytopenic purpura (Niiya et all 2009)	2009
Muscle	Duchenne muscular dystrophy mouse	AAV8 encoding minidystrophin	IP	Reduced muscle pathology and functional benefit to the transduced diaphragm (Koppanati et al., 2010)	2010
Spinal cord	Mouse	EIAV encoding β-galactosidase	Intrathecal injection at E16	Transduction of dorsal roots and dorsal root ganglia (Rahim et al., 2010a)	2010
Nervous system	Mouse	AAV9 encoding GFP	Vitelline vessel injection	Global transduction of nervous tissue throughout the brain, eye and peripheral nervous system (Rahim et al., 2010b)	2010
Liver	Early and late-gestation sheep	AAV8 encoding hFIX	IP injection by USS	hFIX expression in blood up to 6 months but no immune tolerance (David et al., 2011)	2011
Liver	Late-gestation macaque	AAV5 and 8 encoding hFIX	UV injection by USS	hFIX expression in blood and liver for at least 1 year, non-neutralizing immune response (Mattar et al., 2011)	2011
Muscle	Late-gestation macaque	AAV9 vector	UV injection	High level of transgene expression in cardiac and skeletal muscles (Mattar et al., 2011)	2011
Skeleton	Mouse	AAV9 vector	Uterine artery injection	Enhanced mineralization was demonstrated on X-ray images of the chest and forepaw in lethal murine Hypophosphatasia. (Sugano et al 2012)	2012

Adapted from (Mehta, Abi Nader et al. 2011)[29]

[29] AAV, adeno-associated virus vector; cftr, cystic fibrosis transmembrane conductance regulating protein; EB, epidermolysis bullosa; eGFP, enhanced green fluorescent protein; EIAV, equine immune

It is evident from Table 2[30] that there have been many developments in the last ten years. As stated earlier changes in vectorology have made some of the recent advances possible (See Mckay, Rahim et al. 2011). It should be noted that FGT progression has not been linear. The development of gene therapy has been hindered by several incidents, most notably the deaths of Jesse Gelsinger[31] and Jolee Mohr.[32] These incidents have had a negative effect on the progress of all gene therapy protocols (Deakin, Alexander et al. 2009). FGT also has had its own issues where a high incidence rate of liver tumours in fetal and neonatal mice was observed after the application of early third-generation equine infectious anaemia virus vectors with self-inactivating configuration (Coutelle 2008). One also has to consider that any treatment in pregnancy is clouded by high profile incidents involving pregnancy such as the Thalidomide and Epilim.[33] Despite not being a FGT trial, these incidents highlight the possible negative media and public reaction to an adverse result. Despite these concerns, FGT is progressing again. The progress of FGT as seen in Table 2 and the currently identified organs which would be targeted at a prenatal phases of development, indicates that FGT will progress to the clinic because of the increasing success in animal models. In order to understand how FGT has reached this point some basic medicine in terms of fetal development, inheritance and vectorology will now be explored. In doing so, the process and development of FGT as a practice can be contextualised, and at the same time it can provide information to be used later in the thesis to enable understanding of the debates surrounding regulation.

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anaemia virus; GSD, glycogen storage disease; hFIX, human factor IX clotting factor; HSCs, haematopoietic stem cells; IA, intra-amniotic; IM, intramuscular; IP, intraperitoneal; MPS, mucopolysaccharidosis; UV, umbilical vein; USS, ultrasound.

[30] Up to date as of Spring 2012.

[31] Jesse Gelsinger, died in a Phase 1 dose escalation study involving ornithine transcarbamylase deficiency which it has been debated was a result of poor subject selection which if executed safely and efficiency would have resulted in Jesse not being a trial subject (Kimmelman 2008).

[32] Jolee Mohr died during a clinical trial using gene therapy to treat rheumatoid arthritis, but later tests showed the death was not a result of the gene therapy (Tanne 2007).

[33] See (BBC 2002) for details upon the thalidomide incidence which resulted in birth defects between 1957 and 1961; and (Hirsh 2011) for details regarding the soon to be dropped Epilim case where the users of the epilepsy drug 'Epilim' during pregnancy alleged that the drug caused the birth defects in their children.

2.4 Basic medicine and fetal gene therapy techniques

2.4.1 Introduction to fetal development

After fertilisation has occurred between the male and female gametes the embryonic development stage starts. At 36 hours after chemotaxis[34] and fertilisation the ovum begins mitosis until it reaches the blastocyst stage at day 5 of development (Pawlowski, Sheehan et al. 2007).[35] Here, the embryo is merely a group of identical cells, all with the potential to become any part of the embryo. At day 6, implantation occurs and the embedded embryo starts to develop its central nervous system after about 14 days of development. It is at this point of development that the primitive streak[36] is visible (McLaren 1986: 15). The neural tube begins to close after 22–23 days, and by day 42 the cerebral cortex begins development. By day 56, the fetal stage begins (Tortora and Grabowski 2001).

Table 3. Timeline of fetal development

End of Month	Approximate Size and Weight	Representative Changes
1	0.6cm	Eyes, nose and ears are not yet visible. Vertebral column and vertebral canal form. Heart forms and starts beating. Body systems begin to form with central nervous system begin form from the primitive streak by day 15.
2	3cm 1g	Eyes far apart and fused. Nose is flat. Ossification begins while limbs become more distinct with digits being formed. The internal organs continue to form and immune system is still underdeveloped.
3	7.5cm 30g	Eyes almost fully developed but with fused eyelids. Ossification continues. Limbs are now fully formed and fetus

[34] Orientation or movement of an organism or cell in relation to chemical agents (National Institute of Health 2011b).

[35] An undifferentiated embryonic cell that has developed for five to six days after fertilisation (National Institute of Health 2011b).

[36] An elongated band of cells that forms along the axis of an embryo early in gastrulation by the movement of lateral cells toward the axis and that develops a groove or 'streak' along its midline through which cells move to the interior of the embryo to form the mesoderm (National institute of Health 2011b).

		has detectable heartbeat. Unfelt fetal movement occurs and urine starts to be excreted.
4	18cm 100g	Rapid body development while taking on human features and joints begin to be formed. Fetal immunocompetence is established (13-16 weeks). Head is disproportionate in size compared to body
5	25-30cm 200-450g	Head becomes less disproportionate. The fetus also begins more frequent movements which start to be felt (the quickening). Continued rapid body development
6	27-35cm 550-800g	Head becomes even less disproportionate to body and eyelids separate. Substantial weight gain and skin is wrinkled.
7	32-42cm 1100-1350g	Head and body more proportionate despite wrinkled skin. Birth now would be premature but capable of survival. Fetus begins to rotate to upside-down position. Testes start to descend to scrotum
8	41-45cm 2000-2350g	Subcutaneous fat is deposited and skin becomes less wrinkled
9	50cm 3200-3400g	Additional subcutaneous fat and nails continue to grow

(Tortora and Grabowski 2001: 583)

A basic timeline of fetal development can be seen in Table 3. From day 56 of gestation the fetus develops in the mother's uterus in a sac, which develops from a thin membrane formed by the eighth day of fertilisation called the amnion (Tortora and Grabowski 2001). The sac fills with amniotic fluid, which is initially from the mothers blood, but is predominately filled with fetal urine and contains essential nutrients for fetal development (British Medical Association 2004). From week eight, until the fetus coming to term, the fetus grows in length up to 20 times and increases in weight by 1700 times (See Table 3). Around week 12 the fetus starts to develop its own movements and resembles something 'human' like (Cunningham, Gant et al. 2001), but it is not until week 32 that the internal organs are almost fully developed (British Medical Association 2004). The normal term time is 40 weeks, although some babies have been known to survive after as little as 22 weeks of gestation (New Scientist and Reuters 2007). To further understand FGT the next section gives a brief explanation of inheritance and vectorology.

2.4.2 Understanding of inheritance and vectorology

Each human being inherits 46 chromosomes arranged into 23 pairs (British Medical Association 2004). Pair 23 of these chromosomes determines our sex with XX for female and XY for male. Half of the chromosomes in a fetus are inherited from the mother and half from the father. However, a child also inherits maternal DNA from plural mitochondria that are situated within the cytoplasm of the oocyte from which they develop from (Howard Hughes Medical Institute 2006).

Each chromosome that makes up a pair is called a homolog and contains genes that control the same trait (Tortora and Grabowski 2001). Genes that control the same trait are situated on the same location on homologous chromosomes and are called alleles. These can be either dominant or recessive, and can affect both the genotype (genome) and phenotype (physical or outward expression) of a person (Tortora and Grabowski 2001). The example of eye colour shows the different permutations of genotypes and phenotypes (see Table 4).

Table 4. Results of punnett square for brown or blue eyes

Alleles present[37]	Genotype	Phenotype
BB	Homozygous dominant	Brown eyes
Bb	Heterozygous	Brown eyes
Bb	Homozygous recessive	Blue eyes

Genetic diseases can by inherited either through sex determining chromosomes or through genes that are located on a non sex determining chromosome called an autosome (Senut and Gage 1999). As stated above, the inheritance of genetic conditions is not as simple as eye colour since conditions can be monogenetic,

[37] B = dominant allele; b = recessive allele

polygenetic and multifactorial.[38] An individual will inherent a genetic condition from the germ cells of their genetic parents, though it should be noted that genetic conditions can arise as a result of new mutations which neither parent has and can result in incomplete development of organs.

Within the body there are two types of cells: somatic and germ line. Somatic cells are any body cells that compose the tissues, organs, and parts of that individual other than their germ cells (National Institute of Health 2011b). Germ cells are those cells involved in reproduction such as an oocyte, sperm cell or one of their antecedent cells (Debyser 2003, National Institute of Health 2011b). Any therapy therefore targeted at somatic cells will not be inherited by the next generation. In order to treat any of these types of body cells vectorology must be used to transfer the correctly functioning gene into the host's cells.

Table 5. Table indicating the scientific properties of various vectors currently used within gene therapy

	Adenovirus	AAV	Retrovirus	Lentivirus	HSV	Naked DNA
Maximum insert size	30 kb	3.5-4 kb	7-7.5 kb	7-7.5 kb	35 kb	unlimited
Titers (viral particles/ml)	10^{12}	10^{12}	10^{8}	10^{8}	10^{8}	unlimited
Infectivity	broad	broad	dividing cells	broad	broad	broad
Applications for CNS	ex/in vivo	ex/in vivo	ex vivo	ex/in vivo	ex/in vivo	ex/in vivo
Integration	no	yes/no	yes	yes	no	poor
Stability of expression	short	long	long (silencing)	long	latency?	short
Immune response	extensive	unknown	low	low	medium	none
Preexisting host immunity	yes	yes	unlikely	unlikely (AIDS patients?)	yes	no
Safety	I, T	I, T	IM	IM ?	I, T	none

I = inflammation
T = toxicity
IM = insertional mutagenesis

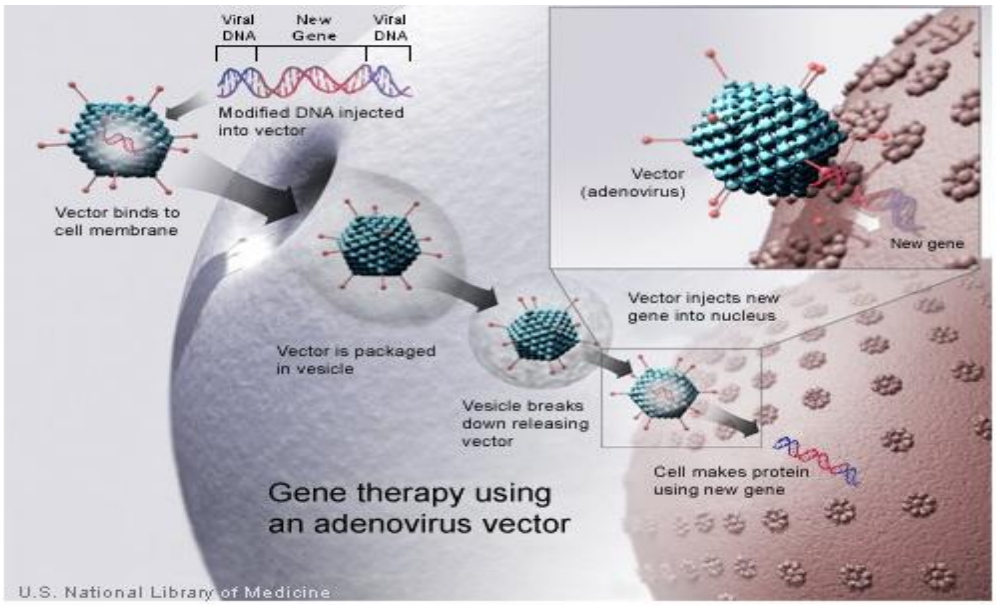
(Debyser 2003: 497)

Vectorology is the use of a vector, often a virus, in order to correct dysfunctional genes. A viral vector is a protein particle derived from a replicative virus that

[38]Monogenic conditions relate to, or are controlled by a single gene and especially by either or both allelic pair, whereas polygenic or multifactorial conditions have characters or a mode of inheritance dependent on a number of genes at different locations (National Institute of Health 2011).

contains genetic information in the form of RNA or DNA (Debyser 2003: 495). There are non-viral vectors as well but the success of these vectors has been limited (Mckay, Rahim et al. 2011). The main classes of viral vectors are adenovirus, Adeno-Associated Virus (AAV), retrovirus (such as HIV), lentivirus, Herpes Simplex Virus (HSV) and naked DNA (See Table 5). The choice of viral vector is determined by the size of the gene of interest, the required duration of gene expression, the target cell and biosafety issues (Debyser 2003).

Diagram 1. Diagram illustrating how gene therapy using an adenovirus works



(National Institute of Health 2011a)

Vectors are used to act as a carrier of a new 'correctly functioning' gene into the host's DNA or cell nucleus (depending on whether an integrating or non integrating vector is used)[39] in order to rectify their dysfunctional gene. This process can be seen in Diagram 1 for a non integrating vector called an adenovirus. Full integration and therefore the length of expression are determined by the vector used.

Having outlined the basic medical and technical aspects of FGT, and introduced the idea of correcting genetic conditions *in utero*, a logical next question to ask is for what conditions can this be used? In order to answer this question regulation is

[39] Integration within this context refers to vector integration into the hosts DNA.

important as not only does it provide the answer to this question, but it helps outline procedures and responsibilities that must be adhered to.

2.5 Regulating fetal gene therapy outside of the clinic

As identified within 2.3, FGT is a subspecialty of gene therapy and therefore gene therapy regulation is applicable to FGT. However, due to its specific and unique target for treatment it has additional regulation that is not applicable to gene therapy in general. The legal definition of a 'gene therapy medicinal product' is any biological medicinal product which has the following characteristics:

> (a) it contains an active substance, which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence;
> (b) its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.[40]

It should be noted that the definition of a gene therapy medicinal product no longer includes vaccines against infectious diseases.[41] Legally, any product that is classified as a gene therapy medicinal product is classified as an Advanced Therapies Medicinal Product (ATMP) under the Advanced Therapies Regulation.[42] These regulations were translated into domestic regulation by the Medicines for Human Use (Clinical Trials) Regulations 2004. Any gene therapy medicinal product that is manufactured or supplied within the UK is covered by the Medicines Act 1968. Where the medicinal product is for human use Directive 2001/83/EC is also applicable.[43]

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[40] Directive 2003/63/EC (amending Directive 2001/83/EC) and European Commission Directive 2009/120/EC of 14 September 2009 amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use as regards advanced therapy medicinal products (Directive 2009/120/EC). For full directive titles see Appendix F - List of Analysed Documents.
[41] Directive 2009/120/EC Article 2.1.
[42] Regulation (EC) No 1394/2007. ATMP's can include any of the following medicinal products for human use: (1) a gene therapy medicinal product, (2) a somatic cell therapy medicinal product, or (3) a tissue engineered product. Regulation (EC) 1394/2007 Article 1.
[43] Amended by Directive 2002/98/EC, Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC.

Where FGT practitioners are conducting clinical trials involving a gene therapy medicinal product they have more general responsibilities in conducting their clinical research, as identified in the Medicines for Human Use (Clinical Trials) Regulations 2004. Under these regulations, all clinical trials involving Medicinal Products, including ATMPs, must have a clinical trial authorisation granted by the Medicines and Healthcare products Regulatory Agency (MHRA). Where a medicinal product will be used across Europe approval from the European Medicines Agency (EMA) will be required.[44] The MHRA will assess the safety of the trial as well as regulatory compliance (Gene Therapy Advisory Committee 2010). In addition, an UK clinical trial cannot commence until a Research Ethics Committee (REC) has provided a favourable opinion for the study (Gene Therapy Advisory Committee 2010).[45] For all gene therapy protocols in the UK GTAC is the only UK ethics committee empowered to approve clinical trials of gene therapy medicinal products.[46] According to GTAC guidelines, in order to be ethical, the risks of the physical procedures would need to be known (Gene Therapy Advisory Committee 1998: 6). They will weigh up the foreseeable risks and inconveniences against the anticipated benefit for the individual trial subject and other present and future patients (Gene Therapy Advisory Committee 2010). As with all gene therapy the intervention must only be to somatic cells.[47] Any intervention that seeks to alter the germ cells of the patient or third party is deemed illegal.[48] All efforts to prevent inadvertent germ line alterations must be taken (Clothier 1993). However, such regulation relies upon current scientific knowledge and the presumption that any germ line alteration would be against human dignity.

[44] Regulation (EC) 726/2004 and European Parliament and Council Directive 2001/83/EC of November 2001 on the Community code relating to medicinal products for human use (Directive 2001/83/EC). For full title of European legislation see Appendix F - List of Analysed Documents
[45] Medicines for Human Use (Clinical Trials) Regulations 2004 s.14.
[46] Medicines for Human Use (Clinical Trials) Regulations 2004 s.14(5).
[47] Medicines for Human Use (Clinical Trials) Regulations 2004 s.19(1).
[48] Medicines for Human Use (Clinical Trials) Regulations 2004 s.19(3).

Table 6. List of organs that are currently being targeted by fetal gene therapy

Organ to be targeted	Current optimal vector	Injection routes	Limiting factors
Lung	AAV	Intra-amniotic	Large dilution effect of AF; relies on fetal bone marrows (BMs)
		Intrapulmonary	Expression remains local to injection site
		Intratracheal	Transthoracic injection and fetoscopic tracheal delivery from mid-gestation onwards
Blood	Lentivirus	Umbilical vein	
		Intraperitoneal	Increased risk of germline gene transfer to peritoneal cavity when performed early in gestation
Skeletal muscle	AAV	Intramuscular	
		Intraperitoneal	Also targets diaphragm
		Hydrothoracic	Technically difficult in man
Liver	AAV Lentivirus	Intraperitoneal	Rapid division of fetal liver may limit level of transduction by vectors that only minimally integrate such as AAV
		Intrahepatic	Transduction of liver injection sites only
Brain	AAV Lentivirus	Intraventricular	Technically difficult in man
		Umbilical vein or intraperitoneal	Relies on vector crossing the blood–brain barrier; may be gestational age dependent
Skin	Lentivirus	Intra-amniotic	Delivery early in gestation required to target deeper epidermal layers
Sensory organs	Lentivirus	Intra-amniotic	Early stage of gestation critical to reach developing ear or eye
		Otocyst or retinal injection	Technically difficult in man
Gut	Lentivirus	Intra-amniotic	Large dilution effect of AF; relies on fetal BMs
		Intragastric	Potential limiting effect of gastric fluid on vector
		Oropharyngeal	Fetoscopically guided
Heart	AAV	Intraperitioneal	
Renal	Lentivirus	Intra-amniotic	Transgenic protein expressed in kidney, but produced elsewhere
	?	Urinary tract	Never evaluated
Uteroplacental circulation	Adenovirus	Uterine artery	

AAV, adeno-associated virus vector; AF, amniotic fluid.

(Mehta, Abi Nader et al. 2011: 729)

Additional regulation is in place for FGT indicating that a target disorder or disease would need to be life threatening, or associated with severe disability, and for which no suitable treatment is available after birth, in order to justify intervention in utero (Gene Therapy Advisory Committee 1998). Therefore recent relatively successful advances in adult gene therapy for haemophilia b (Nathwani, Tuddenham et al. 2011) would mean that an in utero approach would not be permitted. Nevertheless, a FGT practitioner could develop a fetal approach to treatment for conditions in organs such as identified in Table 6. Such regulations mean that the only point of intervention, which would rectify a future child's condition, would be in utero. In developing a fetal approach the mechanics of delivering the product must also be

identified and, therefore, a prospective look at FGT in the clinic is necessary. However, in looking forward issues surrounding emerging technologies, scientific progress and regulation must also be addressed since these issues will help guide the methodology of the thesis.

2.6 Looking forward

In looking forward towards prospective clinic trials of FGT, and then future normalisation of FGT as a viable practice, various issues arise which include: the viability of FGT as a practice; will it be successful; and will the public accept it. However, two predominant issues arise that are relevant immediately to regulation: How can it be done? And, is regulation capable of regulating scientific progress?

2.6.1 The theoretical mechanics of future fetal gene therapy interventions

Currently the options available to those who are in receipt of their own genetic information before pregnancy has occurred have preventive options such as: (i) having no children, (ii) taking the risk and hoping that their child will be unaffected, (iii) adopting a child, (iv) using assisted reproductive technologies such as prenatal diagnosis with selective abortion, or sperm donation, or the use of pre-implantation diagnosis after in vitro fertilisation of intracytoplasmic sperm injection (Fletcher and Richter 1996, Pembrey 1995). Nevertheless, in the future FGT will be another treatment option and the following questions would need to be answered: Is the disease in question amenable to treatment? Would the treatment be preferable to termination or non intervention where there is a valid pre clinical model? Do FGT practitioners' feel after considering factors, such as risk/benefit calculations, and the chance of ethical approval, that a mother's consent is still valid? Would the intervention occur at the correct time (Mattar, Choolani et al. 2011)? These questions are not an exhaustive list but merely indicate the complexity of questions that must be asked. For example, Diagram 2 indicates the imperative of time within the mechanics of any future FGT intervention.

Diagram 2. Flow diagram illustrating the future mechanics of fetal gene therapy within the clinic

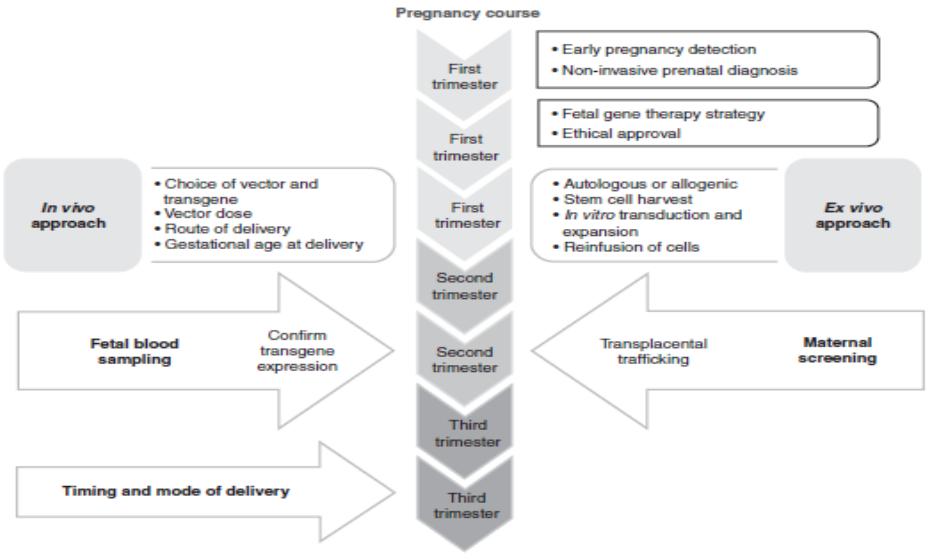


Figure 1. Proposed schema of *in vivo* and *ex vivo* FGT planning in the course of an affected pregnancy.

(Mattar, Choolani et al. 2011: 1262)

It is clear from Diagram 2 that the mechanics of any FGT whether in vivo or ex vivo will have to occur early in pregnancy, near the end of the first trimester, but possibly into the second trimester. Therefore, the availability of prenatal diagnostic tools such as amniocentesis and ultrasound are critical in diagnosing these conditions early enough within pregnancy for an effective treatment regime to be implemented. However, the implementation of that treatment strategy could change as FGT progresses and develops. It is the development of a technology that can cause regulatory problems.

2.6.2 Regulating fetal gene therapy and scientific progress

Although the current FGT regulations appear to be already decided it is clear that emerging or developing technologies pose different questions for regulation as they progress from the laboratory to the clinic and then into normalised medical practice. In identifying the theoretical mechanism of future FGT, as well as the broader regulatory framework that FGT would be governed by, there are still further issues about the ability of the current regulations to cope with the transition from the laboratory into the clinic.

Statutes and regulations, almost by definition, are designed to handle regulatory concerns existing at the time of promulgation. It is not surprising that emerging technologies often exacerbate regulatory gaps or introduce new concerns that create new regulatory lacunae (Mandel 2009: 6). These developments have the ability to outpace the capacity of individuals and institutions to adapt (Winner 1978: 3). As Ellul notes, these types of technologies potentially could change tradition and the way in which we live in order to accommodate these new technologies (Ellul 1965). As a result tradition is banished to the past due to the necessity of new techniques (Welsh 2000). Technologies such as FGT have the ability to shape humans rather than being shaped by humans. This has been interpreted by some as the rise of autonomous technology (Winner 1978). These technologies can lead to future shock[49] because of the greatly accelerated rate of change, thus leading to a negative impact upon society (Toffler 1971). Although this thesis is not arguing that technology is autonomous in the way that either Ellul or Winner suggest, important issues arise out of their work relating to how to regulate such areas and how to investigate such emergent technologies in order to control them, and thus stop the development of autonomous technology (Winner 1978). For example, in the effort to wrest back control one should evaluate the danger of what might happen in the next half-century, and distinguish between what humanity wants to keep and what it is ready to lose (Ellul and Bromiley (trans.) 1989).

In order to manage the dynamic of emerging technology promise versus risk, it is important to move the point of first regulation earlier in a technology's development (Mandel 2009). In other words ethical analysis and debate should happen before the technology advances. However, within the governance of scientific progress, evolution and flexibility must still be possible, otherwise in trying to control scientific progress there is a danger of stifling it completely. Progress inevitably has uncertainty within it that can only be known through investigation. However, areas of scientific progress, such as FGT, can polarize debate and, hence, opinions about

[49] Future shock is a time phenomenon that arises from the superimposition of a new culture on an old one, yet within one's own society (Toffler 1971).

how an area should be regulated. This is partly because progressing technologies are problematic and have persistent uncertainty surrounding potential risks (Falkner and Jaspers 2012: 2). It is potential rather than quantifiable predicted risk that has the ability to hinder progress.

It appears, therefore, that within areas of scientific progress such as FGT an explorative stance should be taken, because there is no current human practice that could address the uncertainties and potential risks, and could be used here in order to achieve an understanding of FGT. This explorative stance, however, causes methodological problems such as sample size and population identification, but it would seek to redress the one direction exchange that could occur due to the potentially autonomous technology (Ellul 1965). These methodological issues will be returned to more fully in chapter 3, but they highlight the difficulty of trying to regulate within an area that is predominately reactionary to current practice. They also illustrate that the regulation currently in use is potentially inadequate to cope with emergent or progressing technologies (Mandel 2009). Therefore, addressing how scientific progress is currently managed is a fundamental theme that must be addressed.

One such method within regulation to control such technology is the precautionary principle.[50] There is no universal definition of precautionary principle, but the purpose of the precautionary principle is to create an impetus to take a decision notwithstanding scientific uncertainty about the nature and extent of the risk (Health and Safety Executive 2002: 2) At a regulatory level precautionary principles have been seen as paralyzing (Sunstein 2003) as well as drawing a growing amount of negativity within certain debates such as climate change (Giddens 2009). It is argued that such a principle would lead to halting scientific progress because not all risks can be contained, thus the most precautionary approach should be adopted (Sunstein 2005). Those, such as Sunstein prefer a cost benefit analysis, which is heavily dependent on market pressure and scientific evidence (Sunstein 2003, 2005).

[50] As opposed to precautionary reasoning which is used to identify a possible agent (see 5.7.2).

However, risk-benefit analyses, may be of limited value because they rely heavily or entirely upon what can be quantified (Kopelman, Resnick et al. 2004). They can also lead to catastrophic damage when damage does occur (i.e. the Gulf oil spill) as well as having underlying questions regarding who an expert is and what is considered expert scientific evidence (for the example of herbicide farmers regarding the use of 2, 4, 5 – T (Irwin 1995)). However, precautionary principles do not have to be zero risk principles, but can aim to achieve lower or more acceptable risks or hazards (World Commission on the Ethics of Scientific Knowledge and Technology 2005). This can be achieved by taking into account the possible uncertainties and evaluating the impact of those potential uncertainties. The precautionary principle can control potential problems that progressing technologies might pose, as well as take into account more than scientific uncertainties, because it shifts the burden onto those wishing to progress technology and thus helps control technology (Kopelman, Resnick et al. 2004).

2.7 Conclusion

Developments within gene therapy and the ever increasing ability to diagnose both physical and genetic fetal abnormalities have meant that FGT is becoming more applicable. FGT is a practice with huge potential despite its uneven development which has been due to incidents which have significantly impeded experimental medicine concerning gene therapy and prenatal therapeutic approaches. These in turn have had a knock on effect upon FGT. However, it has developed now into a practice in its own right out of the developments within fetal therapy and gene therapy. Despite this development it is still very much in its infancy as no clinical trials have been conducted to date. Therefore the practice still remains one without human application and which, it has been shown, would be limited to certain medical conditions. Nonetheless this restriction has not stopped the implementation of animal models and the identification of the future mechanics of prenatal interventions. These proposed future mechanics seek to operate within the rules of consent that currently operate within medicine despite the two not necessarily being compatible. Some of the issues already highlighted in this chapter will be addressed in the following chapters.

It is apparent in addressing the issue of trying to regulate FGT as a practice that is progressing into the clinic that FGT has the potential to expose regulatory gaps, something which technology always seems to do. It is this regulatory challenge rather than the scientific challenges to the progress of FGT that the thesis will explore. In order to explore the regulatory challenge the starting point within an emerging area must be to establish a methodology. Given the uncertainties within exploring an emerging area it is clear that the methodology must take a broad multidisciplinary approach in order not to restrict the analysis of potential data. This exploration becomes easier having established a basic understanding of the historical development of FGT, as well as outlining the basic techniques involved within a potential future practice. The next chapter will present the methodology adopted in the thesis.

3 Methodology

3.1 Introduction

After conducting the literature review, several key areas arose relating to FGT. These key areas included: personnel who created in utero practices involving stem cell and genetic technologies; the regulation of FGT; the thoughts of personnel who provide access to such technologies; and personnel who were affected, both directly and indirectly, including current and future generations. Within those areas it was clear that there were emerging themes that lead to the following research questions:

- Are the intergenerational issues of FGT taken into account by both direct and indirect stakeholders?
- Can intergenerational issues override the reproductive rights of the mother?
- Have intergenerational issues impacted upon the clinical applications implicit and manifest in this work?

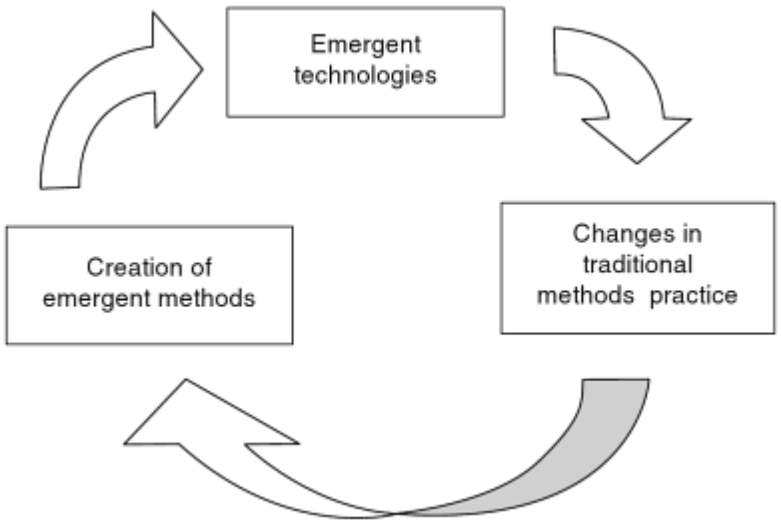
In identifying that intergenerational issues are relevant to FGT, the impact of those issues upon FGT must be investigated. From the above research questions, the key figures that emanate from FGT are: regulators, FGT practitioners, patients, directly affected third parties such as future parents and those indirectly affected, such as the public(s). However, given the breadth of the stakeholders affected by the intergenerational issue the reproductive rights and duties can be viewed through that of the legislator/regulators, FGT practitioners, patient and patient groups. Despite the relevance of the explicit views of patients within reproductive rights, those views are not the contention of this thesis because the current position of FGT means that those patients do not yet exist. Nevertheless, those patients' views are implicitly dealt with within the thesis through the analysis of autonomy. Therefore, consideration of their possible positions is taken into account. Having identified relevant parties and concepts from the literature review, the next phase was to identify data collection tools to answer the research questions.

This chapter will outline the following: why a multidisciplinary approach has been taken and the tools used (3.2); the robustness of both the documentary and interview data (3.3 and 3.4); identify access and ethical issues (3.5 and 3.6); and finally introduce the analytical framework (3.7). It will then conclude and lead into the data chapters.

3.2 Identifying data collection tools

Evolving technologies present different challenges to social research. They extend the boundaries of qualitative and quantitative research because they change the way in which we view human life as well as influencing the research questions that should be asked (Hesse-Biber 2011). Therefore, as FGT seeks to answer new questions the answers lie beyond any single discipline. From a methodological perspective, emerging technologies change the way in which sampling is conducted, how a sample is identified and what a representative sample might be (Hesse-Biber 2011). As identified above, identifying patients is still not possible because no criterion has been established to identify them. Taking into account autonomous technology and the potential inability to regulate, a different method is needed to explore progressing technologies because as technology progresses it challenges traditional social science methods (See Diagram 3). There researchers must develop new research skills (Hesse-Biber 2011). One such method that can cope with the challenge of progressing technologies is a multidisciplinary approach.

Diagram 3. Interplay between emergent technologies and methods



(Hesse-Biber 2011: 9)

Consequently the thesis adopted a multidisciplinary approach which included: exploration of legal instruments, an ethical theory as an analytical tool, social scientific tools to identify and access stakeholders, such as regulators, and the use of documentary analysis and semi structured interviewing of FGT practitioners. The

aim of utilising such an approach was to clarify issues as well as highlight possible issues that need resolution. For example, chapter 5 identifies the maternal fetal divide which highlights the intergenerational aspect of medicine and scientific progress within medical legal practice. The next generation is then explored within the prospective regulation of FGT and the views of FGT practitioners in order to identify any further issues, such as long term follow-up. Following the identification of issues from both sources, the PGC is used as an analytical tool with which to evaluate whether a particular issue presents ethical problems and how it may be resolved. Therefore, the PGC also identifies if the maternal fetal divide may warrant re-evaluation in relation to issues such as long term follow-up.

Having identified the broader research tools, the more specific tools for the thesis were identified. The initial data collection methods identified were: interviews, observation, and documentary analysis. However, the data collection methods used were that of semi structured interviewing and documentary analysis. These methods were chosen because the practice of FGT is still in its infancy and has not reached the point of clinical trials. Therefore, participant observation and patient interviewing would be impractical at this stage.

It was felt that acquiring a picture of regulation before conducting the interviews would be helpful in providing vital background information, as well as providing areas which could be questioned within the interviews. Therefore, the documentary analysis was conducted first. The regulatory picture is often communicated through documents such as legislation, codes of practice; therefore, documents can help fill out and confirm what the interview data reveals. As Silverman (2006) identifies, there are four advantages of using textual data:

1. Richness. Close analysis of written texts reveals presentational subtleties and skills.
2. Relevance and effect. Texts influence how we see the world and the people in it and how we act.
3. Naturally occurring. Texts document what participants are actually doing in the world – without being dependent on being asked by researchers.
4. Availability. Texts are usually readily accessible and not always dependent on access or ethical constraints. Because they may quickly

> be gathered, they encourage early data analysis (Silverman 2006: 157).

Conducting the document analysis first also helped inform the interview process and identify what questions should be included.. For example, it was clear from the data that the definition of human dignity and its use within the clinic should be included within the interview, because of its frequent explicit and implicit use within regulation. It was also clear that questions regarding fetal tissue engineering should be excluded, because it fell outside of the remit of thesis.

The documentary analysis was divided into textual analysis of medical and legal literature regarding fetal interventions, exploration of a general overarching principle in bioethics (namely human dignity) and then an exploration of prospective FGT regulation. The first two modes of analysis narrow the field to concentrate on the maternal fetal divide and the PGC. The maternal fetal divide provides a reference to the present day, thus a benchmark with which to assess if FGT will change current thinking. The introduction of an ethical analysis is returned to within chapter 10, where it provides an analytical tool to assess whether regulation and the maternal fetal divide can withstand scientific progress.

Semi structured interviewing was chosen as a data collection method in order to fill in any gaps left by the documentary analysis. More importantly the interview data collection method was used to confirm whether the picture gained from the documentary analysis was one being reflected within the world of the FGT practitioners. However, interviews do not provide the complete view of whether or not intergenerational aspects are influential within a FGT practitioners world; but they can still provide access to the meanings and values that persons attribute to their work (Miller and Glassner 2004). Such information can then be used to ascertain what issues are important to FGT practitioners. The interviews were semi structured in order to provide consistency throughout the interviews and make the analysis of the data more credible as there was an underlying theme throughout the interviews. Importantly, using this technique does not hinder the narrative/opinion that can be extracted from the interviewee (Thorne 2000).

Given the multidisciplinary nature of the thesis and different data collection methods triangulation (Keats 2000) was used to compare the results from the different data collection methods. This can increase the reliability of the conclusions drawn from the data since both collection methods focus on the same social phenomena (Atkinson, Coffey et al. 2003). It also gives a more detailed and balanced picture of the situation, which each individual data source cannot do on its own (Altricher, Feldman et al. 2005: 114). Therefore the credibility and reliability of the conclusions should be increased (Bazeley 2002). Although, triangulation has been criticised due to over simplifying social reality and ignoring the reflexivity of the researcher (Atkinson, Coffey et al. 2003); such obstacles can be overcome by being a reflexive researcher and acknowledging the limitations of triangulation. However, without triangulation this thesis cannot address the scientific progress of FGT because the differing viewpoints on FGT are all needed to explore the impact of FGT. Without using triangulation and a mixed method approach all of these different perspectives would not have been considered. Triangulation has given the thesis an overview of social regularities from a larger sample (the documents) while understanding personal perspectives through detailed study of a smaller sample (the interviews) (Bazeley 2002).

The interviews were conducted with FGT practitioners between October 2010 and April 2011. A FGT practitioner was any person who worked with and/or researched FGT.[51] These qualitative interviews were conducted with university based FGT practitioners, eliciting narrative reconstructions about their work, particularly the influence of human dignity, regulatory and intergenerational aspects within their field (DeVault and McCoy 2002). The FGT practitioners were selected by purposive sampling, which relies on the researcher selecting the sample due to the traits that the potential candidates will possess, which within this study means being involved with FGT (Bryman 2008: 458).

13 interviews were conducted consisting of 10 males and 3 females from either clinical or scientific backgrounds. Due to the small and exclusive nature of the

[51] See 1.2.3.

sample, the data will be presented in a neutral way and a slightly asocial approach was used to maintain the anonymity of the interviewees. Within the sample there was a range of field experience from two to over 30 years of research. The sample covered five nationalities thus showing the international nature of FGT within the UK. There were two distinct backgrounds with the interviewee either having a predominantly clinical experience (nine interviewees) or a predominantly basic science experience (four interviewees). Four of the interviewees were currently conducting their PhD's. However, only one interviewee followed the 'typical' PhD route, which followed directly after undergraduate work. The three other PhD interviewees had embarked upon specialised training before conducting PhD research. Therefore, years of experience rather than educational status was drawn upon to distinguish the interviewees. The interviewees were a pleasure to interview and once the data was obtained, the interviews were transcribed and analysed thematically.

3.3 Robustness of the data: documentary data

Before assessing the documentary data, the types of documents that were used in the thesis must be identified. A document within the context of the thesis refers to legislation, both primary and secondary; International Conventions and Declarations; regulatory reports and case law from the Jurisdictions of the European Union (EU), ECtHR and England and Wales. These documents were needed because the UK is located within a web of international institutions, which can directly influence regulation (such as through EU regulations) and indirectly through position statements (such as through the UN). In addition, given the globalised nature of FGT, these institutions have provided international guidance upon the area of biotechnologies which cannot be ignored.

In order to gather the appropriate documents from the sources mentioned and once the literature review was completed, a list of appropriate documents was made. It was initially made by referring to key words within Halsbury law. Then through using the key word search, narrowing down to a specific point such as 'Conduct of Clinical Trials: Good clinical practice and protection of clinical trial subjects.' Within that section a list of appropriate legislation could be ascertained. Appropriate

textbooks such as Grubb (2010) and Jackson (2009) were also used to ascertain relevant case law. Consequently, the list grew to over 200 documents. However, within that list, annotations were made in order to justify the inclusion or exclusion of those documents within the list. For example, Directive 98/32/EC was not included because it deals with issues regarding the selling of medicinal products to the public, which was not the concern of the thesis. In doing so, the documents listed could be initially analysed to ascertain their relevance to the research questions. As a consequence of looking at the relevance of certain cases, the formulation of the final list used within the thesis also grew in a biological way, because of the way that cases refer to other cases, which may be relevant or have precedence over the case being tried. Therefore, some documents did not appear within the initial document list, but were included within the final list of documents, which can be seen in Appendix F - List of Analysed Documents. The use of search engines such as Westlaw helped discover cases that the literature had not uncovered due to apparent insignificance. For example, the case of *Peters v University Hospital of Wales NHS Trust*[52] is just as important as *Burton v Islington Health Authority*[53] and *Mackay v Essex Area Health Authority*.[54] The *Peters* case was found through the case finder tool within Westlaw due to being specifically related to the Congenital Disabilities (Civil Liability) Act 1976. Having a flexible basis for the document source before and during the analysis, meant that a more encompassing and focused sample could be created, thus resulting in a more valid and representative document sample.

Having acquired the documents in question, Scott (1990) proposes the use of four criteria with which to assess the quality of a document that is being researched:

1. Authenticity. Is the evidence genuine and of unquestionable origin?
2. Credibility. Is the evidence free from error and distortion?
3. Representativeness. Is the evidence typical of its kind and, if not, is the extent of its untypicality known?
4. Meaning. Is the evidence clear and comprehensible (Scott 1990: 6)?

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[52] *Peters (a child suing by his Mother and Litigation Friend Alyson Peters) v University Hospital of Wales NHS Trust* [2002] WL 31257309.
[53] *Burton v Islington Health Authority* [1993] Q.B 204.
[54] *Mackay v Essex Area Health Authority* [1982] 1 Q.B 1166.

The documents used within the thesis would fit into what Scott terms as 'official state documents'. Representativeness relates to the sample of the documents and is dealt with above. In using documents as a source of data one has to accept that there is an implicit assumption that institutions publish texts that are in some way either true or false, or that each document itself represents a reality of its own (Silverman 2006). Such a question relates to Scott's questions about authenticity and credibility.

When using documents as a source of data there is the underlying assumption that documents, such a legal judgements, reveal something about an underlying social reality, to the extent that when institutions publish documents they are representational of that institutional reality (Bryman 2008). However, the writer of a document, as well as the reader, is likely to have a particular view (political, academic etc) that they want to convey; thus, bringing the question of authenticity and credibility into question. Authorship of official documents is often a common criticism of official documentation. Sources of documents often lack an implied authorship, which tries to create an independent reality outside of the individual reader or observer (Coffey and Atkinson 2004). For example, when reading EMA guidance scientific certainty appeared prevalent until questions were asked regarding safety and long term follow-up. Therefore one must accept that despite the impression of objectivity that some documents may state issues such as political motivation or scientific certainty must be taken into consideration (Scott 1990).

Generally, utilising documents as a source of data can lead to unobtrusive measures in which neither the sender or receiver is aware that the document is being analysed (Weber 2006). Such a general statement in relation to legalistic or regulatory documents is not explicitly true as documents from legislative sources are expected to be scrutinised by those involved in some way, such as barristers, solicitors, business and the general public. Despite the claim that documents should be available for analysis by social science researchers (Bryman 2008), and not just for personal reflection:

> One must be quite clear about what they [documents] can and cannot be used for. Documents are 'social facts' in that they are produced, shared and used in socially organised ways. They are not, however, transparent representations of organizational routines, decision-

> making process or professional diagnosis. They construct particular guides of representations using their own constructions (Coffey and Atkinson 2004: 58).

Therefore, no matter how 'official' a document is it cannot be taken to be firm evidence of what they report (Coffey and Atkinson 2004). The 'facts' in legal judgment is a classic example of this as 'the facts' within a case are what the judge deems has occurred based on the rules of evidence. Case law also has the added inadequacy of only presenting cases in conflict. For example if in Vo v France[55] Mrs Vo had decided not to pursue her case to the ECtHR that does not mean her 'case' did not occur, merely that it did not need judicial intervention to resolve. Therefore, the 'facts' of any case must still be contextualised more widely.

Despite documents being 'social facts', in that they are produced shared and used in socially organised ways; they are not transparent representations of decision making processes or of professional diagnosis (Coffey and Atkinson 2004: 58). However, a documentary reality is fundamental to the practice of governing, managing and administrating forms of society, such that business, government, professions and agencies, (such as GTAC), use documents as a form of action (Dorothy 1974). Therefore, regardless of whether a document truly reflects the facts or practice of an organisation one can say it is authentic and credible in its representation of a social practice or reality.

Through reading documents a researcher can ascertain answers to their research question. They can also gain an understanding about how medical practice should be regulated. In fact, legal cases act as the link between the regulatory authorities interpretation of legislation; because, no matter how clarified and crystallised legislation is, the implied readership of any document brings their own cultural knowledge and unique biography to the text which needs adjudication (Coffey and Atkinson 2004). Therefore, the meaning of a document through language and text is important. However, case law provides clarification to the majority of abstract concepts within regulation, which is built upon rules of interpretation within legal

[55] *Vo v France* (Application no. 53924/00).

systems. For example, where an ambiguous term such as 'reasonableness' is used the judiciary have three rules, which they can use to establish what Parliament meant by the term. These rules are the literal,[56] golden[57] and mischief rules.[58] The choice of which rule to use is subject to each judge's own interpretation, but ultimately if the result is one Parliament did not intend then Parliament can provide further guidance upon the area. Therefore, unless legislation or further guidance has been enacted, one can assume that the judicial interpretations of the legal elements of a case are valid.

When using documents as a source of data, one has to be aware of 'genre mixing' (Fairclough 2003). For the present purpose this means that documents can be used to transcend more than one specific topic or point, by linking other specific points together within the same document. Within the multidisciplinary thesis there are elements of ethics, medicine, sociology, law and politics. A classic example of this is the case *Re MB*.[59] It is a leading case about consent to medical treatment, but it is also about the rights of a pregnant woman and a fetus within England and Wales. It also analyses the various implications for the interpretation of the European Convention on Human Rights 1950 (ECHR) within medical treatment. Some documents may be difficult to read as each document anticipates which genre it may be read in (Fairclough 2003). For example, science and legislation mix within specific gene therapy protocols such as Directive 2001/18/EC as the draftspersons anticipated who would read the regulations. Thus technocratic language specifically aimed at scientists was prominent, thus making it difficult for a non-scientist to understand. This is not to say that documentary data should not have been used here, since it provided useful and potentially valuable resource for the thesis, but recognising potential genre mixing should be acknowledged as a potential issue,

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[56] Where a judge may read the words within the act as their literal meaning within the context of the act and give them that one meaning, regardless of the result (Martin 2001).
[57] Where the literal rule gives an absurd result, ordinary words must be given their ordinary meaning and technical words must be given their technical meanings; unless an absurdity would result from the application of the rule (Martin 2001).
[58] Where a later Act has been implemented with the objective of resolving a previously defection in law, and there is an ambiguity in the apparent application of the Act, the mischief rule can seek to address the defect or mischief for which the Act was passed to remedy (Martin 2001).
[59] *Re MB (Caesarean Section)* [1997] 2 FLR 426.

especially within cutting edge areas of science which potentially transcend fixed barriers.

3.4 Robustness of the data: interview data

Inevitably when using a data collection method such as interviewing, the credibility of such data is called into question. These questions include:

a) 'How do we know the informant is telling the truth', and are the truths we are interested in stable across situations and perspectives?
b) The 'incompleteness' of interview data as compared with the data that could be gained from participant observation.
c) The difference between what people say and what they actually do (Hammersley 2005: 1).

Given that Social Science frequently uses interviews as a means of data collection, 'truthfulness' could be seen as a major problem (Atkinson, Coffey et al. 2003). Finding the 'truth' behind interview data is problematic because one must accept the transmission of epistemic properties thesis (Lackey 2008),[60], which highlights the problem of subscribing meaning to words and beliefs in transmitting their position to the listener (Lackey 2006). This can be affected by: the current emotional state of the informant; the informant's hypothetical reaction to questions posed; the actual tendencies of the participant within the given situation (Dean and Whyte 2003: 351). Therefore, cross questioning the interviewee, combined with other interview data will make this concept consistent throughout, thereby eliminating it as a substantial problem. In accepting that one can transmit their epistemic position and properties in speech to another listener or reader, then the information acquired is valid (Lackey 2006).

Within verbal interviewee responses there can be distortion of expression and use of language (Audi 2006). In order to overcome this issue accepting each interview as a form of evidence or account creates a reliable form of interview data. The problem of distortion can be avoided by using dictionaries, both linguistic and technical (in terms of medicine and genetics) as well as giving clarification of issues within the

[60] That it is necessary for a speaker A to have knowledge of p so they can transmit p via testimony to a hearer B, or as Lackey describes: In order to give another person a full bucket of water, I must have a full bucket of water to hand over, which also applies to knowledge (Lackey 2008: 47).

interview. Triangulation methods such as cross examination through questions focused on the same variable, or in other instances concerning FGT, can increase confidence in, and validity of, the interview data (Denzin 1989).

In seeking to understand the veracity of these interviews the 'truth value' of a qualitative study should be evaluated by its credibility rather than by internal validity as measured within quantitative/scientific research methods (Appleton 1995). Therefore, the question is: how plausible or credible is the interviewee's opinion (Atkinson, Coffey et al. 2003)? In assessing the truth or credibility of interviews one must consider the factors that can be expected to influence the interviewee's reporting of any given situation under the interview circumstances (Dean and Whyte 2003: 352). Such factors include: the motives behind the participant's responses; the lack of spontaneity and reduction of the participants' freely expressed opinions; the desire to please the interviewer with their answers; and idiosyncratic factors which may result in only certain facets of the respondents' feelings being expressed (Dean and Whyte 2003: 352-353). However, of more concern is the use of institutionally constructed answers (DeVault and McCoy 2002: 767). Therefore, recognising quoted standard policy as an answer, which may not be their own opinion or typical of their working practices, is of fundamental importance.

Within interviews, the reactivity and neutrality of interviewers is an issue because the interviewer is an integral part of the process (Marshall 1996). Different researchers will have different influence over the interviewee (Arksey and Knight 1999). Nonetheless, the interviewer is an integral part of the process (Marshall 1996); therefore, interview data has been criticised because non verbal communication and explanation can result in bias (McCormack and Hill 1997). However, being an active interviewer can elicit better interview data than a neutral or passive interviewer. Therefore, recognising that as an interviewer you are a participant, dominating the interview with one's own views and preconceived ideas about the views of the participant can be avoided (Rubin and Rubin 2005: 19). In recognising the role of the interviewer in this way, meant that leading questions could be avoided; thereby, resulting in data that is a closer reflection of the participant's views:

> The interview, unlike most other techniques, requires interpersonal skills of a high order (putting the respondent at ease, asking questions in an interested manner, noting down the responses without upsetting the conversational flow, giving support without introducing bias); at the same time the interviewer is either limited or helped by his or her own sex, apparent age and background, skin colour, accent etc (Oppenheim 1992: 65).

Therefore, to increase the validity of the interview data, rapport, trust and openness between the interviewer and interviewee was built (Arksey and Knight 1999). In doing this within this study, the participants had the freedom to express the way that they saw the influence of intergenerational aspects within FGT

In recognising that there is a difference between what people say and what they do, it must be conceded that there could be missing data from interview data. It is argued that within a scientific setting, one can only acquire the tacit knowledge of a practice through participant observation (See Collins and Evans 2007). However, the interviewee's account is treated as constitutive; therefore, 'reality' is constructed in the telling of the account and is not independent of it (Hammersley 2005). Therefore, one can treat each interview as having their own validity subject to the investigation of any factual claims, thus providing consistency between interviews. Critically, as stated above, FGT is not at a stage where one can observe a patient in a clinic in terms of in utero therapies. Therefore, any complementary ethnographic work could be considered post thesis.

As identified in 3.2 13 interviews were conducted. This appears to be a small number of interviews. However, FGT is an emergent field which has few groups in the world devoting their primary research time to FGT. Therefore, the world population size is below 500 interviewees. Across Europe there are four research groups devoting their time to FGT. Therefore, despite the initial 13 interviewees appearing to be an insufficient size, it emerges as a high percentage amount of not only FGT practitioners in the world, but an even higher percentage of those who are frontier FGT practitioners. In addition, all 13 interviewees are part of the FGT potential first world clinical application that will occur in the near future, thus making these interviewees part of a small and elite population group with significant professional weight within FGT.

Once the 13 interviews were conducted the data was transcribed. In order to get closer to the interview data the interviews were transcribed by the author of this thesis. The interviews were transcribed verbatim, or as close as possible. For example, within one interview outside building work made some comments inaudible, therefore could not be transcribed. Typically due to the interviewees' working constraints the interviews aimed to be no more than an hour long. Yet, due to both interviewer and interviewee getting engrossed within the discussion the interviews were on average 65-70 minutes long.

There are also difficulties in representing speech as text, because there are an endless number of decisions that must be made. Although these decisions appear mundane, they have serious implications for how we might understand discourse and frame reality (Tilley 2003: 758). Decisions over what is coded, categorised and used, influence what 'story' is portrayed to the reader (Silverman 2004: 127). This is affected by the large number of intuitive analytical decisions made (Gorum 2004). Therefore, consistency is pertinent, not just within data collection but through the whole research process (Rubin and Rubin 2005). Therefore, transcription quality was an issue to ensure that the data was the verbatim accounts of what transpired (Poland 2001). In order to achieve the verbatim account, after the interviews were transcribed the interviewees were given several options in terms of how they were represented within the thesis. As a result, a more clarified account is gained with issues regarding misrepresentation of the data being avoided.

Qualitative interviewing with purposive sampling, invokes issues of generalisation and representation. Within the context of FGT, representation is not necessarily a major problem within the UK because of the small community of FGT practitioners. Generalisation and representation could become a more pertinent issue with regards to the international aspects of FGT. However, given the small number of international groups working specifically upon FGT, as well as the collaboration of the research groups interviewed with other FGT groups makes generalisation less problematic. However, generalisation is problematic due to the small, specific nature of the project within the larger context of science and technology, especially

with regards to qualitative research (Payne and Williams 2005). This is an accepted limitation of the project. However, given the small and close nature of FGT, one can ascertain practices which are relevant to all FGT practitioners by situating the findings within the wider context of research such as gene therapy (Perakyla 2004). Therefore, the extent to which the findings from the thesis are relevant to settings other than the one from which they are derived, the transferability of the research is increased (Jones and Sumner 2007).

Having identified the strengths and weaknesses of the data collection methods several other methodological issues must be addressed. These include issues of access, ethics and analysis. The chapter will now address these issues in order and then be concluded.

3.5 Access issues

There were no problems in acquiring documents for this study as they were readily available through resources such as Westlaw, Lexis Nexus, the government online legislative site called opsi.gov and other regulatory bodies. Given the use of CAQDAS (see below), the only relevant access issue relates to electronic access to documents that are not available to the public in that form. However, in such circumstances paper copies of the documents were available through either interlibrary loans or through contact with the appropriate authority. Those documents were then scanned into the programme, thus solving the issue.

Having used purposive sampling to identify possible research participants an immediate and very serious problem occurred. Due to the narrow definition of FGT the potential interviewee sample was a select few, not just in the UK, but within Europe. The consequence of such an exclusive and elite 'club' presented a potential major issue over access. When the potential pool of interviewees is so small, getting the initial approach wrong could result in being locked out and potentially blacklisted. Therefore, the possibility of acquiring no interview data at all was a relevant consideration.

Other associated issues that could have potentially limited access to the interview sample were that: elites may often be unwilling to give up time, if they consider that that time can be spent more productively on 'proper' non trivial projects (Zukerman 2003); and, medical researchers having their own intricate networks, which are often obstructive, unless accessed through a gate keeper of some sort (Odendahl and Shaw 2002).

Access to the intended interviewees was not as problematic as initially feared. Due to the readily available information, gathering contact details was easy and freely available. There was a high return rate and general willingness to be involved in such a project. That enthusiasm translated into the interviews and helped the collection of truly interesting and intriguing data. The arrangement of the interviews was also not as problematic as expected. Due to the status of the interviewees flexibility was needed on the interviewer's part to ensure that the interviews could be arranged. Nevertheless, the interviewees were all accommodating in trying to make the best arrangements for all parties involved.

Interviewing elite scientists in any field requires 'studying up' on knowledge about the field, which social scientists have been accused of not adequately taking into account (Ostrander 2003). A major part of the 'studying up' was done through the fundamental understanding of developmental biology, inheritance, and review of the Clinics in Perinatology especially on FGT as demonstrated in the literature review of the thesis. The preparation was useful especially given the specific scientific language used within the interviews as well as references to particular incidents that have affected the discipline. This helped build rapport and lead to further interesting conversations.

3.6 Ethical issues

The basic ethical principle governing data collection is that no harm should come to the respondents as a result of their participation in the research (Oppenheim 1992). Therefore, when conducting qualitative interviews several key areas of research ethics should be adhered to: informed consent, confidentiality, anonymity and data storage.

When conducting the interviews, the interviewees were provided with a participation information sheet about the thesis (See Appendix A – Participant Information and Consent Form); therefore, making it possible to obtain informed consent of the participants and safeguard their privacy and welfare (Arksey and Knight 1999). The participant information sheet covered: the aim and purpose of the research, identified the interviewer, contact details, topics the interview will cover, their rights, safeguards to confidentiality and anonymity, and the right to withdrawal at any time and dissemination of information (Arksey and Knight 1999). Given the problems of transcribing interview data, in order not to misrepresent the participant's views, they were given the right to check the transcribed interview.

Informed consent within the thesis was not particularly problematic because of the interview sample. Therefore, the key ethical concern when utilising a qualitative interview technique is adhering to the principles of confidentiality and anonymity. The two concepts are often spoken of together but are in fact two separate concepts. Within the thesis anonymity refers to the process of not disclosing the identity of an interviewee in relation to a particular view or opinion; whereas confidentiality is the process of not disclosing to other parties opinions or information gathered in the interview process (Clark 2006). With regards to confidentiality the British Sociological Association states:

> Personal information concerning research participants should be kept confidential. In some cases it may be necessary to decide whether it is proper or appropriate even to record certain kinds of sensitive information (British Sociological Association 2002).

Therefore appropriate precautions were taken due to the small sample population to avoid the chance that individuals could be easily identifiable by using sensitive data as this could have lead to 'reluctant' interviewees (Alder and Alder 2002). This emanates from the idea that the interviewee may sustain professional loss as a result of revealing possibly unprofessional or non-compliant research practices if these become public knowledge. Therefore, protecting the identity of the interviewee is a high priority (Lee-Treweek and Linkogle 2000), and links to the concept of anonymity. Because of the small sample anonymity plays an important role in assuring that the interviewees will not suffer loss. In order to achieve as much

confidentiality as possible blanket anonymity was used. Therefore, specific data relating to location, research area and location of the research group was made anonymous. Because of the unique nature of the thesis the research location was also made anonymous in order to fully protect the interviewees' identity. As mentioned above, this was due to the possibility of identifying the interview participants, but also due to confidentiality. There are ethical issues with data storage within a digital age and the personal information concerning research that must be kept confidential. The British Sociological association states:

> Appropriate measures should be taken to store research data in a secure manner. Members should have regard to their obligations under the Data Protection Acts [...]. In some cases it may be necessary to decide whether it is proper or appropriate even to record certain kinds of sensitive information (British Sociological Association 2002).

To ensure that all personal information as well as the interview data itself, will be kept secure, the data will be kept on data encrypted hard drive for five years subject to the Data Protection Act 1998, University regulations and the British Sociology Association guidance on ethics.

The ethics of documentary analysis is rather more straightforward. In general, the ethics of utilising documents within research is not accompanied with an in depth ethical review, especially in relation to policy documents which have be vetted and checked, and unlike using electronic blogs (Sixsmith and Murray 2001). However, anonymity of legal cases as well as misrepresentation of documents should be considered.

When collecting together relevant legal cases the reporting of such cases are subject to judicial proceedings and institutional vetting. Within judicial proceedings, Article 6(1) of the ECHR[61] means that openness is a fundamental issue within judicial proceedings (Mlola 2008). However, all cases must be balanced within the context of Article 8 of the ECHR and thus medical information and the identity of the patient

[61] The right to a fair trial which is incorporated into domestic law through the Human Rights Act 1998.

is considered as being an uncontroversial topic (Mlola 2008).[62] Therefore, where parties have been stated as a synonym or letter, anonymity has already been executed within the case itself. However, that does not mean that sensitive information of minors or none competent patients is not made public, but provisions for the protection of vulnerable individuals has to be taken into account and weighed up against the public interest.[63]

Another valid consideration is how ethical is it to construe documents or interview data when it may not be possible to have all necessary information. Misrepresentations can occur when the researcher does not have available the totality of communications or documents (Sixsmith and Murray 2001). However, given that the documents utilised here were all publically available without any redactions, misrepresentation should not occur in this thesis if the quotations used are not presented to exclude the important context and message that document is trying to portray. As with interview data, constructive misrepresentation of opinions is unethical and should be avoided.

3.7 Analytical framework

For the interview data a thematic approach was taken. The thematic framework of analysis followed the mechanics of analysis that are similar in all thematic analysis:

- Decide on a theme.
- Decide what counts as evidence of a theme.
- Code a passage to indicate that the passage is an example of that theme.
- Relate what types of people said which themes and relate to other interview data (Gorum 2004: 189-190).

The approach taken to the analysis is comparable to that taken by Cribb et al (2008), with the data being collected before applying the above thematic approach. Grounded theory is often associated with the analysis of qualitative interviews and the practice of grounded theory is implicit within a thematic approach. However, a thematic approach does not commit or contract the analyser to produce a deductive theory from the data. The analysis is complemented by the semi structured

[62] See *Z v Finland* (1997) 25 EHRR 371; *W v Edgell* [1990] Ch 359.
[63] See *Campbell v MGN Ltd* [2004] UKHL 22.

interviewing. The themes that were chosen related to the literature review that was conducted prior to the interviews, with sub themes being used to obtain a more comprehensive analysis of the data (Aronson 1994). Therefore, in order not to stifle the emergence of themes a holistic approach was also used in conjunction with literature related themes.

Documents are normally viewed as little more than containers of 'content', that are sources of information, whether that be textual, imagery, or another document (Prior 2003, 2009). It should be noted that when conducting a literature review, as well as specific research into documents from legal institutions content analysis is conducted. However, it is not conducted in the typically structured social science manner. According to Hall and Wright (2008) empirical legal methods, such as case law rhetoric, are standard applications of social science methods. Hall and Wright advocate a quantitative content analysis of legal sources, which would systematically select, code and quantitatively analyse documents. However, such an approach in the given circumstances would focus upon a pseudo measurement, which would fail to appreciate the value or subtleties of case law and regulation (Mendelson 1963). Law is practice built upon interpreting language, which is not a precise practice; therefore, using a tool that seeks to be precise and certain appears to be flawed.

A particular problem with using content analysis with legal documents is that there is an assumed equality between the documents (Hall and Wright 2008). Such equality does not exist between cases, legislation and regulatory guidelines. Such documents are not only subject to their institutional hierarchical chain, but interact with each other at a national level. One must also situate a case within England and Wales, relative to the jurisdictions of Scotland and Northern Ireland, which can be heavily persuasive; but, also within a context of the EU, Council of Europe and worldwide institutions. These hierarchies appear linear (see Appendix C – Institutional Structure), but issues surrounding precedent and the binding of previous judgements (See Appendix D – UK Court Structure) indicates that cases conducted within the same court may result in different changes in the law. Therefore, content analysis of like cases does not necessarily pertain to strong conclusions. The creation of a 'kick

back to Parliament' clause within the HRA 1998[64] further complicates the interplay between the documents.

However, utilising elements of a quantitative content approach adds to the analysis and evaluative outcome of the thesis, as tools such as word frequency and key word frequency result in favour of who can provide useful information. For example, human dignity appears as a key component within the thesis, yet in the sample cases within England and Wales 'dignity' only appears twice. Concepts that stem from dignity such as autonomy and the right to life appear much more frequently. Therefore it is essential to use a thematic and interpretative approach within the content analysis. Content analysis can also utilise a more qualitative approach. Qualitative content analysis comprises of searching for underlying themes within the documents in a more interpretative manner than its quantitative sibling (Bryman 2008). Therefore, content analysis within the thesis refers not just to quantitative content analysis, but also qualitative content analysis because of the nature of the documents that have been selected. By utilising a qualitative content analysis approach, akin to the thematic approach taken within the interview data; the ability to compare and contrast between the documentary and interview data became easier because the data results were directly comparable.

From this method a series of dominant themes arose from the data. They included human dignity, intergenerational interests, autonomy, safety, foreseeability, funding, and uncertainty. However, within the interview and documentary data the emergent themes were centred on two distinct themes: human dignity and scientific progress. Therefore, each data set was divided into those two categories. Within each category, each theme was elaborated upon and referred back to the maternal fetal divide to analyse the consequences for future regulation. That process was conducted in a similar manner for both documentary and interview data thus making comparison of the data sources easier (chapters 6-9).

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[64] A declaration of incompatibility through the Human Rights Act 1998 s.4(1). For further debate over whether or not judges make law or if the separation of powers truly exists see cases such as *CR v United Kingdom*; *SW v United Kingdom* [1996] 1 FLR 434, *R v Rimmington; R v Gondstein* [2005] UKHL 63 and Benthams 'dog law'.

The analysis was conducted with the help of the Computer Assisted Qualitative Data Analysis Software (CAQDAS) program Nvivo. Within the Nvivo programme the data was coded according to theme and sub themes according to the system explained above. The key to utilising any CAQDAS program is to understand that CAQDAS programmes provide useful and helpful tools for storing and organising work. They also provide useful insights into the data gathered, but only as far as the user of that CAQDAS programme has inputted the information themselves. In other words, merely using a CAQDAS program is not analysis (Coffey, Holbrook et al. 1996). Nvivo, like any other CAQDAS program, has its own strength and weakness that should be taken into account (Barry 1998). Nevertheless, because the data was analysed thematically, utilising a CAQDAS programme made the process, comparison and analysis of the data with a code and retrieval system easier to retrieve data in relation to themes as well as looking at occurrence of a theme in relation to several key indicators such as position, qualification and gender. However, due to confidentiality issues (outlined above) unfortunately the extent to which those results could be used was limited.

3.8 Conclusion

To conclude, the methods used within the thesis were documentary analysis and semi structured interviews. Each data source has its strengths and weaknesses, but together the data results will be stronger and more reliable than had only one data source been used. There will always be issues about the use of each data source. For example, documents will always go out of date as quickly as they are printed, thus the 'reality' they paint is in constant change; and, there will always be the issues with interview data regarding truth and whether one can transfer information about what they do through words. There were ultimately few if any ethical or access issues concerning the thesis. The thematic approach provided a useful tool to apply to both sources and also provided a flexible mode of analysis that ensured consistency between the two data sources. By conducting the document analysis before the interviews it helped inform the areas for discussion, as well as providing a sound platform which was used to either confirm or rebut the picture gained from the

documents. The use of the CAQDAS programmes proved to be an excellent tool for comparing the two data sources.

Having collect the data and analysed it, the next step was to organise the results and report on them. The following six chapters are the result of the multidisciplinary approach adopted to analyse how the scientific progress of FGT interplays with rights, duties and regulation. Chapters 4 and 5 provide the focusing of the thesis and provide useful data for chapters 6 to 9. Chapters 6 to 9 form the social scientific engagement with the field. It was decided that because of the symmetry between the data sources as well as the distinct divide between the data relating predominately to human dignity or the research procedure; that the results should portray those similarities and distinctions. Therefore, each data source, documentary (regulation) and the interview data, has two chapters: one relating to human dignity; and the other relating to scientific progress. Because the documentary analysis was conducted first the comparisons are drawn within the reporting of the interview data.

Data Chapters:
4 The Maternal Fetal Divide?
4.1 Introduction

Having seen that FGT is a recent development, new and interesting debates have been raised in accordance with its advances. For example, within FGT there is often debate surrounding who is the patient and what interests are being considered? Is there a conflict of interests where a mother refuses fetal beneficial treatment? In trying to establish answers to such questions the maternal fetal divide is important. The legal and medical institutions that are examined within this chapter may have different approaches to the maternal fetal divide but they both draw guidance from the principle of autonomy. The different approaches to the maternal fetal divide emphasize different aspects of the possible divide and different ways of resolving conflicts. A comparison between the development of the legal and medical constructions also indicates areas where medical development impacts upon legal institutions. Importantly for the thesis it identifies current medical and legal perspectives of the fetus which can be used to ascertain how rapidly progress can impact upon regulation (chapters 6 and 7) and practice (chapters 8 and 9).

As stated in 1.2.1 FGT could be a misleading concept as it fails to highlight the mother within the procedure (Wu and Ball 2009). However, within medicine, law and sociology the role of the mother is a key component when discussing the fetus. Identifying the maternal fetal divide is important as it frames the ethical and social debates and, as will be shown, it is not only the possible moral, theoretical or philosophical divides that are important, but also the physical divides.

In analysing the maternal fetal divide, several key perspectives emerge. These perspectives include: medical, philosophical, legal and ethical positions.[65] Within these different perspectives the maternal fetal divide is based upon the moral status of the fetus. However, even where the fetus has no legal or moral status, other operating duties may infer that the fetus has interests; thereby creating a conflict

[65] It should be noted that there are religious constructions of the maternal fetal divide. However, the thesis will focus upon the four perspectives mentioned.

between the mother and fetus. The main focus of this chapter will be upon the evolution of the maternal fetal divide within the institutions of law and medicine. The philosophical debate will be conducted in chapter 5, where Gewirth's Principle of Generic Consistency, will be introduced as the ethical framework of analysis.

It should be noted that within this chapter the maternal fetal divide encompasses more than just what medicine tells us about pregnancy as it includes the rights and interests of the fetus according to those other than the mother. In other words, the divide is facilitated by the medical practitioners, courts and other interested parties that claim there is a divide, or conflict, to be resolved. In highlighting interests, defining interest becomes important. As discussed within1.2.2, an agent has an interest when another being has a duty towards them.

The first section (4.2) will situate the maternal fetal divide within the context of medical decision making within England and Wales, which means identifying autonomy. It will not analyse whether or not the concept of autonomy is justified or correct but it will identify the key components of the concept. Section 4.3 will investigate the medical perspective of the maternal fetal divide. It will highlight birth (4.3.1), biological factors (4.3.2) and introduce the 'fetus as a patient' concept (4.3.3) as formed by Chervenak et al (Chervenak and McCullough 2003, 2011, Chervenak, McCullough et al. 1994). Once the fetus as a patient has been discussed, the final section 4.4 will discuss the legal perspective of the maternal fetal divide. It will discuss the debate surrounding abortion (4.4.1) and refusal of medical treatment (4.4.2) focusing upon the leading case of *Re MB* (4.4.3)[66] and human rights (4.4.4) and show how those areas inform the maternal fetal divide.

4.2 Autonomy of the patient

Within the 20th century, the right of a competent patient to make their own decisions about their medical treatment has arisen as a fundamental concept so that it needs little explanation about it underpinning a patient's interest in self determination and

[66] *Re MB (Caesarean Section)* [1997] 2 FLR 426.

bodily integrity (Scott 2002).[67] This principle is better known as patient autonomy. This principle is in stark contrast to paternalism where a decision about a person's medical treatment is not made by the patient but by another competent authority, such as a doctor. That is not to say that paternalism is not an issue within the decision making process of a patient. However, medical ethics has migrated away from the paternalistic 'doctor knows best', to that of individual autonomy, thus placing more pressure upon the fiduciary duty[68] of doctors (Jackson 2006). Now, doctors should use their expertise to advise patients about the relevant choices available to them, letting the patient decide on the course of action to take (Brooks and Sullivan 2002).

Within medicine treatment of a competent patient cannot occur unless they have given consent to the proposed treatment, thereby respecting their autonomy and bodily integrity (Jackson 2006). The decisions taken by that person should be respected, even if it conflicts with medical advice or results in their own death.[69] In terms of refusing treatment, the law and codes of ethical practice emphasize that adults with mental capacity can refuse medical treatment (BMA Ethics 2009).[70] Without their consent the medical intervention will be illegal and the physician in question will be liable for trespass to the person and maybe guilty of criminal charges.[71] The right of a patient to make their own decisions is now directly protected by various articles within the Human Rights Act 1998 (HRA), such as the right to life (Article 2) and the right to a private and family life (Article 8) (Mason, McCall Smith et al. 2006).[72]

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[67] The philosophical debate surrounding the remit of 'autonomy' will not be dealt with here as it forms part of agency within the ethical framework of analysis proposed by Alan Gewirth's Principle of Generic Consistency (PGC) within 5.5.

[68] A person, such as a trustee or doctor, who holds a position of trust or confidence with respect to someone else and who is therefore obliged to act solely in their interest (Martin 2001).

[69] See *Re T (Adult: Refusal of Treatment)* [1993] Fam 95.

[70] Mental Capacity Act 2005.

[71] As identified by Lord Donaldson MR in *Re R (Wardship) (A Minor) (Consent to treatment)* [1992] Fam 11. The case concerned a local health authority wishing to treat a mentally ill 15year old girl without her consent. It was held that the doctors could proceed without her consent if they received consent from someone with parental responsibility.

[72] For full list of rights see Human Rights Act 1998 Sch 1.

The right to make one's own decisions is dependent on having capacity to do so. Any adult[73] that presents themselves within a medical situation is presumed to have capacity and this is thoroughly ingrained within law[74] and medical practice (See British Medical Association 2009, General Medical Council 2009b).[75] However, a person is deemed to lack capacity if they are unable to: understand the information; retain the information; use or weigh the information as part of a decision; communicate that decision.[76] Those under the age of 16 are automatically presumed to lack capacity.[77] However, under certain conditions, those under the age of 16 will be able to consent to treatment by being 'Gillick' competent.[78] For those under 16 years old, the right to refuse medical treatment can be overturned by a Court of Protection Order.[79] If a person is deemed incompetent, then medical treatment can be conducted without the consent of that person if it is deemed in the best interests of that patient[80] and considered the least restrictive alternative.[81] The best interests of a patient includes taking into account the beliefs of the person in question, the person's past and present wishes and other factors.[82]

Within medical situations, 'patient autonomy' is often referred to and therefore the term 'patient' is also a concept that will show a divide and possible conflict within decisions made during pregnancy. The term 'patient' is often synonymous with

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[73] A person who reaches the age of 18 is considered to be at the age of majority (or adulthood in layman terms); but, those aged 16 and 17, also have the right to consent to treatment under the Family Law Reform Act 1969 s.8(1).

[74] *Re MB (Caesarean Section)* [1997] 2 FLR 426, *Re R (A Minor) (Wardship: Consent to treatment)* [1992] Fam 11, *Re T (Adult: Refusal of Treatment)* [1993] Fam 95 and the Mental Capacity Act 2005 s.1.

[75] Outside of medical situations consent and autonomy have a more restricted remit and cannot act as a defence to actual or grievous bodily harm. See *R v Brown* [1994] 2 WLR 556 where it was held that a person could not consent to sado-masochistic practices.

[76] Mental Capacity Act 2005 s.3(1)(a)-(d). Section 3(1)(a)-(c) codified the test for capacity that is used within the common law and was established within *Re C (Adult: Refusal of Medical treatment)* [1994] 1WLR 290. Also, these provision do not apply to those under the age of 16 (Mental Capacity Act 2005 s.2(5)).

[77] Family Law Reform Act 1969 s.8.

[78] A child is deemed Gillick competent, where the child achieves a significant understanding and intelligence to enable them to fully understand what is proposed. See *Gillick v West Norfolk and Westbech Area Health Authority* [1986] 1 AC 112.

[79] *Re R (Wardship) (A Minor) (Consent to treatment)* [1992] Fam 11, *Re W (A Minor) (Wardship: Consent to treatment)* [1993] Fam 64, Mental Capacity Act 2005 s.16.

[80] Mental Capacity Act 2005 s.1(5).

[81] Mental Capacity Act 2005 s.1(6).

[82] See Mental Capacity Act 2005 s.4.

being ill (Thomson 1986) but within the thesis it will be used not to infer illness but merely an agent receiving a doctor's service.[83] However, within the context of the FGT, often the mother is not ill; it is the fetus that needs the direct medical intervention; for example, a fetus suffering with a congenital hernia.[84] In not making illness a necessary condition of the term 'patient', it allows for the term 'patient' to be used in relation to the mother, as well as the fetus (as will be shown below).

The terms 'patient' and 'patienthood' also create correlating duties for a physician, of which fiduciary duty and patient autonomy are of key importance (Buchanan 2008). The fiduciary duty inferred by the patient's status becomes important within a medical setting as an 'individual' does not infer personhood, which can be seen when the fetus is treated as a patient. Having given 'patient' a remit, the debate surrounding the maternal fetal divide can be conducted. Pregnant women can use many sources of information or moral guidance to view the maternal fetal divide and religion can help inform how a pregnant mother may view the maternal fetal divide. However, in making an autonomous decision that may be informed by a person's religious orientation, the decision is made within the sphere of medicine. Medicine is both a practice that self regulates, but also one regulated by the law. Therefore, how medicine approaches the maternal fetal divide must be examined firstly from a medical perspective and then from a legal one.

4.3 Medical perspective on the maternal fetal divide

Within medicine the maternal fetal divide can be seen on several different levels which have all contributed to debate on the maternal fetal divide. One can either: view pregnancy chronologically so that birth is the only divide between mother and fetus, or; take a biological view of pregnancy, right down to genetics and the interaction between mother and fetus, or; try and assess the number of patients they are dealing with, which introduces the fetus as a patient concept. Each will be dealt

[83] For a detailed study upon illness and patient roles see Parsons (1951) in *The Social System*.
[84] See previous chapter for explanation of congenital hernia.

with in the corresponding order and will start with what is physically the most obvious divide that occurs between mother and fetus: that of birth.

4.3.1 Birth

The most fundamental divide between mother and fetus is birth, whether that is naturally or through a caesarean section. Conservatives may argue that a fetus and baby are essentially the same, whether inside or outside the womb (Singer 1993). However, there is little debate surrounding the use of birth as the division of a mother and her fetus. Once born, the fetus is considered a child; therefore, morally, socially and legally the maternal fetal conflict becomes that of a child's best interest versus parental autonomy. It is not the contention of this thesis to examine gene therapy upon children, but the area is still connected to the issue of FGT. Nonetheless, one must look further within the institution of medicine to see how the possible maternal fetal divide is treated. Another way of considering if there is a maternal fetal divide is to view pregnancy biologically. If so, it can indicate how emergent medicine could possibly view the maternal fetal divide.

4.3.2 Biological perspective on the maternal fetal divide

From a purely genetic perspective, when a woman is pregnant there are two genetically unique entities occupying one visible body. However, the idea that the fetus acts as a parasite until the right time is not strictly true. Despite immunological reasons why the fetus and mother are two distinctly separate entities, there is interplay between the two entities. The relationship between mother and fetus, which has often been referred to as a parasitic relationship, does not reflect the true relationship between mother and fetus, which is closer to that of parabiosis or symbiosis (Liley 1983). In fact, it has been recorded that changes in maternal emotions can alter the heart rate of a fetus (Liley 1972). Therefore, the relationship is a two way affair within pregnancy. For example, it is acknowledged that the placenta induces many of the hormones, including hCG (human Chorionic Gonadotropin) and HPL (Human Placental Lactogen), that regulate pregnancy (Lunenfeld 2004).

However, despite the perceived separation between the fetus and mother, the advent of genetic technology challenges the view of two distinct separate entities. Genetically, the fetus and mother are different, but fetal DNA can be detected within a pregnant women's blood stream and tested through cell free DNA technologies (Wright and Chitty 2009).[85] However, the DNA is fragmented and therefore limited in use (See Norbury and Norbury 2008).[86] Despite the interaction and evidence of fetal cells within a pregnant woman, the pregnant woman's immune system can still react as if fetal cells were foreign cells and induce a 'graft vs. host' response similar to that within gene therapy. Although not clinically proven, it highlights the immunological response of a mother to her own fetus (See Johnson and Bianchi 2004). In short, the mother's body is placed under extreme demand and does not biologically gain a benefit from the fetus.[87]

The traditional view of the placenta keeping mother and fetus completely separate is not strictly true. A substantial amount of maternal T cells (white blood cells), transcend the placenta into the fetus (Mold, Michaëlsson et al. 2008). The result is that the fetus becomes immunological tolerant to the mother's cells, while also priming the immune system of the fetus before it is born (Reinberg 2008). Therefore, there is interaction between the two genetically separate entities because the fetus is dependent on the mother for nutrition. The fetus cannot live without the mother (until the point of viability, see below), but the mother can live without the fetus.

If a mother wishes to carry the fetus to term, the fetus has a degree of control over inducing labour. Labour is onset by the fetus realising hormones, which inhibits menstruation before labour and also induces birth (see above). In fact, Liley claims that the fetus is actively in charge of pregnancy (Liley 1983) and therefore has its

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[85] For a review of the ethical, legal and social impact of cell free testing technologies see Hall et al (2009).

[86] It should be noted that recently it has been reported that the fetal genome can be obtained through none invasive testing (See Leese 2012).

[87] 'Her' denotes a person of female genetics at birth. Clarification is needed because it is possible to change gender to a male, but still retain female organs such as a uterus and become pregnant through assisted reproductive technologies. The most famous of such cases is Thomas Beattie who has given birth to two children (Tedmanson 2009).

own personality (Liley 1972). It is through representations of the fetus as an individual with agency and biological control over pregnancy that one can find the historical foundations of the maternal fetal conflict (Casper 1998). The fetus biologically and visually through ultrasound technologies presents the FGT practitioner with a dilemma. How does a FGT practitioner approach the two biologically separate entities? How many patients are they treating, especially when the treatment proposed is purely for the benefit of the fetus alone? In trying to answer these types of questions, the fetus as a patient emanated as a viable solution to these questions.

4.3.3 The fetus as a patient

As stated earlier the term patient is flexible and has been used to refer to a fetus that a doctor is treating and has as their primary concern. In order to establish the fetus as a patient, the fetus should be framed as a distinct, separable and separate from the pregnant woman's body in which it resides in (Casper 1998). However, it will be shown that being distinct, separable and separate patients does not mean that there are two independent persons or patients. By introducing the fetus as a patient concept, how it came to be used within medicine and how it is formulated, its effect upon the maternal fetal divide can be discussed. In order to introduce the fetus as a patient concept proposed by McCullough and Chervenak, the concept must be placed within the technological developments that have occurred since the concept resulted from such developments within fetal surgery. The fetus as a patient (or fetal patient) is a concept that has been developed within the last 40 years. Developments in fetal diagnosis and therapy, which have increased fetal outcomes in cases such as congenital diaphragmatic hernia, illustrate how three trends have facilitated the move to the concept of the fetus as a patient within the FGT debate (Harrison 2003). The trends were possible due to: technological developments in imagery such as the real time ultrasound imagery in the 1970's, which could diagnose in utero congenital anomalies (Han and Hwang 2001) in two, three and now four dimensions (real time

three dimension) (Churchill 2006); and the development of less invasive techniques such as fetendo (The Fetal Treatment Center 2009).[88]

The first trend was the movement of fetal surgery towards physiological manipulation instead of anatomical repair (Jancelewicz and Harrison 2009). The second trend was a result of technological developments into less invasive surgical techniques whereby fetal surgery could move from open fetal surgery, which impacted heavily upon the mother and her pregnant status (Harrison 2003). This meant that fetal surgery could be used for fetal benefit with minimal maternal harm. And finally, the establishment of fetal interventions as clinical trials rather than just a practice manifested through clinical descriptions and/or retrospective analysis (Jancelewicz and Harrison 2009).

To reflect these medical changes the 'fetus as a patient' concept was developed by fetal therapists to alert themselves, and patients, to the reality that treatment of pregnant women can have significant implications for their fetus (Dickens and Cook 2003: 87). Referring to the fetus as a 'patient' rather than an 'unborn child' helpfully highlighted the beneficence rather than rights-based nature of obligations toward early life (McCullough and Chervenak 2008). However, the fetus does not have an independent moral status from others, which can generate obligations (Chervenak, McCullough et al. 2004: 222). The term 'patient' is not based upon the intrinsic independent person, but upon whether or not one can gain a benefit from the application of clinical skill by a physician, whereby a human presents him/herself for treatment that will be more beneficial rather than cause 'harm' (Chervenak, McCullough et al. 1994: 5).

The 'fetus as a patient' concept moves the maternal fetal divide debate within FGT away from issue of rights to the more fruitful terrain of the moral obligations of the clinician to the pregnant woman and fetus (Harris 2000). The debate is shifted away from independent rights to that of dependent moral status (Harris 2000). The major advocates of the 'fetus as a patient' concept view dependent moral status as human

[88] See chapter 2 for development and history of FGT.

beings having obligations to protect and promote an entity's interests because that entity is in a social role that has been created and structured for that purpose (Chervenak, McCullough et al. 1994).

It should be noted that the 'fetus as a patient' concept proposed here differs from the unborn or fetal patient used by Liley (1972). Liley used the increasing biological knowledge surrounding pregnancy to infer a 'natural' fetal patient through biological determinism; thus, legitimizing fetal personhood (Casper 1998, Liley 1972). The fetal patient, in this instance, utilised key physiological and behavioural developments of the fetus to support the patient status placed upon the fetus (Casper 1998). The 'fetus as a patient' that McCullough and Chervenak propose throughout their work draws elements from the principled approached proposed by Beauchamp and Childress (2001). They propose that medical ethics consists of four principles: autonomy, non-malfeasance, beneficence, and justice.[89] These principles become important when the fetus is deemed a patient, because the pregnant woman's beneficence based obligations to the fetal patient can and should justifiably restrict her autonomy (Fleischman, Chervenak et al. 1998). The two initial factors needed for the fetus to become a patient are:

1. It is presented to the physician or other healthcare professional, and
2. There exist clinical interventions that are reliably expected to clinically benefit the child and, later, the person that the fetus is expected to become once born (McCullough and Chervenak 2008: 37).

The 'fetus as a patient' concept depends on the viability of the fetus and the acknowledgement of the mother to continue a viable fetus to term (See Chervenak and McCullough 2007). Therefore, the dependant moral status of the fetus is not based upon intrinsic characteristics of the fetus, but upon viability and *ex utero* support thorough technology and biology (Chervenak and McCullough 2009). Within England and Wales, a fetus is considered viable once it has commenced the 24th week of gestation.[90] Legally, any fetus that is born dead after this point is no

[89] 'Justice' within this context refers to treating like cases a like, but depends on being able to ascertain whether cases are comparable (Jackson 2006).

[90] The time of gestation can be calculated by (1) the first day of the woman's last period; or (2) the date of conception; or (3) the date of implantation; or (4) the first day of the woman's first missed period (Grubb and Kennedy 2000). However, when Parliament introduced the 24 week time limit

longer considered a miscarriage, but a still birth.[91] Once the fetus is viable it acquires interests, which include: avoiding premature death, disease and handicapping conditions; hence, when its interests are threatened, it becomes a 'patient' (Harrison, Golbus et al. 1984).

However, the fetal stage of development starts after 56 days of gestation, therefore the pre-viable fetus has to be considered. As the prefix 'pre' suggests, the fetus would be unable to live if it was born at this stage of its development. In order for a pre-viable fetus to be considered a patient, an extra criterion is needed. The pre-viable fetus is a patient as a function of the pregnant woman's decision to confer the status of 'patient' upon the fetus (Chervenak and McCullough 2009, 2011). More importantly, there is no obligation upon the pregnant woman to confer the status of a patient upon a pre-viable fetus, just because there is a potentially applicable and beneficial fetal therapy available (Chervenak, McCullough et al. 1994: 6). However, with the rise of early genetic interventions, which can be seen as purely for the medical benefit of the fetus, the pre-viable fetal patient is important.

Concepts are more than dictionary definitions or necessary entailments which someone wishes, but encompass the patterns of reasoning that lie behind it. These patterns can include the conversational implications and interpretational predispositions that animate its use (Lyerly, Little et al. 2008). Consequently, despite practitioners claiming that the 'fetus as a patient' treats both mother and fetus as the one patient; it is inescapable that the fetus as a patient depends on two distinct patients. The fetus as a paradigmatic patient is an entity that is individuated physically and fully separate from others (Lyerly, Little et al. 2008). Therefore, it should be considered that by treating the fetus as a patient means that the fetus, in theory, acquires the right to protection, thus making the threshold of viability irrelevant. An irreversibly comatose patient has a right to protection regardless of their brain function or malfunction. If being a patient includes the right to

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upon medical abortions it was on the basis of the medical calculation of the date of the last menstrual period (British Medical Association 2005).

[91] Under the Still-Birth (Definition) Act 1992, which amended the Births and Deaths Registration Act 1926 (definitions) and of the Births and Deaths Registration Act 1953 s. 41 from 28 weeks to 24 weeks.

preventative care, damage to the fetus should be avoided even before viability (Van Bogaert and Dhai 2008). Therefore, the fetus as a patient could extend the conflict between mother and fetus throughout the gestational period.

Throughout the development of the fetus as a patient within prenatal medical practice, the emphasis is on the autonomy of the mother. As Dickens and Cook (2003) state:

> Those who appoint themselves physicians to fetal 'patients,' and then favour the interests of such 'patients' over the duties they owe to the pregnant women who came to them for conscientious care and advice, place themselves in a conflict of interest, and profoundly betray their true patients and professional responsibilities (Dickens and Cook 2003: 87).

Therefore, the mother is still paramount within the 'fetus as a patient' concept, especially where she has confirmed the status of patient upon a pre viable fetus. In fact, subject to a declaration of incapacity upon the mother, the mother's decision upon the course of treatment is still paramount above that of the fetus (Chervenak and McCullough 2003, 2007, 2011, Chervenak, McCullough et al. 2004, Chervenak, McCullough et al. 1994). Therefore, despite the possibility of two patients, there is still only one ultimate decision maker. In fact, as ubiquitous as the construction of the fetus as a patient is, not all practitioners will view or define the fetus as their primary or secondary work object (Casper 1998: 119). However, within the USA, from where many of the leading FGT practitioners originate, the American College of Obstetrics and Gynaecology has issued guidance on how to approach the maternal fetal divide, if there is a conflict. It states that physicians should

> (1) respect her autonomy, regardless of the consequences; or
> (2) counselling and/or referral to a colleague (who is willing to oblige or at least willing to repeat counselling); or
> (3) request a court order (and over-ride her autonomy)(American College of Obstetrics and Gynecology committee opinion 1999: 214).

In fact, with regards to research that is purely for the benefit of the fetus, consent of both parents is needed.[92] Therefore, the maternal fetal divide is heightened when

[92] Code of Federal Regulations: Title 45 - Public Welfare, Part 46, Protection of Human Subjects, s.46.203 and s.46.204.

physician and maternal patient are in conflict over the physician's recommended course of treatment.

As stated above, there is no obligation for the mother to see the fetus as separate from the mother within the proposition of patienthood. Autonomy of the patient only refers to patients that are persons. Considering that the fetus as a patient concept depends on more than clinical expertise; the maternal fetal divide becomes a divide between mother on one side, and fetus/physician on the other. Therefore, reference to the fetus as a patient creates a possible conflict between the mother and fetus, as well as between the mother and clinician (Noble and Rodeck 2008: 222). It could be considered that a clinician can, under the fetus as a patient concept, have two patients with competing interests. For example, 'patienthood' is a normative status that connotes concrete expectations for professional engagement: physicians are duty-bound to be fiduciaries of their patients (Lyerly, Little et al. 2008). When the benefit of treatment is purely for the fetus, then under strict interpretation of fetal patienthood, the FGT practitioner would under their fiduciary relation with the fetus recommend treatment. Under their fiduciary duty to the mother, they should recommend abortion. Therefore, the fetus as a patient creates a divide between mother and fetus, but relies upon autonomy to resolve the conflict.

Ultimately, the fetus as a patient concept is a concept that changes the way in which FGT practitioners address issues within FGT. For example, treatments given to the mother are also put in terms of their prospective benefits and risks for both the women and for their fetus, as the therapist has duties towards both (Dickens and Cook 2003). It moves the maternal fetal divide from a biological or ethical problem to a practical one. Nevertheless, when the maternal fetal divide becomes a conflict, it is up to legal institutions to decide what the maternal fetal divide is. Therefore, how the maternal fetal divide is legally constituted helps create the environment upon which the maternal fetal divide within the clinic is formalised. In order to ascertain the judicial view of the maternal fetal divide, the relevant legal topics must be identified. These are the cases surrounding abortion and the refusal of treatment because these are the cases where it is being advanced by another party that there is conflict between the interest of the fetus and mother. Once those areas are identified

then each area can be dissected to reveal that the legal perspective on the maternal fetal divide is one established at birth and, therefore, does not exist except in limited circumstances such as infant destruction.

4.4 Legal perspective on the maternal fetal divide

Within the legal system of England and Wales the development of the maternal fetal divide has been bound up with the debate surrounding the legality of abortion and enforced caesarean sections. The political and legal debate is immediately connected to these practices; therefore, both frame the maternal fetal divide (Casper 1998). The civil and criminal debates surrounding the legal status of a fetus form one continuous account of the legal status of a fetus. In discussing the possible maternal fetal divide, the debate is framed within the conflict of medical opinion and maternal want. In other words, the cases that are reviewed are only cases where these two opinions differ. These cases are important for the thesis as they will help frame the answers to the research questions as well as assist in understanding whether there is legal room to manoeuvre if the practice of FGT is pointing in a different direction.

The case law establishes common themes surrounding the regulatory approach to the maternal fetal divide. These themes are abortion, refusal of treatment, and human rights. In order to assess these areas, the relevant case law will be identified and explored in the above order. The abortion and refusal of treatment cases involve cases from England and Wales, but because of the nature of human rights, the human rights cases include rulings from the European Court of Human Rights (ECtHR). After analysing each case the legal perspective will lead to the conclusion that, due to the mother's autonomy, the maternal fetal divide does not exist except in limited circumstances. Even at a European level, there is a reluctance to enforce that the fetus is a legal life under the ECHR. Therefore, the maternal fetal divide starts at birth.

As stated earlier in the chapter, it is the right for the mother to act autonomously over her own body that has emerged as the key element in defining any conflict between mother and fetus. In acting autonomously, the legal debate is concerned with the right to refuse treatment as well as to receive medical services, which directly affects

the fetus in areas such as abortion. These rights can be seen as negative or positive,[93] which makes abortion a useful area to explore to ascertain if there is a divide and/or conflict at a legal level. However, the case law refusal of treatment includes treatment of incompetent pregnant women, which also provides significant evidence as to how the maternal fetal divide is framed. Classically, case law regarding the enforcement of treatment to incompetent pregnant women concerns caesarean sections. However, the maternal fetal divide is also prevalent within abortion law. Given the interplay with FGT and abortion as a 'treatment option' abortion law and how abortion law has developed is extremely important because potentially any intergenerational interests would impact on abortion being a viable option where FGT is available.

4.4.1 Abortion

An historical perspective on the law surrounding abortion is the best way in which to understand the current abortion regulations. It outlines the progression from abortion being an illegal practice before the 20th century, to essentially abortion on demand, under certain conditions, under the Abortion Act 1967. This account includes looking as far back as Coke's 17th century definition of murder. This is important for the thesis as it establishes who are defined as legal people capable of protection under English law, and thus potentially how FGT could be regulated. Historically within the abortion debate the fetus had no rights or interests until the point of quickening[94] which, once it had occurred, curtailed the mother's autonomy. Essentially viability and humanity was shown to exist at the point of the quickening, thereby creating a conflict between the mother and fetus where the mother did not wish the pregnancy to continue. Therefore, the biological 'life' of the fetus could override that of the mother's autonomy.

Despite abortion post quickening being illegal at this point in history, a fetus was not considered a person and did not accrue any rights until being born. Therefore,:

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[93] See 1.2 for further elaboration of terms.
[94] The point at which fetal movements are felt by the mother and is normally felt after 16-18 weeks of gestation.

> If a woman be quick with childe, and by a potion or otherwise killeth it in her wombe; or if a man beat her, whereby the child dieth in her body, and she is delivered of a dead childe; this is a great misprision, and no murder . . ."(Coke 1628-1644: Pt. III, ch. 7, p. 50).

This was because the fetus was not a reasonable creature, in *rerum natura*. The case of *Attorney-General's Reference (No. 3 of 1994)*[95] confirms that the above stance is still applicable today. Therefore, until the damaged fetus is born, there is only one 'person' that an accused is criminally liable to, except in certain circumstances.

Nonetheless, the criminal law included restrictions upon maternal autonomy within the Offences Against the Person Act 1861. Section 58 made it unlawful to administer a poison or noxious thing to procure an abortion; while section 59 prohibits supplying or procuring poison or instruments for the purpose of criminal abortion. Viability no longer applied as medical knowledge had proved that the quickening was no longer a special point within pregnancy. Therefore, the maternal fetal divide rested purely on the knowledge of being pregnant. Fetal interest in a continued pregnancy to birth was paramount over the mother's autonomy and bodily integrity. Further legislation made it illegal to procure an abortion of a child that was capable of being born alive, with the person being served with a charge of 'child destruction'.[96] Viability, once again became the point at which a fetus gained protection from being wilfully terminated by its mother.

However, within *R v Bourne*,[97] a 14 year old girl became pregnant following a rape. With the consent of both parents Dr Bourne performed an abortion upon the girl and was subsequently charged under the 1861 Act. Dr Bourne was acquitted with the trial judge linking the Offences Against the Person Act 1861 and the Infant Preservation Act 1929. Importantly, the case recognised that the priority within the maternal fetal relationship is that of the mother, not the fetus. Therefore, legislation reflected the change towards autonomous decision making with the introduction in the Abortion Act 1967. The change in legislation reflected the ability of medical practitioners to perform abortions safely as well as changing attitudes towards

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[95] *Attorney-General's Reference (No. 3 of 1994)* [1998] A.C 245.
[96] Infant Preservation Act 1929 s.1(1).
[97] *R v Bourne* [1939] 1 KB 687.

women's rights. As far as the criminal proceedings are concerned the maternal fetal divide can still be seen in recent cases that have placed weight upon damage and trespass to the pregnant woman rather than on pure harm to the fetus as a person.[98]

The criminal law does, however, recognise the maternal fetal divide. The *Attorney-General's Reference (No.3 of 1994)*, indicates that there is a maternal fetal divide because:

> (i) B caused the death of a person, the child, S. Otherwise he could not have been convicted of manslaughter.
> (ii) He did so by an act done with intent to cause grievous bodily harm to a person, the mother. (Metcalfe 1997: 831)

The maternal fetal divide is reflected in third party intervention within the criminal law but not where the mother chooses to inflict injury. For example, a person will be guilty of murder and infant destruction where injury inflicted to a victim also results in the death of their fetus. The conviction of Carl Whant for the murder of Nikitta Grender and the infant destruction of her fetus highlights the divide between mother and fetus at law (BBC News 2012). This is partly due to the amendments made by the Human Fertilisation and Embryology Act 1990, which uncoupled the Infant Preservation Act 1929 from the Abortion Act 1967, thus removing the 'capable of being born' limitation and hence liability of abortions of fully handicapped children (House of Parliament 1990). Therefore, despite Coke's definition of murder not being applicable to fetuses because they are not 'people' clearly criminal liability, not just civil liability, can be imposed under the Infant Preservation Act 1929. Using the term 'infant' rather than fetus implies that beyond viability the divide is more than an emotional divide, and seeks to protect the fetuses because they will be infants. In order to further assess if there is a maternal fetal divide or conflict, the maternal fetal divide must be viewed through the lenses of medical decisions.

After 24 weeks, the ultimate decision of curtailment of fetal life can only be where; the fetus has a serious genetic disease; the continued pregnancy will cause permanent physical or mental injury to mother; the benefit of a continued pregnancy places a

[98] *R. v Magira* [2009] 1 Cr. App. R. (S.) 68.

greater risk than an abortion.[99] However, the initial limit under the Abortion Act 1967 was 28 weeks, but this was reduced following an increase in knowledge about pregnancy (House of Commons Science and Technology Committee 2007). [100] Yet the same amendment meant that a 'life' could be ended if there were sufficient conditions, thus highlighting not only the tension between restriction of choice and autonomy as medical knowledge develops, but also the importance of scientific progress upon the regulation of choice and autonomy. Therefore, there could potentially be an impact upon FGT regulation as it progresses.

Abortion places the maternal fetal divide debate within the frame of positive rights. However, that is merely one aspect of the maternal fetal divide within the law of England and Wales. Importantly for the thesis, it is the negative right of autonomy, or right to refuse, that is of paramount importance to the maternal fetal divide. The debate surrounding negative rights moves the debate away from the regulation of abortion and into the general regulation of autonomy within pregnancy. This is important as the research questions clearly indicate that there is a question about enforcement of treatment for the sake of future generations. If this is occurring within case law then an avenue for enforcing treatment in the interest of future generations would be possible. If this is not so then regardless of the benefit of a treatment, maternal autonomy would place the maternal fetal divide solely in the hand of a mother and no other interested party. Interestingly, the evolution of significant case law appears from 1992 in the case of *Re T*,[101] through to the cases of *Re MB*,[102] and the exception to this in *Re F (In Utero)*.[103] This latter case, however, is dealt with within *Re MB*,[104] which is the leading authority on the maternal fetal divide.

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[99] Abortion Act 1967 s.1(b)-(d).
[100] Human Fertilisation and Embryology Act 1990 s.37
[101] *Re T (Adult: Refusal of Treatment)* [1993] Fam 95.
[102] *Re MB (Caesarean Section)* [1997] 2 FLR 426.
[103] *Re F (In Utero)*[1988] Fam 122.
[104] *Re MB (Caesarean Section)* [1997] 2 FLR 426.

4.4.2 Refusal of treatment

It was not until 1992 that the legal system within England and Wales had to address the possibility of an exception to the principle of autonomy within competent women (Scott 2002). The possible exception to the principle of autonomy was mooted by the case *Re T*.[105] *Re T* concerned a 34 week pregnant woman who had been admitted to hospital due to a road traffic accident. Although not part of a religious group herself, her mother was a Jehovah's Witness. One afternoon, when only her mother was with her, she stated spontaneously to a nurse that she did not want a blood transfusion, that she had been a Jehovah's Witness and retained some beliefs. She reiterated her refusal to blood transfusions both to the midwife and to a doctor. Her fetus was delivered still born. Later T's condition deteriorated and she was sedated and placed on life support. The case primarily considered patient autonomy; how to assess capacity to consent and if there is any undue influence upon a person's consent; due to her pregnant nature, the case considered the rights and interests of the fetus against the refusal of blood transfusions by Miss. T:

> An adult patient who, like Miss. T, suffers from no mental incapacity has an absolute right to choose one rather than another of the treatments being offered. The only possible qualification is a case in which the choice may lead to the death of a viable fetus. That is not this case and, if and when it arises, the courts will be faced with a novel problem of considerable legal and ethical complexity.[106]

At the time of Lord Donaldson's statement, the Abortion Act 1967 was amended by the Human Fertilisation and Embryology Act 1990 s.37, which reduced the time limit for medical termination of pregnancy from 28 weeks to 24 weeks.[107] The caveat of viability was quickly challenged in *Re S (Adult: Refusal of Medical Treatment)*,[108] where Sir Stephen Brown P was called to adjudicate whether doctors could override a refusal of treatment by a pregnant woman on religious grounds. Although the case was swiftly banished to legal history, the case drew criticism for allowing the declaration of the doctors to treat S without her consent. The case also

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[105] *Re T (Adult: Refusal of Treatment)* [1993] Fam 95.
[106] *Re T (Adult: Refusal of Treatment)* [1993] Fam 95, 102.
[107] Within the case off *C v S* [1987] 1 All ER 1230 (see below), medical evidence claimed that a fetus could be considered viable at 21weeks. At the same time the Still Birth (Definition) Act 1992 amended the legal definition of a miscarriage to 24 weeks for a consistent approach within the law towards viability.
[108] *Re S (Adult: Refusal of Medical Treatment)* [1992] 4 All ER 671.

drew criticism for Sir Brown P's wrongful interpretation of the American case *Re AC,*[109] which involved very different facts.[110] Several cases involving incompetent women followed this judgement with enforced caesarean sections being carried out as treatment under the Mental Health Act 1983 s.63.[111] The maternal fetal divide was alive with regards to caesarean sections, placing the legal force with the fetus and its interest in living. However, the question of whether or not viability was enough to invoke a conflict between mother and fetus which was able to override a competent mother's negative right to treatment was not fully reconsidered until the case of *Re MB*, thus consigning *Re S* to the history books.

4.4.3 Re MB

MB was a pregnant woman who refused blood transfusions both before and during her pregnancy because of her needle phobia. When she was 40 weeks pregnant it was found that the fetus was in the breech position. The serious risk of brain damage or death to the baby was explained to MB if the fetus was delivered vaginally. She agreed to have a caesarean section, she was admitted to hospital where she and her partner agreed to the operation and signed a consent form. However, when successive attempts were made to carry out the operation she panicked at the last moment because of her needle phobia and withdrew her consent. Finally, when MB was in labour and not responding to either the midwife or the consultant, she once again consented to, and then refused anaesthesia. The health authority subsequently applied for and was granted a declaration from the High Court that it would be lawful for the consultant gynaecologist to operate on her, using reasonable force if necessary. Later that night the Court of Appeal dismissed the patient's appeal from that order, reserving its reasoning till the following morning. In the leading judgement by Butler Sloss LJ, the maternal fetal conflict was addressed, firstly by assessing the case law that preceded the case stating:

> There are decisions, which give some acknowledgment to the effect harmful acts have upon the fetus[...] [However,] none [..] lends any

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[109] *Re AC* 533 A 2d 611 (DCApp 1987).
[110] *Re AC* concerned the District of Columbia enforcing a caesarean section against the wishes of a terminally ill mother, in an attempt to save the life of the fetus, which died hours after delivery.
[111] See *Norfolk and Norwich Healthcare (NHS) v W* [1996] 2 FLR 613 and *Tameside and Glossop Acute Services Trust v CH (a patient)* [1996] 1 FLR 762.

> support to the proposition that the court should take into account the interests of the unborn child at risk from the refusal of a competent mother to consent to medical intervention.[112]

Butler Sloss LJ, then went on to address fetal interests within pregnancy and if the court can protect those interests. She states:

> The fetus up to the moment of birth does not have any separate interests capable of being taken into account when a court has to consider an application for a declaration in respect of a caesarean section operation. The court does not have the jurisdiction to declare that such medical intervention is lawful to protect the interests of the unborn child even at the point of birth.[113]

She reiterated dictum from *Re F (In Utero)*, involving a pregnant woman who was mentally disturbed and led a nomadic existence. The local authority was concerned that she would neither take sufficient care nor seek medical attention for the wellbeing of the child at the time of birth and thereafter. The local authority applied for the fetus to be declared a ward of court. The local Authority lost on the grounds that because a fetus was not a person, a writ could not be issued on the fetus' behalf. However, *Re F (In utero)* also considered the possibility of the court being asked to order delivery of the baby by caesarean section. Balcombe LJ stated:

> If Parliament were to think it appropriate that a pregnant woman should be subject to controls for the benefit of her unborn child, then doubtless it will stipulate the circumstances in, which such controls may be applied and the safeguards appropriate for the mother's protection. In such a sensitive field, affecting as it does the liberty of the individual, it is not for the judiciary to extend the law.[114]

Re F (In Utero) confirmed the decision taken a year earlier in the case of *C v S*,[115] whereby a father sought to stop his girlfriend from obtaining an abortion. However, it was held that the fetus had no status and the rights of a fetus are crystallised at birth.[116] No other party could interfere with competent maternal choice unless parliament felt it appropriate. Therefore, *Re MB* confirmed that within the institution of law and medical decisions, despite dealing with two entities, there is not a division between mother and fetus when the mother is deemed competent. In other

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[112] *Re MB (Caesarean Section)* [1997] 2 FLR 426, 441.
[113] *Re MB (Caesarean Section)* [1997] 2 FLR 426, 444.
[114] *Re F (in utero)* [1988] Fam 122, 143.
[115] *C v S* [1987] 1 All ER 1230.
[116] *C v S* [1987] 1 All ER 1230, 1234.

words, there is only one set of interest to take into account, that of the mother's. Therefore, where the mother is competent no other interested parties such as fathers or 'future children' can override a mother's choice regardless of the benefit to anyone/anything else. Therefore, regardless of how good fetal therapies are they cannot be enforced upon a mother. The case highlighted the possible influence of human rights within refusal of treatment cases, which must be considered at a supranational level because under the Human Rights Act 1998, the decisions of the ECtHR are directly applicable to the maternal fetal divide within the UK. To assess the supranational level, once again the case law involving the fetus and decisions regarding pregnancy will be analysed, which results in the maternal fetal divide once again being dependant on birth.

4.4.4 Human rights and the maternal fetal divide

In 1951, the UK ratified the ECHR,[117] which binds all ratifying nations to convention rights and rulings of the ECtHR and European Commission of Human Rights (Bradley and Ewing 1997). The UK is also a signatory to the EU, which acts at a supranational level over the UK and is separate from the ECHR.[118] The regulatory competence of medicine within the EU falls under the Treaty on European Union, implying that such protection falls within the competence of national legislation and, therefore, not strictly of concern at the EU level. The ECtHR, also applies a margin of appreciation with respect to their decisions in relation to convention rights.[119] Therefore, the ECtHR is a useful tool for analysing the maternal fetal divide.

It was not until October 2000, through the HRA 1998 that convention rights were enshrined within the domestic law of England and Wales. The rulings of the ECtHR

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[117] The full official title is 'Convention for the Protection of Human Rights and Fundamental Freedoms as amended by Protocol No. 11 (1950)' and did not come into force within the United Kingdom until 1953. Under the Treaty of Lisbon amending the Treaty on European Union and the Treaty establishing the European Community [2007] OJ C306/01 Article 6(2), all members of the EU now accede to the ECHR.

[118] The United Kingdom joined the then European Community in 1973 after passing the European Communities Act 1972. The European Union was created in 1992 under the Maastricht Treaty (or Treaty on European Union 1992).

[119] *Vo v France* (Application no. 53924/00) [82].

and European Commission, pre HRA are still applicable. However, applicants must still exhaust all avenues of appeal before an application to either court is admissible. More recently, under the Lisbon Treaty there is a Charter of Fundamental rights, which runs parallel to the ECHR and should adopt the same interpretations and case law of the ECtHR (The Law Society 2008).[120]

The earliest case where the maternal fetal divide was called into question was in *Brüggemann and Scheuten v Federal Republic of Germany*.[121] The European Commission on Human Rights had to consider the relationship between the pregnant woman and her fetus in the context of Article 8 of the Convention, the right to respect for private and family life. Two German women challenged the criminal restrictions upon abortion in West Germany. The Commission found that there are limits to the Article 8, because:

> Pregnancy cannot be said to pertain uniquely to the sphere of private life. Whenever a woman is pregnant, her private life becomes closely connected with the developing fetus.[122]

The Commission did not find it necessary to assess, or conclude, whether or not the fetus has rights within Article 2, but the judgement was the first of many with regards to the maternal fetal divide. Article 2, the right to life, has been a key factor in the maternal fetal divide debate because neither life nor human had been defined within the ECHR;[123] therefore, a fetus could potentially have a separate, conflicting/competing interest in the right to life from that of its mother. The question of whether the status of a fetus is separate from its mother, and therefore engaging competing rights, was raised within the case of *Paton v United Kingdom*,[124] where the maternal fetal divide was considered in relation to Article 2.

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[120] The Treaty of Lisbon 2007, amends article 6 of the Treaty on European Union 1992, to provide for recognition of the Charter, which was originally proclaimed by EU institutions at the Nice Inter-Governmental Conference in December 2000 (The Law Society 2008).
[121] *Brüggemann and Scheuten v Federal Republic of Germany* (Application no. 6959/75, Commission Decision of 12 July 1977).
[122] *Brüggemann and Scheuten v Federal Republic of Germany* (Application no. 6959/75, Commission Decision of 12 July 1977) 116.
[123] *Bruggemann and Scheuten v. Federal Republic of Germany* (Application no. 6959/75, Commission Decision of 12 July 1977).
[124] *Paton v United Kingdom* [1980] 3 EHRR 408.

In 1978, Mrs Paton found out that she was eight weeks pregnant and decided to have an abortion. Her husband did not agree with the proposed abortion and applied for an injunction to prevent the abortion from being carried out. Having exhausted all appeal avenues within the legal system of England and Wales, Mr. Paton then applied to the ECtHR to rule upon the matter. The case alleged many ECHR infringements, but is relevant to the maternal fetal divide by identifying the legal interpretation of a fetus in relation to the ECHR. In identifying if the Article 2 of the ECHR applied to the fetus the court identified that:

> The 'life' of the fetus is intimately connected with, and cannot be regarded in isolation from, the life of the pregnant woman. If Article 2 were held to cover the fetus and its protection under this Article were, in the absence of any express limitation, seen as absolute, an abortion would have to be considered as prohibited even where the continuance of the pregnancy would involve a serious risk to the life of the pregnant woman. This would mean that the 'unborn life' of the fetus would be regarded as being of a higher value than the life of the pregnant woman. The 'right to life' of a person already born would thus be considered as subject not only to the express limitations mentioned in paragraph 8 above but also to a further, implied limitation. [...] The Commission finds that such an interpretation would be contrary to the object and purpose of the Convention.[125]

The interpretation of *Paton* was followed in *Re F (In utero)* and *C v S*. Therefore, the maternal fetal conflict is only acknowledged and that is all. A fetus has no legal rights and nor does any other party where a mother is competent and making a decision voluntarily. However, *Paton* did not issue a definitive decision upon a viable fetus as the question of viability was considered to fall outside the remit of the case.

The most recent decision of the ECtHR that is relevant to the maternal fetal divide is the case of *Vo v France*.[126] Following the medical negligence by her doctor, Mrs Vo suffered injury to her amniotic sac, which in turn required the termination of her pregnancy, which she maintained she fully wanted. The fetus was on the borderline of viability when the termination occurred. It was argued that Article 2 of the ECHR applied to a fetus at this stage of development. The doctor, who performed the

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[125] *Paton v United Kingdom* [1980] 3 EHRR 408, [19-20].
[126] *Vo v France* (Application no. 53924/00) (2004) 79 BMLR 71.

procedure, was charged with causing unintentional injury, but was acquitted on the grounds that the fetus was not, at that stage, a human person. On appeal, the acquittal was upheld by the Court of Cassation within France, thereby exhausting all Mrs. Vo's remedies within the French legal system and appealing to the ECtHR.

The convention, however, is clear upon the status of the fetus.[127] However, given the technology that is now available more than 50 years after the original convention was written, and the *Paton* case, it does not completely answer the question of the maternal fetal divide. The court drew precedent from *X v United Kingdom,*[128] where a husband petitioned the European Commission on Human Rights on behalf of the fetus that his wife wished to abort.

> [I]f one assumes that this provision applies at the initial stage of the pregnancy, the abortion is covered by an implied limitation, protecting the life and health of the woman at that stage, of the 'right to life' of the fetus.[129]

The above statement reaffirmed the decision of *Paton* and within the *Vo* case the judgement went further in identifying the implication of the ECHR for the fetus and states:

> [I]t is neither desirable, nor even possible as matters stand, to answer in the abstract the question whether the unborn child is a person for the purposes of Article 2 of the Convention.[130]

The *Vo* case highlights that there is no moral conscience about the status of the fetus across Europe. More importantly, it signifies that for the purpose of the ECHR, the right to life does not apply to the fetus in law. The Court is still not willing to answer the question of whether a fetus is a person or answer questions in relation to viability.

Therefore, the fetus is not considered distinctly separate or different from its mother. The comments provided to the court in the *Vo* case, indicated that this should be the case even when fetal damage occurs (Center for Reproductive Rights 2003). Thus,

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[127] *Bruggemann and Scheuten v. Federal Republic of Germany* (Application no. 6959/75, Commission Decision of 12 July 1977).
[128] *X v. United Kingdom* (Application no. 8416/79, Commission decision of 13 May 1980).
[129] *X v. United Kingdom* (Application no. 8416/79, Commission decision of 13 May 1980) 253.
[130] *Vo v France* (Application no. 53924/00) [85].

the maternal fetal divide is essentially ruled out apart from the possibility of viability. Nonetheless, the language used by the ECtHR frames the maternal fetal debate in relation to competing interests, but has yet to rule in favour of a fetus; therefore confirming that fetal interests are not of concern with regards to maternal rights.

In fact, other pieces of legislation related to fetal issues confirm the lack of maternal fetal divide. In terms of property rights, despite the biological difference between mother and fetus, the Human Tissue Authority (HTA) considers that fetal tissue is of maternal origin; therefore, whether fetal cells are extracted for analysis, or are removed from a stillborn fetus, the cells are still considered maternal tissue (Human Tissue Authority 2009: [157]).[131] The same consent rules apply to fetal tissue as to the mother's tissue, and due to the sensitivity attached to research on fetal material, it is good practice to always obtain consent for the examination of fetal tissue and for its storage or use for all scheduled purposes (Human Tissue Authority 2009).

It is worthwhile identifying that a mother has no civil culpability for decisions made while pregnant once that fetus is born. According to the Congenital Disabilities (Civil Liability) Act 1976, if a child is born disabled as a result of an action or actions during the pregnancy or birth, the child may sue the person responsible but not the mother.[132] The only instance is contained within section two whereby the mother owes the same duty of care to the fetus as she does to any other road user. The reason for the exception is due to compulsory car insurance (Jackson 2006). The legal construction of the maternal fetal divide is best summed up by Butler Sloss:

> Although it might seem illogical that a child capable of being born alive is protected by the criminal law from intentional destruction, and by the Abortion Act from termination otherwise than as permitted by the Act, but is not protected from the (irrational) decision of a competent mother not to allow medical intervention to avert the risk of death, this appears to be the present state of the law. Moreover, if

[131] Under the Human Tissue Act 2004 s.37, the HTA can issue directions on procedures and practices that are governed by the act. Currently the HTA is on *Directions 2009/002* and were approved by Parliament in July 2009.
[132] Congenital Disabilities (Civil Liability) Act 1976 s.1(2).

> the competent mother by refusing medical intervention is delivered of a handicapped child, she cannot be sued by that child for her decision not to take steps to protect it at the moment of birth.[133]

Therefore, the maternal fetal divide is acknowledged within law in relation to fetal interests, but the result is that there is effectively no maternal fetal divide until the birth of the fetus. Only in certain criminal circumstances is the maternal fetal divide an important enough issue that regulation creates a divide in order to prescribe liability to more than one entity. In comparison to the development of knowledge surrounding pregnancy, it appears that the legal maternal fetal divide has not developed in accordance with principles such as the fetus as a patient or the development of medical knowledge surrounding pregnancy. Rather case law is centred under legal personality and autonomy. The importance of this is that there is a danger that FGT could progress in line with medical practice and the legal maternal fetal divide could be left behind, as identified by Ellul (1965) and Winner (1978).

4.5 Conclusion

The fundamental difference between the construction of the maternal fetal divide within law and medicine is the way that the interests of the fetus are taken into account. The fetus as a patient within medicine creates a divide between mother and fetus, which is beyond the biological divide of pregnancy. It recognises and tries to treat two patients, despite claiming only to treat one combined patient of mother and fetus. The advent of FGT makes the maternal fetal divide even clearer, as increasingly it is the fetus that needs treatment, with the mother receiving treatment as a proxy. Because of the fetus as a patient concept the maternal fetal divide results in 'parental', not just maternal, consent being an issue for FGT practitioners within the USA. However, within the legal institutions of England and Wales, although FGT practitioners may utilise the fetus as a patient model to try and treat the fetus, there is no divide at law, except within a few exceptions. In other words, until birth, despite the acknowledgement of two sets of competing interests, at both the UK and European Human Rights level, the rights and interests of the mother are paramount.

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[133] *Re MB (Caesarean Section)* [1997] 2 FLR 426, 441.

No other parties are relevant, even when a mother is making a decision which conflicts with their duties. In fact, the lack of maternal fetal divide within the law is shown by the way that fetal tissue is treated as maternal tissue, not tissue in care of both parents. If the maternal fetal divide was apparent within the legal institutions of England and Wales, the medical and legal debate within pregnancy would centre on weighing up maternal and fetal interests, not viability or birth. As a result of the two different constructions of the maternal fetal divide a tension is created between not only mother and fetus, but between institutions.

The maternal position appears not to have developed as viable therapies that can be administered safely to mothers have been developed, yet medical knowledge has been influential in restricting maternal choice. The reduction of the abortion limit under section 1(1) of the Abortion Act 1967 from 28 weeks to 24 is a clear indication of that. However, medical knowledge of fetal therapies has not had the same impact in terms of enforcement of treatment.

These principles are important because in order to assess the regulation of FGT and answer the research questions, the maternal fetal divide helps establish the implications of the data as well as establishing the relevant parties within FGT. They also provide an insight into how the legal interpretation of the maternal fetal divide has progressed in accordance with the rise of autonomy rather than with the rise in medical knowledge surrounding the fetus. This indicates that an autonomy orientated position would evolve within the clinic rather than a fetus orientated position. However, biotechnologies have also had power to impact upon choice within the clinic. The next chapter will investigate ethics as a method to mitigate the impact of progressing biotechnologies, and provides the philosophical foundation to the debate about the maternal fetal divide.

5 Justifying the use of an Ethical Principle

5.1 Introduction

Having seen in chapter 4 the medical and legal manifestations of the maternal fetal divide that operate within FGT, regulating and practicing in such an area can be potentially precarious. It is clear from international declarations, academic writings and other associated documents that ethics is seen as one way to regulate progressing biotechnologies, which would include FGT. Ethics can codify societal responses towards such areas, assess whether current regulations are adequate to the demands of scientific progress and can promote responsible uses of science (Directorate-General for Research and Innovation 2012). Theorising about ethics helps provide consistency, identify what guidelines or standards should be used to make appropriate judgements, and help guide the correct application of the appropriate theory (LaFollette 2007).

Importantly for the thesis, utilising a prospective theory, which can go beyond the current risk and safety factors reduces the real danger of polarising opinions when technologies and/or practices are introduced and discussed is preferable (Peterson 2001). Considering that technology has the power to produce long term consequences beyond the 'now' as well as have its own autonomy (Ellul 1965, Winner 1978), an ethical theory should not be contingent upon time or place (Groves 2006). This is important when considering the intergenerational aspects and long term consequences of FGT whereby applying an ethical critique to the debate will clarify issues that may be technically feasible in the future (Peterson 2001). To add legitimacy to the ethical analysis that follows in this thesis a connection must be made between ethics, the practice of medicine and the regulation of FGT. By identifying the connection an appropriate ethical theory to analyse FGT emerges which is presented in the last sections of this chapter.

Section 5.2 of this chapter looks at the international influences on FGT and shows that within the globalised industry 'human dignity' emerges as a guiding principle in both international and domestic regulatory practices, including patients' rights. Section 5.3 asks what is human dignity and examines the question under Schulman's

four categories. Section 5.4 evaluates different moral theorists in order to find a foundation for human dignity. Here Alan Gewirth's Principle of Generic Consistency (PGC) emerges as the standard with which to assess whether human dignity has been violated. The PGC has been used by several academics in bioethics as well as in human rights theory and in the assessment of reproductive issues (Beyleveld 2012, Beyleveld and Brownsword 1998, Beyleveld and Brownsword 2001, Kohen 2005, Pattinson 2002). Section 5.5 explains and presents the PGC in three stages. This is followed by an examination of the Contingency argument, the Principal of Proportionality and the Precautionary Principle. The final section 5.8 presents the marginal groups under PGC before the conclusion of the chapter.

5.2 Human dignity as a guiding principle

Post World War II there have been many international instruments designed to protect human rights. These instruments were a reaction to the eugenic practices of Nazi Germany. The first international instrument to condemn such human atrocities was the Charter of the United Nations 1945 where the preamble states:

> We the people of the United Nations, determined to save succeeding generations from the scourge of war, which twice in our lifetime has brought untold sorrow to mankind, and to reaffirm faith in fundamental human rights, in the dignity and worth of the human person, in the rights of men and women and of nations large and small.

Shortly after the introduction of the Charter of the United Nations 1945, the United Nations proclaimed the Universal Declaration of Human Rights 1948. Within Article 1, the term 'human dignity' appears, by proclaiming that 'all human beings are born free and equal in dignity and rights.' In 1950 the ECHR was ratified but this, however, made no explicit reference to human dignity as the foundation of human rights (Beyleveld and Brownsword 1998). In fact, human dignity and freedom were only confirmed by the ECtHR as being the very essence of the convention in 2002.[134] However, other international declarations including the International Covenant on Economic, Social and Cultural Rights, 1966 (ICESCR) and the International Covenant on Civil and Political Rights 1966 (ICCPR) saw the

[134] *Pretty v United Kingdom* [2002] (Application no. 2346/02) [65].

foundations of freedom, justice and peace as being intrinsically linked with human dignity.[135] These instruments are relevant to patients' rights but are less applicable to the practice FGT. Therefore, more specific international instruments must be investigated to ascertain whether human dignity is relevant to FGT.

The United Nations Educational, Scientific, and Cultural Organization (UNESCO) Declaration on the Human Genome and Human Rights 1997 states 'Practices, which are contrary to human dignity, such as reproductive cloning of human beings shall not be permitted.'[136] The declaration also states, that germ line interventions could be contrary to human dignity.[137] Such statements are relevant to the practice of FGT because germ line interventions may provide the best solution to eradicate certain genetic conditions within FGT and therefore understanding if germ line interventions truly violate human dignity is of importance. Although the UK is not a signatory to the Convention on Human Rights and Biomedicine 1997, the Preamble requires signatories:

> To take sure measures as are necessary to safeguard human dignity and the fundamental rights and freedoms of the individual with regards to the application of biology and medicine.

This was confirmed a year later by the Council of Europe Protocol in relation to human cloning.[138] Therefore, at a European level, human dignity is a fundamental part of regulating biotechnologies. Internationally, UNESCO's Universal Declaration on Bioethics and Human Rights, continues the theme of human dignity within bioethics. The principles of respect for human dignity, human rights and fundamental freedoms appear as foundations to the declaration.[139] Human dignity

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[135] The ICCPR and ICESCR do not use the term 'human dignity' within their respective preambles, but see the foundations of their declarations arising from 'the recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family.'

[136] United Nations Educational, Scientific, and Cultural Organization Declaration on the Human Genome and Human Rights 1997 Article 11.

[137] United Nations Educational, Scientific, and Cultural Organization Declaration on the Human Genome and Human Rights 1997 Article 24.

[138] Preamble to Council of Europe, Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings 1998.

[139] United Nations Educational, Scientific, and Cultural Organization Universal Declaration on Bioethics and Human Rights 2005 Article 3.1.

appears eight times within the declaration as a guiding principle; therefore, it is a fundamental concept within biotechnology and FGT.

Although within the UK there is a heterogeneous and multi-layered framework, which sees a conflict between utilitarianism and 'human rights' (Rendtorff 2002), the concept of dignity is still prevalent.[140] It is evident within consultation documents regulating new genetic technologies that academics within the UK utilise the term 'human dignity'. For example, the first report from the Joint House of Commons and House of Lords Committee, concerning the Human Tissue and Embryo's Bill[141] stated:

> A total of 38 of the 42 comments (90%) raised objections to the creation of hybrid embryos altogether. Several did so, on the basis of religious, ethical or moral convictions, regarding it as "contrary to human dignity" [...] (Joint Committee on the Human Tissue and Embryos (Draft) Bill 2007: 109).

The concept of 'human dignity' has not just been utilised by academics and others giving evidence for consultation, but also by the committees charged with ultimately scrutinising bills. For example, earlier in the assessment of human reproductive technologies the House of Commons Science Committee stated:

> The demand to regulate morally controversial techniques goes beyond possible harms to individuals or even society. The concern here is more that the use of the treatment offends human dignity rather than any harms that might result from it (House of Commons Science and Technology Committee 2005: 20).

Previous reports concerning the maternal fetal divide, such as embryo and fetal research, have attributed some status to the human embryo and had something akin to 'dignity' in mind. The Polkinghorne Committee Report 1989, which was set up to review and overhaul the code of practice governing fetuses and fetal tissue acknowledged a 'special status' of the fetus (Keown 1993). They go on to say that the fetus is entitled to respect broadly comparable to that of a living person. The Warnock Report (1984), also concluded that the embryo had special status because

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[140] It should be noted that within the United Kingdom devolution has and is continually occurring, but ultimately Parliament has the right to legislate where powers of legislation have not been devolved.

[141] The Human Tissue and Embryos Bill proposed changes to the Human Tissue Act 2004, such as the establishment of a new body called Regulatory Authority for Tissue and Embryos (RATE), but were subsequently dropped. Therefore, the Bill changed its name to reflect those changes and was subsequently called the Human Embryology and Fertilisation Bill 2008 (White 2008).

of having some intrinsic moral importance; thus, must be treated with respect (Jackson 2006). It should be noted that the eventual conclusion of the Warnock committee was essentially a compromise position in order to appease many diverse factions of society (Jackson 2006). Although not specifically a reference to human dignity, the intrinsic nature of humanity is evident.

Furthermore, the Human Genetics Commission (HGC) has stated that in order for respect of persons to be fulfilled, there has to be respect for the equal value, dignity and moral rights of individuals regarding personal information and genetics (Human Genetics Commission 2002). The HGC report on reproductive choices and genetics reaffirmed the significance of dignity within autonomy (Human Genetics Commission 2006). However, GTAC, which governs the ethical approval process of FGT, makes no specific reference to human dignity. But GTAC is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, which implemented the European Clinical Trials Directive.[142] The Directive established that the accepted basis for the conduct of clinical trials in humans is founded on the protection of human rights and the dignity of human beings, with regard to the application of biology and medicine.[143] However, GTAC is a Research Ethics Committee (REC); therefore it's priority is to safeguard the rights, safety, dignity and well-being of people participating in research (National Patient Safety Agency 2009). Therefore, dignity should be an integral part of scrutinising proposed FGT research.

In addition, within the regulation of biotechnologies, vis-à-vis FGT, human dignity emerges as an ethical or moral principle that needs exploration. However, as seen in chapter 3, the regulation of medicine within England and Wales is based upon the principle of autonomy (Jackson 2006). Therefore, any construction of human dignity should include 'autonomy' within it. The World Health Organisation (WHO) recognises that patients have the right to be treated with dignity; and, it was from the fundamental dignity and equality of all human beings that the notion of

[142] Directive 2001/20/EC.
[143] Directive 2001/20/EC s.2.

patient rights was developed (World Health Organisation 2010). Therefore, by exploring human dignity will inform the debate within FGT and the related concepts of patient autonomy. Consequently, it is not exaggerating to characterize it as the overarching principle of international biolaw (Andorno 2009). The international instruments appear to present three ideas about human dignity. Firstly, there is something inherent or intrinsic about human dignity; secondly, it applies to everyone equally; and finally, because it is inherent in every human, it cannot legitimately be taken away (Andorno 2009).[144]

The benefit of utilising human dignity is that it is not contingent upon current social thinking and can be used regardless of time or place. Contemporary human rights and autonomy based theories too often forget this element of the debate, thus leading to incomplete debate and regulation (Dupré 2009). By adding this dimension, issues related to the intergenerational aspect of FGT can also be critiqued and discussed. Despite all these references to human dignity, and as an important concept within the regulation of FGT one has to establish: what is human dignity? The next section explores this more fully.

5.3 What is human dignity?

It should be noted that the terms dignity and human dignity can indicate who can possess dignity. For example, the term human dignity excludes all those outside of the homosapien species without debate, whereas dignity is inclusive of anything that can possess dignity. Guidance about what human dignity is, is merged within the various sources of human dignity which Schulman (2005) identifies as: classical antiquity, biblical religion, moral philosophy (Kantian), and 20th century constitutions and international declarations. The focus within this section will be upon classical antiquity, biblical religion, and moral philosophy as this will help inform the documentary analysis which does not include these sources.

[144]It is not the contention of this thesis to deal with the consequence of such 'dignity' in relation to high primates, but it is important to note that as research develops upon higher primates the difference between 'humans' and certain primates will becoming increasingly smaller.

Dignity within classical antiquity can be traced back to Roman times. Dignity is akin to worthiness and associated with rank, honour and excellence (Schulman 2005). Such a concept of dignity has been viewed as empirical or external dignity (De Baets 2007, Gewirth 1998). Therefore, dignity becomes contextualised depending on time, relative space, and social position. Given the increased complexity that biotechnologies add to the debate on FGT, it should be clear that associating dignity with rank and honour, turns dignity into a contingent property based upon social class and a form of excellence (Schulman 2008). The failure of contingent propositions will be seen within 5.6. More importantly, however, is whether such a position contradicts human dignity (Andorno 2009, Beyleveld and Brownsword 2001). Deciding who has dignity based on social position, makes dignity exclusively concerned with the dignified conduct of a social group, not of humanity. Therefore, as a source for defining human dignity it will not be used.

Guidance for defining dignity can also be found from biblical sources (Schulman 2008). However, although biblical guidance is noteworthy, it remains bound to a notion of 'god', and does not provide any further grounding of human dignity, which could be useful for debate. Therefore, biblical sources will not inform the derivation of human dignity within the thesis. The search to construct human dignity should therefore take place within the moral philosophy part of Schulman's identified sources.

'Human dignity' consistently emerges as an abstract concept which needs to be defined or grounded. Human dignity has been associated with genetic uniqueness. Therefore, dignity is genetic uniqueness and has been seen within the cloning debate as a way in which dignity can be violated. However, if genetic uniqueness grounded human dignity then monozygotic twins would violate human dignity by their mere existence. More importantly, our genes do not, on their own, bind our future life to a particular course (Caulfield 2003). Therefore, the concept of human dignity must be grounded within a theory that is dependent on something other than genetics. Kass (2008) identifies that within moral philosophy there is still tension about what human dignity is.

> There are differences of opinion about exactly what it means and what it rests on, a difficulty painfully evident when appeals to "human dignity" are invoked on opposite sides of an ethical debate, for example, about whether permitting assisted suicide for patients suffering from degrading illnesses would serve or violate their human dignity. There are also disagreements about the extent to, which considerations of human dignity should count in determining public policy (Kass 2008: 297).

These types of questions appear to further complicate what is entailed in human dignity but as Schulman (2008) identifies, there are several possible answers to the problems that Kass observes:

> One possible answer discussed in our report is that it is morally permissible (and perhaps even admirable) for such a patient, who finds the prospect of years of dementia humiliating or repellent and who is reluctant to become a burden to his family, to forgo medication and allow heart disease to carry him off in a more dignified and humane way. Another possible answer is that it is morally impermissible, because deliberately hastening the end of one's life, even by an act of omission, is incompatible with the equal dignity and respect owed to all human life. A third answer is that respect for the dignity and autonomy of all persons requires us to defer to the personal choice of a competent individual in such intimate matters, regardless of how he or she might decide (Schulman 2008: 4).

It is important to identifying a common thread for human dignity from these answers that can guide regulators, practitioners and individuals in the maternal fetal divide. Within moral philosophy according to Ashcroft (2004) there are four distinct groups within which a person can be situated in when talking about dignity:

1. Those who consider dignity talk as incoherent and unhelpful
2. Those who find dignity as illuminating, but still reducible to autonomy such as Beyleveld and Brownsword do utilising Gewirthian theory.
3. Persons who consider dignity as being part of a family of concepts
4. Those who see human dignity as a metaphysical property, which grounds human rights (Ashscroft 2004: 679).

Those within Ashcroft's first group argue that, despite human dignity being identified as being embedded in the modern debate surrounding genetics and medical ethics, it can appear as an ungrounded or a circular concept that is based upon humanity, although it is unclear what it is about our humanity that gives people dignity (Feinberg 1980). Because of this lack of clarity Helga Kuhse forwards:

> [H]uman dignity plays a very dubious role in contemporary bioethics discourse. It is a slippery and inherently speciesist notion, it has a tendency to stifle argument and debate and encourages the drawing of moral boundaries in the wrong places. Even if the notion could have some use as a short-hand version to express the principles such as 'respect for persons,' or 'respect for autonomy.' It might, given its history and undoubtedly long-lasting connotations accompanying it, be better if it were for once and all purged from bioethics discourse (Kuhse 2000).

Ruth Macklin would agree with Kuhse, as she argues that the concept of dignity is a useless tool and is the equivalent to respecting autonomy (Macklin 2003). However, dignity only becomes useless if it is not entrenched in a theory that goes beyond the intrinsic and abstract nature of dignity. English lawyers may fit into this first group of people, but one has to accept that dignity is an important part of regulation and practice (Brownsword 2003). Therefore, as Van Der Graaf and Van Delden identify, it is the job of ethicists to clarify the position of dignity within the social, legal and ethical debate (Van Der Graaf and Van Delden 2009). Given that the second, third and fourth groups identified by Ashcroft are not mutually exclusive a tension between autonomy, rights and duties emerges. Therefore, an ethical theory that transcends these groups would be preferable. Key theorists and academics that utilise human dignity to inform their theories[145] include Immanuel Kant, Jürgen Habermas, Leon Kass, Charles Foster and Alan Gewirth. These will be examined in turn below.

5.4 Moral theorists and human dignity

Within early moral philosophy, Immanuel Kant utilised human dignity as the very basis for his theory Categorical Imperative:

> [T]hat, which constitutes the condition under which alone something can be an end in itself has not merely a relative value, that is, a price, but an inner value, that is, *dignity* [...]Morality, and humanity insofar as it is capable of morality, is that, which alone has dignity (Kant, Gregor et al. 1998: 42).

From dignity Kant goes on to construct his Categorical Imperative. Without engaging with the complete work of Kant the Universal rules within the Categorical Imperative has two formulas: The Formula of Universal Law; and The Formula of

[145] For a well written synopsise of those who utilise human dignity see Foster (2011).

the End in Itself. The Formula of Universal Law indicates that one should act only on a maxim that at the same time one would want it to become a universal law (Kant, Gregor et al. 1998: xviii); and The Formula of End in Itself (Kant's most recognised principle) means that persons should act in a way, to others and themselves, never just as a means, but at the same time an end (Kant, Gregor et al. 1998: 43-44). Both these rules are moral absolutes (Pullman 2002). However, Schulman (2005) argues that because of the narrow and constricted account of Kant's principle, it cannot cope with modern day biotechnological advancements because it is difficult to apply, and is too rigidly focused within the deontological and consequentialism debate. These arguments against employing a Kantian model appear as toothless accusations. Bioethicists have claimed to use Kantian theory successfully as a method of analysis of modern biotechnology (President's Council on Bioethics 2008). Also, regardless of ethical theory, one will be placed within deontological or consequentialist reasoning..

Kant attributed inherent dignity to being rational and autonomous, but saw beings as things in themselves, not subject to natural phenomena (Kant, Gregor et al. 1998). Therefore, Kantian theory does not allow persons to decide right and wrong from any empirical reference, but purely from rational thought which presents difficulties, because persons are subject to both phenomena and noumena (Gewirth 1983). More importantly, Kant's Categorical Imperative derives it acceptance from the logical implication of acceptance of morality. Starting from the acceptance of morality makes Kant's theory contingent; therefore, those such as moral error theorists[146] and moral subjectivists[147] can easily disregard the Categorical Imperative by dismissing that morals exist (Joyce 2007).[148] This fatal flaw makes the Categorical Imperative unusable as a foundational theory within the thesis, because a more defensible theory should be used.

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[146]Someone who thinks that although our moral judgments aim at the truth, they systematically fail to secure it. The moral error theorist stands to morality as the atheist stands to religion (Joyce 2007).
[147]Someone who believes that moral facts exist but holds that they are, in some manner to be specified, constituted by our mental activity. The slogan version comes from Hamlet: "there is nothing either good or bad, but thinking makes it so" (Joyce 2007).
[148] Further discussion about the weakness of contingent arguments is conducted within 5.6.

Habermas (2003), on the other hand, recognizes that as genomic technologies increasingly become available, the choices of those technologies bears on the future of human nature. Biotechnologies such as genetic engineering pose ethical issues across the human species. Such issues concern not merely our self-understanding as members of a particular culture or tradition, but how to understand our basic human dignity (Habermas 2003). The core of human dignity, and thus the basis for a human-species ethics, lies in the capacity of human beings for autonomous self-determination. The foundation to Habermas's theory is his species ethics, which seeks to answer questions relating to the contemporary debate by addressing what it is to be human. Central to Habermas's species ethics (2003) is the need to understand what it is to be human and how being human is affected by new contemporary biotechnologies which seek to make life an artefact rather than the product of some form of natural process. Such technologies are an affront to his species ethics and thus dignity. However, the species ethics Habermas utilises is:

> [T]he most speculative idea in a book that is characterized by an innovative élan and a significant number of promissory notes. For it is entirely unclear, to begin with, how this species-ethics is supposed to generate the individual obligations demanded by the gravity of genetic interventions or how we are supposed to imagine this process of reflection and self-clarification occurring on a global scale (Anderson 2005: 821).

More importantly, the species ethics relies on one considering the genome as a programme rather than as an intricate thing that interacts with more than just genetics, but with the environment and ultimately the public. His argument also fails to distinguish why assumed consent, with regards to enhancements, is any different to that of measures seeking to treat or correct an individual's gene back to within 'normal functioning'. It may rule out certain practices, but it blurs the boundaries between methods that seek to enhance and those considered therapeutic (Rorty 2003). Considering these problems Habermas' species ethics will not be utilised to ground human dignity. However, Habermas does raise a serious and fundamentally important thought process about how modern day technologies are impacting upon our perception of theoretical notions such as dignity. He questions whether we ought to change the genome of future generations. This thesis engages with such

issues; therefore, such a reflective stance to instigate dialogue is important because it can help provide resolutions to many of the issues identified later in the thesis.[149]

A contemporary academic who considers that human dignity is a key component within modern advances in genetics is Leon Kass. Kass sees modern advances in biology and medicine as invoking an inhuman basis (Kass 2002, 2008). Kass, as does Habermas, sees modern biotechnology as dehumanising, which other bioethicists are blind to. In order not to make the same mistake Kass (2002) argues that human dignity should be rooted in a proper anthropology that goes beyond the said dignity of 'persons,' to reflect and embrace the worthiness of embodied human life (Kass 2002: 18). The dignity he seeks uses our awareness of need, limitation, and mortality in such a way that people naturally formed a way of life that has engagement, depth, beauty, virtue and meaning, not despite our embodiment, but *because* of it (Kass 2002: 18). However, despite Kass's movement to a more natural, biological and anthropological vision of biotechnologies, he never actually defines what human dignity is, thus leaving the concept without useful meaning. Despite defending this allegation in later writings, by claiming everyone can in fact readily recognize dignity, both when it is shining and when it is extinguished (Kass 2008); such a defence lacks any substance beyond one's own interpretation of their own 'human dignity.' By Kass's own admission:

> The dignity of being human is rooted in the dignity of life itself and flourishing in a manner seemingly issuing only in human pride, completes itself and stands tallest when we bow our heads and lift our hearts in recognition of powers greater than our own. The fullest dignity of the god-like animal is realized in its acknowledgement and celebration of the divine (Kass 2008: 329).

Such a statement makes human dignity nothing more than a reworded religious theory. Considering the inherent problems with such a theological approach (see above), the interpretation of human dignity forwarded by Kass will not be followed.

A relatively new approach to human dignity is that of Charles Foster. He claims, quite simply, that human dignity is the bioethical theory of everything and that

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[149] See 7.4 and 8.4.

human dignity can provide the answers to medical and bioethical questions that other theories cannot (Foster 2011: 1). He considers human dignity to be connected to human flourishing (Foster 2011: 4). It is not another name for the authoritarian imposition of some powerful group's vision of human flourishing, all in the legitimating name of human dignity (Brownsword 2012). Human dignity, according to Foster, is a neo-Aristotelian concept based virtue.

However, although he criticizes autonomy based approaches such as those taken by Beyleveld and Brownsword due to their alleged limitations, the paradigm that Foster suggests does not seek to provide answers. In fact, he warns the reader against searching for answers within the book (See Foster 2011: 11). Therefore, the notion of human dignity expressed by Foster appears to be a set of well thought out questions without any answers. Also, the neo-Aristotelian 'virtue' ethic fails in the same way as the use of dignity within Roman times. To the end that the thesis is seeking to establish answers (although it may pose more questions as well!) this approach will not be used.

Another contemporary theorist associated with human dignity is Alan Gewirth. On first appearance Gewirth is seemingly more concerned with human rights theory than human dignity. However, contemporary theorists have connected dignity to Gewirth (Beyleveld and Brownsword 1998, Beyleveld and Brownsword 2001) and have seen dignity as the basis of his theory (Steigledger 1998). Gewirth does not object to human dignity being the foundation of rights; but for different reasons than the above theorists. Gewirth sees reason and voluntariness or free will as generic features of the basis of human dignity (Gewirth 1998: 168). According to Gewirth, if 'X having dignity' is equivalent to 'X having human rights', then it does not add substantially to the attribution of rights (Gewirth 1983). However, human dignity derived from an logically necessary form of moral theory can help identify what human rights social and legal institutions ought to recognise or facilitate (Gewirth 1979); therefore, providing a helpful critique of the FGT debate.

Gewirth goes further to identify that human dignity within international declarations are only implicit (Gewirth 1996). However, an explicit reference to human dignity

can be derived from the explicit dialectically necessary mode of derivation of the Principle of Generic Consistency (PGC) (Gewirth 1996: 66).[150] The argument is dialectic (as opposed to assertoric) when it begins from statements presented as being made or accepted by an agent and examines what they logically should do, rather than statements made by the writer themselves (Gewirth 1996: 16). This adds theoretical and analytical strength to human dignity because, unlike a contingent basis, a dialectically necessary foundation cannot be dismissed by not accepting the basis it stands upon (See Kant above). The link between human dignity and the PGC is that violating the PGC is to violate human dignity. Dignity serves as the grounding or antecedent to human rights (Gewirth 1992: 14). As Gewirth states:

> [T]he idea of human dignity can serve as the justificatory basis for regarding the needs of human agency as sufficiently important or compelling that they can provide, in turn, an adequate justificatory basis for human rights (Gewirth 1998: 174).

There has been widespread criticism of Gewirth's Principle of Generic Consistency, with the majority being defended by Beyleveld, and Gewirth (as will be shown below) offers the most robust theory that is associated with human dignity.

Therefore, in identifying that the PGC can be utilised to identify whether actions or practices violate human dignity; the PGC can be taken to govern the making of all such judgements surrounding FGT and how FGT practitioners, patients and regulators should approach the subject. It can govern all relevant persons and the relationship between them because the PGC governs the rules of moral agency and moral patients, or those to whom one has a moral obligation (Pullman 2002); thus, making the PGC most suitable to address the issue of human dignity.

5.5 Principle of Generic Consistency (PGC)

Before the Principle of Generic Consistency (PGC) can be explained some opening remarks and clarifications should be made. These issues include the dialectic necessary method that Gewirth utilises how Gewirth defines morality; what 'rights' are under the PGC, and; the constitution of the Generic features of Agency. It

[150] Here dialectic refers to statements made from an agent's point of view. See 5.5.1 for further explanation.

should be noted at the outset that where a person has 'lost their dignity' behaviourally they are not someone who can be treated as without dignity (Rolston 2008). Having dignity and being treated with dignity are two closely linked debates, but the thesis will focus on the construction of dignity in general, because this reflects the documents and literature of the thesis.

5.5.1 Starting premise under the PGC

Firstly, the PGC is not foundationalist in the sense that it begins from self evident moral or evaluative statements. The PGC is grounded in statements of action, which are prudential (Gewirth 1983: 14). A prudential claim, or right, is a justified claim, or entitlement, whose justificatory basis or criterion is the self-interests or purposes of the rights holder or claimant themselves (Gewirth 1985: 302). Despite starting from prudential statements, the PGC is a moral theory through prudential reasoning, due to the second stage of the PGC. The move from prudential reasoning to moral reasoning is not motivational but logical (Gewirth 1978: 146). The movement is logically necessary if there is a sufficient condition that justifies an agent having generic rights,[151] then logically those rights are held by all others satisfying that condition (Gewirth 1978: 146).[152] However, the movement from a prudential right to a correlative ought judgement (or instrumental duty), does not indicate a movement from a prudential to a moral theory (Gewirth 1978: 145). Therefore, a key and fundamentally important question is: How can the PGC be a moral principle if it is derived from claims or judgements that are themselves not moral? The key to this transition is the principle of universalisability, which is considered later in the chapter. However, to summarise:

> [The] generic rights referred to in the antecedent are prudential; but the generic rights referred to in the consequent are moral. The antecedent's rights are prudential in that the agent claims them with a view to serving or upholding his own interests or purposes. But the consequent's rights are moral in that, in setting them forth, the agent has now to uphold or take favourable account of the interests or purposes of other persons -namely, of all prospective purposive

[151] See Stage II and the principle of universalisability combined with the Argument for Sufficient Agency.
[152] Being based on logic makes the reasoning a necessary independent valid condition that is not contingent.

> agents, whose generic rights, and hence whose possession of freedom and well-being, he is now logically committed to endorsing. Thus the logically necessitated generalization of the agent's prudential right claim yields a moral rights judgment because the latter, generalized judgment upholds the interests of persons other than or in addition to the original agent […] (Gewirth 1985: 304).

In order to progress through the stages of the PGC, Gewirth uses the dialectically necessary method (Gewirth 1978: 42-47), which is taken from the internal viewpoint of a prospective purposive agent (or agent for short). The method is derived from self agreement based on pure thought, rather than debate about which way to act. The dialectically *necessary* method is different to a dialectic *contingent* argument. The dialectic contingent method begins from a singular or general statement or judgement that reflects the beliefs or ideas of a person or group (Gewirth 1978: 42). That belief can be rejected purely on principle where an agent chooses not to adhere to it or believe it. Therefore, the conclusion of a dialectic contingent argument can be coherently rejected. An argument becomes dialectically *necessary* when:

> [...] the statements it presents reflect judgements all agents necessarily make on the basis of what is necessarily involved in their actions [...]. The statements the method attributes to the agent are set forth as necessary ones in that they reflect what is conceptually necessary to being an agent who voluntarily or freely acts for purposes he wants to attain (Gewirth 1978: 44).

Despite a dialectically contingent argument having less force than a dialectically necessary argument, it can provide additional weight to the PGC. Therefore, where regulation is based upon a contingent proposition such as human rights, then the PGC can be taken into account.[153] However, before the PGC can be expanded further terminology and the foundations of the PGC will be discussed.

5.5.2 Morals, rights, duties and voluntariness under the PGC

Gewirth opens his book *Reason and Morality* (1978) by defining morality as:

> A set of categorically obligatory requirements for action that are addressed at least in part to every actual or prospective agent, and that are concerned with furthering the interests, especially the most important interests, of persons or recipients other than or in addition to the agent or the speaker. The requirements are categorically obligatory in that compliance with them is mandatory for the conduct

[153] See 5.6.

> of every person to whom they are addressed regardless of whether he wants to accept them or their results, and regardless also of the requirements of any other institutions such as the law or etiquette, whose obligatoriness may itself be doubtful or variable. Thus, although one moral requirement may be overridden by another, it may not be overridden by any non-moral requirement, nor can its normative bindingness be escaped by shifting one's inclinations, opinions, or ideals (Gewirth 1978: 1).

Therefore, what is moral covers a wide range of situations and importantly covers FGT. What is 'moral' for Gewirth, goes beyond the above definition of morality, and requires moral philosophy to go the next step. Gewirth explains that the intention of moral philosophy is to answer three central questions, with their own sub questions:

> First, there is the *authoritative question*: why should one be moral, in the sense of accepting as supremely authoritative or obligatory for one's actions the requirement of furthering or favourably considering the important interests of other persons, especially when these conflict with one's own interests? Second, there is the *distributive question*: whose interests other than one's own should the agent favourably consider in action? To, which persons should the goods [or benefits] accruing from such consideration be distributed in actions and institutions? Third, there is the *substantive question*: of which interests should favourable account be taken? Which interests are good ones or constitute the most important goods (Gewirth 1978: 3)?

All the above questions appear relevant for the regulation and practice of FGT and human dignity because they require us to answer questions such as: should a mother make moral decisions? If she should, whose interests should be taken into account? The fetus.? The father's? And finally, if they are important, regardless of what those interests are, should those rights be placed above that of the decision maker themselves, in reaching a decision of whether to have FGT? In answering these questions, one can see what the rights and duties of patients should be and how regulators should act in order to facilitate the right balance of interests and goods within FGT. Also, it can be ascertained what rights and duties a fetus, parent, mother or third party may have.

Important elements of the PGC are the Generic Features of Agency (GFA). It is the unjustified violation of the generic features that would constitute a violation of human dignity.[154] Gewirth refers to the GFA in terms of 'action' comprising of:

> [...] in the strict sense that is relevant to moral and other practical precepts, [having] two interrelated generic features: voluntariness or freedom and purposiveness or intentionality (Gewirth 1978: 27).

Therefore, the concepts of voluntariness and purposiveness (Gewirth 1978: 31-37) need defining, as they both can appear abstract and vague. However, within the PGC Gewirth refers to voluntariness as:

> [...] behaviours or movements to be actions in the strict sense and hence voluntary or free, certain causal conditions must be fulfilled. *Negatively*, the behaviours must not occur from one or more of the following kinds of cause: (a) direct compulsion, physical or psychological, by someone or something external to the person; (b) causes internal to the person, such as reflexes, ignorance, or disease, that decisively contribute, in ways beyond their control, to the occurrence of the behaviour; (c) indirect compulsion whereby the person's choice to emit the behaviour by their own unforced and informed choice. *Positively*, the person must control their behaviour by their own unforced and informed choice. This does not mean that whenever they choose to do something they do it, for they may be unable to do it. It means rather that when their behaviour is free and voluntary, their unforced and informed choice is the necessary condition of the behaviour [...] person or agent to whom choices belong may be viewed as an organised system of disposition in, which such informed reasons are coherently interrelated with other desires and choices. [...] it is the person who controls his behaviour by their unforced choice, so that is voluntary (Gewirth 1978: 31).

Therefore, voluntariness involves both positive and negative behaviours, and consequently the PGC involves both positive and negative rights, which accords with the distinction in medicine between refusing life saving treatment and a right to treatment. However, can pregnancy fit Gewirth's freely chosen and voluntariness actions, where examples that indicate the difference between non voluntary choices, are such as being held at gun point, and voluntarily choosing to be fired (See Gewirth 1978: 31-37)?

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[154] The reason that an 'unjustified' violation of the PGC is against human dignity is that where there is a conflict between the rights of two agents, it may be justified to violate the PGC in order to maintain dignity overall.

It could be contended that pregnancy falls into the involuntary category. However, Gewirth indicates that causes internal to the person, such as reflexes, ignorance, or disease that decisively contribute, in ways beyond their control, to the occurrence of the behaviour are not voluntary (Gewirth 1978). However, pregnancy is not a disease and in the majority of cases entered into voluntarily. One has to consider that a pregnancy may be unwanted/unplanned or forced upon a woman through rape. Such cases are clearly in the first place not voluntary. It could be argued that situations that fit the above circumstances cannot fall within the remit of the PGC. However, in general, pregnancy is a freely chosen pursuit by many. When it is not, there is a choice about continuing a pregnancy or not. Regardless of the person's view on the ethical side of pregnancy, given the current state of technology there is a choice about continuing the pregnancy. Although controversial, such a statement is amoral in that it merely states that an agent has a choice once they are aware that they are pregnant. One might consider such actions as a mixed action under Aristotle's construction of voluntary and involuntary actions (Aristotle, Rowe et al. 2002). However, actions within such a circumstance are still voluntarily chosen despite taken under pressure and the outcome is controlled by an analysis of mitigating circumstances (Rees 2000). Therefore, pregnancies and the resultant choices that fall within FGT would be considered voluntary.

Connected to voluntariness is purposiveness. Gewirth goes on to state that purposiveness consists of:

> The behaviours that are the possible objects of these and other moral precepts are hence not aimless but rather goal-directed, at least in the sense that they envisage more or less clearly a certain content to be effected or achieved, even if at one level this content consists only in a certain mode of acting or in observance of certain rules or formal requirements. The persons who engage in this behaviour are regarded not merely as loci of movements, but as controlling their movements for reason they can make their own, because they want to engage in that behaviour either for its own sake or for some result to be achieved (Gewirth 1978: 37).

Therefore, purposiveness indicates an active thought to do something, and is prudential. For example, if I want to go fishing, merely wanting to go fishing does not cast any moral judgement about fishing. In wanting to go fishing, I actively engage in the pursuit of fishing, hence I have a purpose to my action. Having

identified the principle behind an agent, Gewirth introduces freedom, wellbeing and the GFA, which are fundamental principles of the PGC. Therefore, these concepts also need defining. 'Freedom' is frequently used by Gewirth within the PGC and refers to the ability of an agent to control:

> [...] each of their particular behaviours by their unforced choice and [...] his longer-range ability to exercise such control [...]. The loss of disposition or long range freedom, such as by imprisonment or enslavement makes all or most purposive action impossible, while to lose some occurent or particular freedom debars one from some particular action but not from all actions. Nevertheless, the loss of freedom in a particular case deprives one of the possibility of action in that case (Gewirth 1978: 52).

Therefore, facilitating autonomy appears as a key concept in relation to parts of the PGC. Furthermore, there are three levels to an agent's wellbeing within the GFA: basic, non-subtractive and additive goods. The foundations of the GFA are the basic goods, which include:

> [...] the proximate necessary preconditions of his performance of any and all of his actions [...]. [Therefore,] certain physical and psychological dispositions ranging from life and physical integrity (including such of their means as food, clothing and shelter) to mental equilibrium and a feeling of confidence as to the general possibility of attaining one's goals (Gewirth 1978: 53-54).

The basic goods are fundamental for an agent to act (the principle of action). These include life itself, capacities involved to make choices and the mental equilibrium sufficient to translate one's preference into active pursuit of one's purpose (Beyleveld and Brownsword 2001). For an agent to have the possibility of successful action non-subtractive and additive goods emerge as sub categories. Non subtractive goods are those goods needed to be able to act successfully, without thereby being needed for the possibility of acting. For example, the possession of accurate information in order to make informed decisions (Beyleveld and Brownsword 2001: 71). Therefore, non-subtractive goods consist of goods that an agent needs to retain what it already considers as 'good' apart from basic goods (Gewirth 1978). Additive goods consist of whatever an agent needs to increase its existing level of capacity of purpose-fulfilment, and whatever it wishes to have, apart from basic and non subtractive goods (Beyleveld 1991: 17). Such additive goods depend on the individual and can range from the latest mobile phone to having the newspaper every Sunday morning.

Within the PGC, the generic features of freedom and well being are prudential. The PGC maintains that an agent must consider that they have 'strong' or 'claim' rights (Gewirth 1978: 65-67). Claim rights are correlative to duties on the part of others not to interfere with the doing or possession of that to which the rights-holder has the right (Beyleveld 1996). Under certain conditions an agent must concede positive rights, but also must consider that they have negative rights as well. The concepts of negative and positive claim rights are equivalent to those suggested within 1.2. Claim rights should be distinguished from mere liberties (weak rights), which indicate that it is merely permissible to do something, but it can be restricted in certain circumstances.

Where rights are not restricted, an agent can waiver their rights or not exercise them at all. However, the wavering of a duty towards another agent is not permissible. In conjunction with the GFA are the duties of aid and non interference. The duties of aid and non interference are conditional and are subject to the provisos of 'own unaided effort' and 'comparable costs.' Therefore, an agent may have a duty to aid another agent to secure its generic features only where it is unable to do so itself, but only when doing it does not deprive me of the same or more important generic capacities, as measured by the degree of needfulness for action (See Gewirth 1978: 217-230).

The thesis will not refer to the generic features as being divided between substantive (well being) and procedural (freedom), because the division appears to add contingency to the PGC. More importantly, it allows for a simpler presentation of the PGC. The PGC will be presented in three stages and follows the principle of *Reductio ad Absurdum*.[155] In order for the PGC to succeed, it must be shown that it is contradictory for an agent to hold that it is permissible for it to do anything that violates the PGC and consequently human dignity. However, an agent can forward a logically incompatible view with the PGC, but it is logically impermissible to do so. In forwarding an incompatible subjective viewpoint an agent contradicts that it is an

[155] Reducing a proposition to the absurd and thus showing the contradictory nature of the argument.

agent due to the dialectically necessary element of the PGC.[156] In fact, the PGC allows for agent fallibility, and thus may not condemn an agent for acting immorally if their good faith intention had been to act morally in the terms of the PGC (Holm and Coggon 2009: 305). Therefore, an agent must act in a practically reasonable or rational way in accordance with the PGC. The PGC is set out in three stages, moving between each stage through logical deductive and dialectically necessary reasoning.

5.5.3 Stage 1

In claiming that I am a prospective purposive agent (agent):[157] i.e. those who act voluntarily for purposes that they have freely chosen (purposive agents), as well as those who intend to do so, which they have the capacity to do so, which they have some disposition to exercise (Beyleveld 1991: xxxvi), I claim:

1. I do (or intend to do) X voluntarily for a purpose E I have chosen.

Because E is my freely chosen purpose, I attach some positive value to E (which is prudential and not definitive), and because my purposes have a motivating power sufficient to move me to act for E (G 49), I must also claim:

2. E is good,

Meaning only that *I* attach sufficient value to E to motivate me to pursue E (i.e. I value E proactively). To signify this claim and not contradict I am an agent, this must be expressed as (2). If I do not accept (2), then I deny that I am an agent, which is to say that it is dialectically necessary for me to accept (2).

3. There are generic features (needs) of agency.[158]

In order to be an agent a minimal rational capacity must be possessed, including the ability to recognise that to achieve an end I must possess or obtain necessary needs to these end (Beyleveld 1996: 20). Therefore, I must accept:[159]

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[156] There is an exception to this rule as purposes that are chosen under any circumstance whatsoever are excluded (See Beyleveld 1991: 47-56).

[157] Gewirth uses the acronym PPA for prospective purposive agent PPA, but for simplicity the term 'agent' will be used to signify a prospective purposive agent.

[158] Gewirth separates the GFA into conditions necessary for action and conditions necessary for successful action, regardless of what those conditions are.

[159] By the principle 'whoever pursues an end must be prepared to pursue the means necessary to achieve the end'. If I do not accept this principle, I deny that I am an agent (because agents, by definition, do things as perceived means to their chosen ends).

4. My having the generic needs is good for my achieving E *whatever* E *might be* ≡ My having the generic needs is categorically instrumentally good; therefore, my having the generic features is a necessary good.

5.5.4 Stage 2

Because

5. I value my purposes proactively, this is equivalent to me having to accept I categorically instrumentally ought to pursue/defend my having the generic needs.

As it follows from (4) that I must be motivated to pursue my generic features for my purpose and because 'ought' implies 'can', if others interfered with my having generic features, I would not be free to pursue or defend (5). Therefore, because my having the generic needs is necessary for me to pursue having the generic needs, I must hold:

6. Other agents categorically ought not to interfere with my having the generic features *against my will*, and ought to aid me to secure them when I cannot do so by my own unaided efforts *if I wish so*,

Due to the other-referring categorical 'oughts' correlate with claim rights, I must hold:

7. I have both negative and positive claim rights to have the generic needs.

5.5.5 Stage 3

8. It follows (purely logically) that if I am an agent, by not considering that I have a right to the generic features, I deny that I am an agent if I do not consider that my being an agent is sufficient reason for my having a right to have the generic features. I have a right to have generic features → (I am an agent → I have a right to have the generic features).

However, (8) cannot be logically followed unless it is secured by the 'Argument for Sufficient Agency' (ASA) (Gewirth 1978 109-110). The ASA is as follows:

a) If it *does not entail* that I must hold (8) then I must be able to deny 'I am an agent → I have the generic rights' without denying that I have the generic rights.
b) To deny I am an agent → I have a right to have the generic features, is to assert that my having some property D - a quality not necessarily possessed by all agents – is necessary for me to have the generic rights. To deny 'I am an agent → I have a right to have the generic

features' is to assert 'I have a right to have the generic features → I have D'.

c) 'I have a right to have the generic features→ I have D' logically assents to 'I am an agent without D → I do not have generic rights'. In other words, to be consistent with 'I have the generic rights → I have D', I must consider, *even though I am an agent*, that I do not have the generic rights *if I do not have D.*
d) However, on the basis of my having to hold (8), I must, *provided only that I am an agent*, consider that I have a right to have the generic features–, which is to say that I must, *by virtue of being an agent*, consider that I have a right to have the generic features, *whether or not I have D*.
e) 'I must consider, *even though I am an agent*, that I do not have the generic rights *if I do not have D*' contradicts 'I must, *by virtue of being an agent* consider that I have the generic rights, *whether I have D or not*'.
f) Since 'I am an agent → I have D' is to contradict what my having to hold (8) entails, 'I am an agent → I have D' contradicts that I must hold (8).
g) Since 'I am an agent → I have D' is equivalent to denying 'I am an agent → I have a right to have the generic features', to deny 'I am an agent → I have the generic rights' is to deny that I must hold (8).
h) Thus, in order not to deny (8), I must reaffirm, I have a right to have generic features → (I am an agent → I have a right to have the generic features).

Since, I deny I am an agent if I deny (8); consequently every agent also does so, thus making (8) dialectically necessary for every agent. Having secured (8) through the ASA, in order to progress the PGC further, another principle must be introduced: the principle of universalisability. The principle of universalisability, states:

> If some predicate P belongs to some subject S because S has the property Q (where the 'because' is that of sufficient reason or condition, then P must also belong to all other subjects S_1, S_2... S_n that have Q. If one denies this implication in the case of some subject, such as S_1, that has Q, then one contradicts oneself. For in saying that P belongs to S because S has Q, one is saying that having Q is a sufficient condition of having P; but in denying this in the case of S_1 one is saying that having Q is not a sufficient condition of having P (Gewirth 1978: 105).

For example, if I have a right to have my work marked because I am a student, then anyone else that is a student, I must also logically conclude, also has that right because they are students regardless of any other features I may like or dislike. Therefore, using the principle of universalisability it follows that:

9. A possible agent is an agent → All other possible agents have the right to the generic features

10. All other possible agents have the right to the generic features
11. I have a right to have the generic features and other possible agents have a right to have the generic features ≡ All agents have a right to have the generic features ≡ Principle of Generic Consistency.

From these statements, it follows by once again using the principle of universalibilty:

12. Principle of Generic Consistency applies to all agents.

Although the PGC is forwarded as being dialectically necessary and introduced in regards to human dignity, as stated previously the principles of autonomy and human rights are seen as contemporary concepts that must be addressed within FGT.[160] Given that autonomy stems from the concept of human rights, a contingent argument in relation to human rights for the acceptance of the PGC as a critique can also be forwarded. In doing so, those who maintain that there are such concepts as autonomy and human rights, but do not agree with the dialectically necessary argument of the PGC, will still be bound by it through their own contingent acceptance of autonomy and human rights.

5.6 Contingent argument for the PGC

Beyleveld (1996, 2012) forwards a contingent argument dependent upon the acceptance of human rights, which would also make the GFA applicable. The argument is contingent as it relies on the agent to recognise (1) I have human rights. An agent can deny the assertion of (1) and all that follows from (1). However, international institutions and countries, such as the UK and the USA, recognise human rights. Therefore, within the context of FGT any agent denying the existence of human rights can be shown those instruments. For those still denying that human rights exist, but still asserting that autonomy exists, refer to a right that is derived from human rights theory so must still accept the PGC or contradict themselves (Gewirth 1978). Therefore, having a contingent argument based on human rights adds to the strength of the PGC as an underlying principle to guide regulation, practice and individual decisions.

[160] See chapters 6-9.

Starting from the statement that (1) I have human rights, it follows that (la) I am human → I have R-rights. Having already stated the principle of universalisability above, it requires one to concur that (2) X is human → X has R-rights. Therefore, (2a) All human beings have R (rights). Having established (2a) it follows (3) A has a right to y → A has a right to the necessary means to exercise y. From (4) there are generic feature (*GF)* (which are necessary means to the exercise of y, whatever y might be), as a result of (4) one must agree that (5) whatever A has a right to; A has a right to have the GF. Having stated in (2a) that all human beings have R-rights, I must assent to (6) all human beings have a right to have the *GF,* whatever R are. Leading to (7) all humans have a human right to have the GF. (8) Any being granted a claim-right must be capable of exercising it because in order to be able to exercise a right a being must be an agent. It follows that I must assent to (9) All agents have a (claim) right to have the GF (which is the PGC) (Beyleveld 1996).

Therefore, the contingent argument for the PGC from human rights demonstrates that anyone who claims to have a human right to anything would contradict that claim if they did not accept that all agents have a right to have the GFA. Therefore, anyone that accepts human rights must accept and act in accordance with the prescriptive requirements of the PGC (Beyleveld 1996, 2012). Consequently, human dignity is intrinsic within human rights instruments as well as those regulations governing the practice of FGT. Having secured the PGC as the principle that an agent must follow on pain of contradicting that they are an agent, it logically follows to ask: who is an agent?

5.7 Clarifying: who is an agent?

5.7.1 Principle of proportionality

It could be contended that despite the PGC being dialectically necessary, it has no practical significance as it cannot be demonstrated with the same degree of stringency that there are other agents (Beyleveld and Pattinson 2000). Identifying an agent is not as intuitive as it may initially appear and these beings are called ostensible agents. There are a number of marginal groups that may be afforded protection under the PGC, because of their status as ostensible agents. In order to

assess if an agent is an agent, Gewirth proposes that the principle of proportionality should be utilised by agents. The principle of proportionality is:

> When some quality Q justifies having certain rights R, and the possession of Q varies in degree in the respect that is relevant to Q's justification the having of R, the degree in, which R is had is proportional to or varies with the degree to, which Q is had. Thus, if x units of Q justify that one have x units of R, then y units of Q justify that one have y unit of R (Gewirth 1978: 121).

However, there is an inherent problem with Gewirth's principle of proportionality. Gewirth claims that the principle shows the degree to which partial or marginal agents have generic rights. In attributing quasi generic rights to partial agents it does not give generic rights to a lesser extent, but it gives a different quality of protection granted by generic rights (Beyleveld and Brownsword 2001: 119). In order to rectify the problem presented by the principle of proportionality, precautionary reasoning can be utilised.

5.7.2 Precautionary reasoning

The PGC shows that agents are categorically required to treat other agents as having the GFA, and should avoid treating an agent as though it did not have the GFA. Therefore, where X shows behaviours of agency (see 5.8), X is an ostensible agent. The possibility that X may not be an agent is wholly discounted, and X's status as an ostensible agent can be taken as being sufficient that X has the capacities to be an agent (Beyleveld and Brownsword 2001: 121). Accompanied with an adaption of Pascal's Wagers' reasoning about the existence of God,[161] Beyleveld and Brownsword introduce the precautionary principle, which states:

> If there is no way of knowing whether or not X has property P, then in so far as it is possible to do so, X must be assumed to have property P if the consequences of erring in presuming that X does not have P are worse than those erring to the side that X has P (and X must be assumed not to have P if the consequences of erring in presuming that X has P are worse than those of assuming that X does not have P) (Beyleveld and Brownsword 2001: 122).

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[161] Pascal (1966) considers that logic can neither determine nor deny the existence of god; therefore, in weighing up equally possible outcomes, with one of those outcomes being disastrous, one must choose the choice that avoids that disaster, and one must wager god exists. Despite the argument having logical roots, it does not provide for acting in a way that there is a god or proves that there is a God, as it may be equally disastrous or beneficial that god or any other being exists.

Precautionary reasoning moves the argument away from proportionality and towards owing protection to all beings that have uncertainty surrounding their agency in relation to the proportionate degree that they have necessary capacities and characteristics of agency (Beyleveld and Brownsword 2001: 125). It does not make the principle of proportionality redundant, as the duty to which an agent owes an ostensible agent is subject to the principle of proportionality (Beyleveld and Pattinson 1998).

In order to help assess whether there is a possible agent, four categories of empirical evidence are suggested to aid an agent in ascertaining the relative agency of an organism, these are:

1. Patterned organismic behaviour (displayed by living organisms).
2. Behaviour that evidences itself as purposive (as being motivated by feeling and desire).
3. Behaviour that evidences itself as intelligent (as being susceptible to learning by experience).
4. Behaviour that evidences itself as rational (value-guided, and characteristics of an agent)(Beyleveld and Pattinson 1998: 18-19).

Where X shows all of the above characteristics and behaviour, one (any agent) must treat that being as an agent (Beyleveld and Pattinson 2000). If a conflict arises, as is apparent within FGT where an operation is purely for the benefit of the fetus, but has to go via the mother, all things being equal:

> If my doing y to Z is more likely to cause harm h to Z than my doing y to X (and I cannot avoid doing y to one of Z or X) then I ought to do y to X rather than to Z.

Where y = failing to observe a particular duty of protection; and h = mistakenly denying a being the status of an agent, we can infer by this criterion that:

> If my failing to observe a particular duty of protection to Z is more likely to mistakenly deny Z the status of an agent than is my failing to observe this duty
> of protection to X (and I cannot avoid failing to observe this duty to one of Z or X) then I ought to fail to observe my duty to X rather than to Z (Beyleveld and Brownsword 2001: 123).

In short, the rights of an agent who displays more agency relevant features, takes precedence over those who show less agency relevant features.[162]

[162] Further elaboration on the application of these principles is situated within 10.3 and 10.4.

The precautionary reasoning forwarded here has its critics. It is argued that precautionary reasoning is not inherently flawed on an intellectual level, but it does not provide a useful tool for guiding the action of agents (Holm and Coggon 2009). It is claimed that precautionary reasoning pays insufficient attention to the conditions under which it is appropriate; and in practice the rights of a non ostensible agent must yield to those of an ostensible agent (Holm and Coggon 2009: 295). For a full defence of precautionary theory Beyleveld and Pattinson (2010) offer a reply to such claims. More relevant to the debate within FGT is Holm and Coggan's claim that the rights of a non ostensible agent must yield to those of an ostensible agent. However, Holm and Coggan fail to consider that in utilising precautionary theory duties can be imposed on agents towards ostensible agents. Therefore, precautionary theory offers more than just 'rights', but duties towards an ostensible agent without contradicting the PGC, which can provide guidance.

By utilising such precautionary reasoning it can be applied to the so called marginal groups, whose agency status are in question and provide guidance on how to regulate agent conduct. The marginal groups consist of those who are unconscious, the mentally handicapped, children, fetuses, embryos and gametes. The thesis will focus upon children, fetuses, embryos and gametes.

5.8 Marginal groups under the PGC

5.8.1 Children

The marginal groups that are important in relation to FGT are fetuses and embryos. Identifying the position of the PGC in relation to children, one can see how fetuses would be in the future if they develop to term. In assessing rights and duties several groups of agency arise: the potential agent; and the future agent. A potential agent is a being that has the potential to become an agent (Pattinson 2002: 21). A potential agent is different from a prospective agent,[163] as the latter already has the proximate abilities of the generic features of action, even if he is not actually acting (Beyleveld

[163] A prospective agent has the capacity and disposition to agent; therefore, is not differentiated within the thesis from an agent.

and Pattinson 1998: 31). A future agent is a being that will in the future poses intrinsic moral status. The distinction between 'potential' and 'future' agents means that each type of agent will derive protection from two different sources.[164] However, the PGC is applicable to both and therefore the terms may appear interchangeable, but it is the application of the PGC that is important. The first ostensible agents to be considered within the marginal groups are children. According to Gewirth:

> Children are potential agents in that, with normal maturation, they will attain the characteristics of control, choice, knowledge, and reflective intention that enter into the generic features of control. A potential agent is not the same as a prospective agent, for the latter already has the proximate abilities of the generic features of action even if he is not currently acting. Insofar as children are not such prospective agents, they are not among the recipients whose rights to freedom the PGC requires agents to respect fully. But insofar as children are potential agents, they have rights that are preparatory for their taking on the generic rights pertaining to full-fledged agency (Gewirth 1978: 141).

Therefore, children and new born babies are not full agents but have the right to have their potential protected. As they mature they should increasingly participate in decisions affecting themselves (Beyleveld and Brownsword 2001: 130). However, Gewirth's position on children (and the mentally deficient) appears to be only utilised in relation to children, and not to fetuses or embryos (See Gewirth 1978: 141-142).

5.8.2 Fetuses, embryos and gametes

As stated above, the position in relation to the fetus and embryo are the focus of the thesis. There are circumstances where the rights and interests of agents have precedence over the status of an embryo or fetus (Steigledger 1998). Nonetheless, precautionary reasoning imposes a duty upon agents to allow relevant potential agency to develop and where possible assist with that development. For Gewirth, the fetus has generic rights, but embryos and fetuses lack purposivity altogether under the Principle of Proportionality. According to Gewirth:

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[164] Developed further within chapter 10.

> If there were no conflict between fetus and the rights of the mother, the principle of proportionality and the PGC require that the fetus [...] have such a right to well-being as is required for developing potentialities for growth toward purpose-fulfilment.
>
> When there is a conflict, however, the mother's generic rights should take priority. [...] [T]he fetus lacks abilities, except in remotely potential forms [...]. Hence its [the fetus] generic rights, by comparison with the rights of its mother, are minimal (Gewirth 1978: 142).

As the fetus develops it gains more protection. Therefore, a six month fetus will have more right to protection than a three month old fetus (Gewirth 1978: 143).

Gewirth's position on a fetus lacking purposiveness is outdated and contradicts his reasoning in relation to children. It is widely accepted that at some point during pregnancy, a fetus shows the ability to display a response to pain (See Derbyshire 2006). One could consider reacting to pain as evidence of behaviour of agency. Ultimately Gewirth appears to be saying that the principle of proportionality and the PGC justify that the fetus has a right to realise its potential to develop into an agent, from which it may be inferred that the fetus has a right to life and the other conditions necessary to realise its potential to develop into an agent (Beyleveld and Pattinson 2000: 49). However, under precautionary reasoning where X is a fetus or embryo it means that if there is:

1. Evidence that X is a potential ostensible agent, *by itself*, requires agents to grant X moral status (in proportion to the strength of the evidence); and
2. Evidence that X is a potential ostensible agent adds to the moral status secured for X by the degree to which X exhibits the capacity and disposition to do something voluntarily for a purpose that it has chosen (GCA) behaviour (bf). Thus, if Y is apparently only a partial agent with y moral status (by virtue of Y's degree of GCAbf) *but not apparently a potential ostensible agent,* and X is apparently a partial agent with y moral status *and also apparently a potential ostensible agent,* then agents must take more seriously the possibility that X is an agent than that Y is an agent, by virtue of, which their duties of protection to X are greater than their similar duties to Y. (And, of course, the degree to, which evidence of potential to become an agent adds to X's moral status will be proportional to the strength of this evidence) (Beyleveld and Pattinson 1998: 27).

Therefore, a developing fetus should be afforded more protection as it develops, but an embryo should not be afforded any significant protection.

Gametes are afforded no protection. Although genetically part of the human species, protection under the PGC is governed by the ability to express the abilities of agency. Empirically, gametes only show patterned organismic behaviour, which if one was to afford all patterned organisms the protection of the PGC, then it would be ethically and morally impermissible to clean ones home with bleach or to wash oneself, which inevitably kills cells. Therefore, the choice of agents supersedes that of any gamete as they have no protection under the PGC. Gametes only posses passive potential rather than active potential; therefore, it is misleading to say that an unfertilized ovum is potentially a person (Reichlin 1997: 4).[165] Even if this argument is flawed, gametes are fundamentally the agent's own 'property'. Therefore, the choice over the use of gametes fundamentally lies with the agent and as does all associated parental rights that stem from a gamete if they produce a child.

Even if partial agents are not directly protected, they can be indirectly protected through physical proximity to agents and the development of virtues by agents that are needed for compliance with the PGC. Pattinson (2002) outlines five possibilities for the protection of beings with indirect moral status. They consist of: physical proximity; the development of virtues; protection of the sensitivities of others; contractual collective waiver of the freedom to mistreat certain beings; and property (Pattinson 2002: 30). With regards to fetal surgery the most interesting is that of the physical proximity argument and the protection of the sensitivities of others, due to the nature and intergenerational aspect of fetal gene surgery. Therefore, within the debate of FGT it will be interesting to see how the PGC aligns with the practice of practitioners.

5.9 Conclusion

In conclusion, the frequent references to dignity within international instruments, domestic regulation and consultation documents indicate that human dignity is not a

[165] Property is not used in the conventional sense as here it refers to 'under the control of the agent'. Whether the body is 'property' is a vast question and for further reading see articles such as: Harris, J. 'Who Owns My Body' (1996) 16 *OJLS* and Skene, L. 'Arguments Against People "Owning" Their Bodies, Body Parts and Tissue' (2002) 2 *MacQuarie LJ* 165.

concept that can be ignored. Despite there being various sources of dignity, the abstract concept of dignity was shown to be rooted in moral philosophy. After considering Kant, Foster, Habermas, Kass and Gewirth, it emerged that Gewirth's PGC appeared as the most appropriate ethical theory to use in this thesis. It was found that in utilising a dialectic necessary approach, the PGC is an appropriate ethical theory which can be used to assess the current and potential future progress of FGT. Where human dignity is used as a foundation for regulation, the PGC can be used to ascertain whether a violation of human dignity has occurred. The theory imposes duties as well as elaborating rights, which may consequently be taken into account in the examination of intergenerational issues, and must be analysed. In using the PGC as an analytical tool for FGT, it can guide regulation where it is scientifically plausible but uncertain that harm will result then, that action or inaction shall be taken to avoid or diminish that harm (World Commission on the Ethics of Scientific Knowledge and Technology 2005).[166] Such harms include:

- threatening to human life or health
- serious and effectively irreversible
- inequitable to present or future generations
- imposed without adequate consideration of the human rights of those affected (World Commission on the Ethics of Scientific Knowledge and Technology 2005: 14).

Such issues are clearly relevant to FGT as identified in chapter 2. It can guide regulation in these areas (akin to the precautionary issues with 2.62) because where uncertainty and harm are relevant to choice and impact upon marginal groups as well as wider concerns can be taken into account. It does not fall foul of the zero tolerance arguments as the precautionary reasoning seeks to reduce harm under the PGC to the minimum. Therefore, the PGC can be used in making ethical assessments of the choices science and technology present, or in this case the direction of FGT. By making those ethical assessments the concerns raised in 2.6, such as regaining control of autonomous technology through precautionary reasoning (in terms of harm and rights) can start to be addressed.

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[166] The judgement of plausibility should be grounded in scientific analysis. Analysis should be ongoing so that chosen actions are subject to review. Uncertainty may apply to, but need not be limited to, causality or the bounds of the possible harm (World Commission on the Ethics of Scientific Knowledge and Technology 2005: 14).

It may become evident that 'harm' between that of the mother and that of the fetus within the context of FGT is an important issue. Harm is of relevance due to the proximity of intervention for both mother and fetus, but also relevant to possible future generations. Harm within the PGC refers to violations of an agent's generic features, aka human dignity. However, as has been shown above, duties can be inferred upon an agent in relation to a fetus because of their relevant empirical evidence. Under the potential agent definition in PGC the fetus/future generation is not protected, but under the future agent definition there may be an issue within the debate concerning the prohibition of germ line interventions and harm to a future agent. Under the precautionary principle where a marginal group is in need of protection of their generic features it would mean that certain potential practices in FGT may be banned or should not be pursued. How such a distinction affects intergenerational regulation will be interesting. What is clear is that the PGC should be used to critique the debate surrounding FGT due to the PGCs connection to human dignity, and this will be done in chapter 10. Finally, therefore, having seen that the analysis of the issues raised by FGT should be grounded in ethics (in this case the PGC), the data must be collected by documentary analysis and semi structured interviewing as identified within chapter 3.

6 Documentary Data: Human Dignity

6.1 Introduction

Having seen that the data primarily points towards identifying a maternal fetal divide within current regulatory and medical practice as well as revealing a potential overarching principle of human dignity, it has been indicated that the PGC will be a useful analytical tool to assess the maternal fetal divide and the future impact of FGT progress. In order to assess the impact of progress as identified explicitly in 2.6.2, and implicitly throughout the thesis, the regulation and FGT practitioner's views of future FGT needed to be explored. Chapters 6 and 7 are a result of the analysis of institutional regulation from legislators to the EMA. These chapters are important to the thesis because they identify and analyse the regulation under which FGT will be conducted when it progresses to clinical trials. It is these regulations that are charged with controlling FGT and any potential scientific progress that might occur.

During the documentary analysis two main themes emerged: human dignity and scientific progress (or issues relating to the research process). Chapter 6 analyses human dignity and chapter 7 analyses scientific progress. Some of the themes, such as intergenerational issues, cover both themes and therefore there is not a definitive separation of the issues. It should be noted that the documentary analysis was conducted before the interviews took place in order to inform the interviews.

This chapter will identify the following underlying themes: human dignity, the themes underpinning human dignity such as the empowerment of the individual and finally future generational interests. In each of the following sections, except 6.2, the findings or principles identified are then related to the maternal fetal divide and the consequences for FGT practice. Firstly, section 6.2 identifies the sample and the initial document findings. Section 6.3 will then move from identifying the abstract principle of human dignity to identifying principles that facilitate human dignity within FGT. By moving from human dignity as an explicit guiding principle, human dignity is empowered through implicit terms such as autonomy in section 6.4. It appears that autonomy raises the individual within a clinical situation above scientific progress and the wishes of society concerning FGT. It is also seen that

human dignity can constrain action even where choice is available and therefore autonomy can be constrained. Section 6.5 then looks at intergenerational issues, and shows that when possible next and future generations are taken into account, the present individual is raised above their interests because a fetus is not considered an individual. Section 6.6, however, shows that there is some protection afforded to future generations in the regulation and practice of FGT, which is dependent upon maternal choice. The chapter will then conclude that human dignity is implicitly applied through principles such as autonomy. Through autonomy the individual within a clinical setting is raised above all others. However, this principle may potentially be eroded by the research process and by the fetal interests, which will be developed later in chapter 7.

6.2 Initial document findings

In total 127 documents were analysed.[167] The documents were divided into the following categories: primary and secondary legislation governing England and Wales; EU regulation; case law from England and Wales; case law from the ECtHR; governing body policy and consultation documents; and international declarations and conventions. They were selected due to their relevance to issues such as: the maternal fetal divide; the regulation of gene therapy, thus FGT; regulation of genetically modified organisms and clinical trials. An initial word count provided a useful tool to highlight possible emergent themes. Considering the vast amount of documents and words a more useful tool was to use Nvivo's 'tag cloud'. The tag cloud generated a list of the top 100 words in alphabetical order with the most prominent being the largest and boldest. One letter words and single numbers were eliminated to give a better picture of the possible themes that might emerge. The results of that tag cloud are visible in Diagram 4.

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[167] For full list of documents and reason for selection see Appendix F - List of Analysed Documents.

Diagram 4. Top 100 tag cloud

Words such as risk, information, consent and human appear as frequently used words being in the top 100 words. However, it is evident that 'dignity' is nowhere to be seen. In terms of scientific progress words such as treatment, clinical, research and products appear to be frequently used indicating that the documents are relevant to the thesis. Personal words such as 'he' and 'she' appear within the tag cloud, therefore some form of personal ownership may arise from the data. The same can be said for positive words that facilitate action. However, the interpretation of these words must be contextualised as they may infer duties, rather than negative rights for parties. They also place possible restrictions upon researchers or individuals with words such as 'must', 'condition' and 'regulation' appearing. Words such as 'section' and 'article' appear on the tag cloud, which is unsurprising given that the documents in questions divide their relevant parts into articles and sections. However, looking at the frequency of words can be misleading, because within the tag cloud important words such as rights and dignity do not appear. In fact, the term dignity is only used 167 times.

However, relying on the word count for what themes are important misrepresents the documents. Nvivo 8 utilises every word individually within the word count. Therefore, within the tag cloud plurals of the same word are counted as two separate

words unless an apostrophe is used. Therefore, the prominence of words such as risk should be greater as risks and risk' appear later on with their own count of 708 and 17 respectively. As a result the word count for 'risk' is 2817 instead of Nvivo's 2092 count. .

It is important to consider the institutional structure (See Appendix C – Institutional Structure), within England and Wales. Each statute implicitly includes all other relevant statutes unless it states that it is contrary to or outside the remit of an act. The same applies to European regulation. Therefore, the top down approach of documents can be seen by the regulatory references with those at the bottom providing the filler which the reality painted by the document above appears to have missed.

The institutional structure indicates that cross referencing of documents is high between all the documents. Therefore, institutional structure is important. However, it is evident that, because of the hierarchy between the documents, the referencing of other institutional documents becomes more prominent. For example, using a matrix query (See Appendix H – Sampled Matrix Query) it is evident that certain types of documents are referred to by only certain institutions and that, by looking at the amount of referencing, each institution appears to have a certain remit. For example, references to articles and books are solely the domain of judicial cases and policy documents, but institutions reference from a wide range of sources either above or below them in the institutional hierarchy. European institutional documents, on the other hand, only tend to reference their own institutional documents and documents from institutions above them. For example, intergovernmental documents reference themselves; whereas, policy documents, consultations and case law have the broadest range of cross regulatory referencing as they also have the duty to interpret an issue or case in light of all relevant documents.

In order to help guide readers, legislation will often start with procedure formalities, such as those stated above, followed directly by a section titled 'interpretation' or 'definitions'. The purpose of such formalities is to inform the reader about a document's remit. Often within case law and policy documents definitions appear at

the back of the document, but are there none the less as a guide for the reader. The abundance of definitions and facts within a document helps shape and clarify the agenda and stance upon a specific point. The issue of 'remit' becomes important in the context of interests and decisions made upon the rights of others. Through the thematic approach, certain themes arise as guiding principles within that remit. One such theme is that of human dignity. Human dignity can be seen as an explicit and implicit principle. The chapter will now elaborate upon human dignity and how autonomy and intergenerational issues show the implicit nature of human dignity, with the effect of these principles upon the maternal fetal divide.

6.3 Human dignity as an explicit and implicit guiding principle

Within international declarations and conventions human dignity is a key principle. It is inviolable and appears as an intrinsic foundation to declarations. Within the international and intergovernmental institutions human dignity appears as an explicit theme within the documents. It applies to every human being and is a source of empowerment because:

> […] recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world.[168]

The above quote illustrates that human dignity is not an isolated concept. It is an explicit concept that is connected to other principles such as liberty and equality. It is considered a necessity that protects the identity and dignity of all human beings. The mere connotation of human dignity with 'democratic' adds political weight behind it. By associating human dignity with more than just science it also becomes about human action and interaction based on a multitude of preferences, thus making human dignity a complex principle (Häyry and Takala 2005). Human dignity appears as a value that cannot be removed by anyone. Intertwined with the explicit notion of human dignity is biology and/or humanity. When human dignity is used in the explicit sense it appears to encompass the whole of humanity, thus prescribing dignity in human genes (Häyry 2004). Importantly, for the maternal fetal divide, chronologically, there is little to indicate when one becomes a member of humanity;

[168] United Nations Universal Declaration of Human Rights 1948 Preamble.

therefore, becoming entitled to equal treatment. The only indication is within United Nations Universal Declaration of Human Rights 1948 whereby 'birth' is considered a factor in the assessment and attainment of human dignity:

> All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.[169]

However, within the Council of Europe a different point of origin for human dignity emerges as:

> It was acknowledged that it was a generally accepted principle that human dignity and the identity of the human being had to be respected as soon as life began (Council of Europe 1997: [19]).

Other documents confirm the intrinsic link to humanity.[170] Therefore, at an international level there is a lack of clarification regarding the attainment and interpretation of human dignity. Given the political structure in place international conventions are hugely influential in the creation of European Regulations and Directives.[171] These ultimately help construct the regulation of FGT within England and Wales. However, because the highest political institutions only have persuasive force, the legislator has to indicate what founding principles are important. The top of the binding legislative structure is the EU. The preamble of a European document serves as notice to readers about the influences and considerations within the drafting process. Within the preambles the influential nature of the intergovernmental documents is evident; thus, including human dignity is an explicit concept for the institution:

> The accepted basis for the conduct of clinical trials in humans is founded in the protection of human rights and the dignity of the human being with regard to the application of biology and medicine, as for instance reflected in the 1996 version of the Helsinki Declaration.[172]

Therefore, human dignity and human rights are connected within the application of biology. The principle of human dignity is confirmed within other Directives; however, the explicit nature of human dignity is now less prominent. Instead the

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[169] United Nations Universal Declaration of Human Rights 1948 Article 1.
[170] United Nations Educational, Scientific, and Cultural Organization Declaration on the Human Genome and Human Rights 1997, Article 1.
[171] Once transposed under the European Communities Act 1972 s.(2).
[172] Directive 2001/20/EC, Preamble.

recurrent theme of cross regulatory referring (or referral to another relevant institution) makes human dignity implicit at the level of the EU:

> This Directive is based on international experience drawn upon through an extensive consultation, the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells, the European Convention on Human Rights, the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo, 4.IV.1997), with its additional protocols, and recommendations from the World Health Organisation.[173]

The high level of cross regulatory referencing implies that human dignity is an important concept as the documents that are referenced explicitly utilise human dignity. As will be shown in chapter 7, scientific evidence appears as a key theme, which can cause problems when combined with human dignity. However, at an international level, human dignity is explicitly and implicitly used as a founding principle for regulation. Therefore, it is paramount and forces it way into the thinking of those who practice genomic medicine. It is explicitly connected to the themes of rights, liberty and the biology of humanity.

Within England and Wales, human dignity as an explicit regulatory concept for FGT disappears. Only implicit references to human dignity within legislation emerge. It is the inclusion of other documents through cross regulatory referencing, as Directive 2006/17/EC signifies, that human dignity becomes a relevant influence and factor within FGT with sections within the regulation of FGT stating:

> Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.[174]

Because human dignity is such an important principle within the Declaration of Helsinki, it is implicitly one of the important factors for FGT within England and Wales. One could argue the difference between 'must' and 'shall' varies the obligations of a physician, but the implicit inclusion of human dignity within clinical trials means that human dignity is within the regulation of FGT. Themes emerge that help conceptualise what human dignity is and how human dignity can relate to

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[173] Directive 2006/17/EC, Preamble.
[174] The Medicines for Human Use (Clinical Trials) Regulations 2004 Sch 1 Part 2 s.1.

the regulation and practice of FGT. These themes help translate human dignity implicitly into England and Wales, which is important for the maternal fetal divide as international documents are only persuasive unless specifically enacted through ratification or specific reference within legislation. Thus, despite the documents not being binding, because of their influencing power human dignity has the potential to be an enforceable norm within the practice of FGT (Andorno 2009).

6.3.1 First impressions for the maternal fetal divide

On first instance, human dignity has the qualities identified within section 5.2 as being a guiding principle not only for biotechnology and human rights, but specifically for FGT. Human dignity is the rock upon which rights are founded and is firmly tied to a preambular of ideas such as equality and inherent dignity (Beyleveld and Brownsword 2001). It is not contingent upon social rank, thus moving away from the idea that human dignity is empirical or external (Gewirth 1998). Therefore, human dignity has the qualities of various conceptual models. No reference to God appears, therefore, human dignity appears to have the qualities of reason, capacity, genetics and sentience (Häyry 2004). What is clear is that, rightly or wrongly, human dignity is inherently speciest within these documents (Kuhse 2000). That is not to say that animals could not have 'dignity' (Singer 1989, 1993), but within the documents considered here it is purely focused upon the inherent dignity of humans. Nevertheless, further exploration is needed because the differing attributes of several different conceptions of dignity would have different implications for the maternal fetal divide. For example the commencement of 'life' varies between the different conceptions. Humanity at the biological level starts at conception, but sentience could be evaluated as engaging at different points of biological development. Without identifying the most prominent conceptualisation of human dignity such issues and vagueness cannot be reconciled.

The lack of definition is unsurprising as every definition in law is *omnis definitio in iure periculosa est* or perilous in today's language. Thus, the generalised formulation of the principles can ultimately be justified by the need to find a balance between the universalism of some bioethical norms and the respect for cultural diversity (Andorno 2007). Nonetheless, the first principle that emerges is that every

human being possesses an intrinsic worth, merely by being human. The second is that this intrinsic worth should be recognized and respected by others, and some forms of treatment by others are inconsistent with, or required by, respect for this intrinsic worth (McCrudden 2008). Therefore, the interpretation of human dignity is important for the maternal fetal divide because it creates boundaries, which can then be used to assess whether the current frameworks are implementing the maternal fetal divide uniformly.

6.4 Conceptualising human dignity within regulatory institutions: the individual is paramount

Human dignity appears as a hollow concept within the documents, because on initial reading the term human dignity is not explicitly defined. However, principles emerge, which indicate what human dignity might be and how it is adhered to in the maternal fetal divide, research and the rights of others within the FGT context. Within the sample a strong emphasis emerges surrounding how individuals, society and science or medicine should and must be prioritised. It is repeated in several sources regardless of where those documents fit within the institutional structure of regulation.

> The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.[175]

The above extract pronounces the importance of the individual over society despite both being related to dignity. However, an interest being superseded by the rights of the individual says little about the rights of society. It will be shown there is a stark difference between interests and rights within the context of FGT, which can amount to an inherent contradiction. The European institutions use such statements to reinforce the principles that were indicated within the higher political institutions, as is evident from the extracts.

Human dignity being bound to the individual is repeated identically three times within the Clinical Trials Regulation 2004 as well as being repeated identically in other documents. It is confirmed that within the practice of FGT human dignity is

[175] The Medicines for Human Use (Clinical Trials) Regulations 2004 Sch 1 Part 2 s.2.

the paramount consideration. Therefore, individual rights should prevail within the practice of FGT practitioners rather than the dignity of society. Elevating the individual as being the most important principle appears to create a tension between other related themes. On the first interpretation rights, ergo dignity, appears as the key claim against even the economic interests of a country. The result is that there is no tension between human dignity and other factors due to the carte blanche superiority of the individual. The Convention on Human Rights and Biomedicine 1997 Explanatory Report emphasises how powerful the 'individual' can be:

> It did not appear desirable, in the context of this Convention, to make the exercise of fundamental rights chiefly concerned with the protection of a person's rights in the health sphere subject to the economic well-being of the country, to public order, to morals or to national security (Council of Europe 1997: [156]).

Once again the individual is of paramount concern and human dignity appears intrinsically linked to individual rights. More importantly specific documents elaborate on what rights are, such as the ECHR. As a result, the structure and hierarchy of the documents becomes important as the implication is that such pieces of legislation could, in fact, be more significant than other pieces of equal legislation. The HRA 1998 s.4 is a clear indication of the effect of human rights ergo human dignity within institutions.

Despite the apparent carte blanche nature of human dignity to control research and progress within FGT, any conflict between human dignity and scientific progress would still potentially need resolving. Documents across institutional sources deal with the conflict between research, the individual and society, thus highlighting the competing nature of the interests' of others and the complications this can cause. Once again, the European Convention on Human Rights and Biomedical Research 1997 explanatory report elaborates further:

> The first is that of the individual, who had to be shielded from any threat resulting from the improper use of scientific developments. Several articles of the Convention illustrate the wish to make it clear that pride of place ought to be given to the individual: protection against unlawful interference with the human body, prohibition of the use of all or part of the body for financial gain, restriction of the use of genetic testing, [...] (Council of Europe 1997: [14]).

The above extracts highlight the competing nature of the principles that emerge from

human dignity and point out situations in which human dignity must be properly considered. Human dignity is protected if consent and information procedures are adhered to once scientific practice has conducted its own measurement of what is best for the individual. Therefore, the individual is paramount, but an individual's choice is mitigated by principles that they may or may not have control over. It will be shown below how such a position ultimately causes an inherent contradiction within FGT. However, even if the individual is paramount within human dignity who can decide upon what is best?

6.4.1 Who can decide?

It appears that the only person to decide is the individual, which is facilitated by other principles such as informed consent and autonomy. It is the interplay between these principles and scientific progress and risk evaluation, which emphasises the primacy of the individual. An example relevant to children shows how they amalgamate:

> Persons who are incapable of giving legal consent to clinical trials should be given special protection. [...]. Such persons may not be included in clinical trials if the same results can be obtained using persons capable of giving consent. Normally these persons should be included in clinical trials only when there are grounds for expecting that the administering of the medicinal product would be of direct benefit to the patient, thereby outweighing the risks. [...]. Children represent a vulnerable population with developmental, physiological and psychological differences from adults, which make age and development related research important for their benefit. [...]. The clinical trials required for this purpose should be carried out under conditions affording the best possible protection for the subjects. Criteria for the protection of children in clinical trials therefore need to be laid down.[176]

There are many different complex competing themes in the extract above; but, it offers an insight into what criteria need to be fulfilled in order to uphold human dignity. The extract highlights the interplay and tension between consent, protection, risk and 'best interests', which is evident throughout the regulation of FGT. However, the individual is sometimes not deemed to be the top of this theoretical

[176] Directive 2001/20/EC Preamble.

model. Autonomy can be restricted depending upon the issue at stake and the point of development in the technology. The extract clearly indicates that certain elements of the risk evaluation are not done by the individual or proxy consenter. Therefore, there is an inherent conflict between pursuing human dignity through autonomy and scientific progress. The documents place derogation from the model of individual over society and science outside of scientific progress or research and social acceptability. Therefore, the individual is the priority within the context of research:

> Traditionally, reproductive autonomy meant simply the freedom (assuming it was a real freedom) to decide whether to try and reproduce, with whom, when and where. [...] Whilst we would strive to encourage autonomous decision making, we recognise that there may be problems with unfettered and unregulated choices. These problems can include decisions, which may adversely affect broader society and thus be in tension with genetic solidarity and social responsibility. [...]. Perhaps the best formulation is that whilst autonomous decision making should be supported and encouraged, it is legitimate to limit this autonomy where its exercise unreasonably impacts on the autonomy of others, or threatens others with significant harm (Human Genetics Commission 2006: [1.5]).

Therefore, the tension between the individual and society is not just a result of the balancing of primary rights holders, but also results from genetic solidarity and a rights holders own responsibility. The tension can be mediated, but also influenced, by scientific knowledge and social acceptability, which may restrict or promote certain autonomous actions. Therefore, there is a distinction between being constrained to choose and being forced or fraudulently made to act, which is consistent throughout the documents. In identifying the difference between constrained choice and enforcement, if the interests and rights of the individual were always paramount then one should be entitled to choose any procedure regardless of procedural affects. In turn, scientists would be allowed to conduct clinical trials on any condition with any method on anybody. However, the above extract clearly shows that this is not the case as autonomy is a two edged sword which can be constrained and influenced by society. However, the influence for such a decision comes from regulators rather than just from science. Within the research environment once a choice is available the emphasis falls back upon individual autonomy through risk management/assessment and the communication of information to the individual. Such empowerment and negative liberty clearly

emanates from the concept of consent.

6.4.2 Consent facilitating human dignity

Consent emerges as the undercurrent within the documents reinforcing the prioritisation of the individual over science and society. 'Consent' ultimately means patient empowerment and control over their bodies. For example, valid consent means the same as legal consent, which emanates as a strong concept and is repeated constantly within all levels of the institutional framework. Consent is referenced over 2200 times within the sample and appears in virtually every document. The repetition of consent throughout the sample emphasises the importance of consent for the individual. Consent is interwoven with risk calculation and other issues as seen above. Nevertheless, in order to operationalise autonomy, communication of information related to issues of risk and treatment management are needed:

> If one considers the scope of the doctor's duty by beginning with the right of the patient to make his own decision whether he will or will not undergo the treatment proposed, the right to be informed of significant risk and the doctor's corresponding duty are easy to understand: for the proper implementation of the right requires that the doctor be under a duty to inform his patient of the material risks inherent in the treatment. and it is plainly right that a doctor may avoid liability for failure to warn of a material risk if he can show that he reasonably believed that communication to the patient of the existence of the risk would be detrimental to the health (including, of course, the mental health) of his patient.[177]

Once again the priority is the patient which accordingly creates a correlating duty upon the physician in order to facilitate that priority. It also places a duty upon the physician to have current knowledge of treatment practices. The consequence of such duties and indication of best interests is recognised and thus can affect the relationship of the individual with the physician. However, the sample recognises such a situation and the influential Helsinki Declaration states:

> The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.[178]

Such statements do little to illuminate how to resolve competing or conflicting interests which may occur when a treatment option is forwarded. However, the

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[177] *Sidaway v Governor of the Bethlem Royal Hospital* [1985] 1 AC 871, 888.
[178] World Medical Association Declaration of Helsinki 2008 Article 34.

consequential duty of information communication places patient autonomy in the hands of the physician, thus initially outside of the realm of autonomy. Therefore, what is in the best interests of an individual emerges. It is the duty of the physician to consider what is in the best interest of the patient. The Mental Capacity Act 2005 lists the important factors, which include both medical and social interests, to consider for incompetent patients and serves as a guide. Best interests is usually connected with incapacity when the individual is concerned; but, because of the information and clinical research, it is apparent within FGT that best interests or the interests of others becomes a relevant factor due to the maternal fetal divide and the involvement of more than one entity.

It does not, however, appear that by placing the individual as the central focus of the maternal fetal divide one can adequately answer the question of conflict. If fetal life is protected under human dignity, then the autonomous choice of FGT practitioners and mothers can be constrained and possibly lead to enforced practices within maternal fetal conflict (Beyleveld and Brownsword 2001). Therefore, human dignity is about empowerment and constraint (Beyleveld and Brownsword 2001). By creating a hierarchy with the individual taking precedence over society, one is creating the necessary conditions for human dignity to flourish as well as respecting the individual's own dignity (Beyleveld and Brownsword 2001). Therefore, choices within the maternal fetal divide should empower the individual by placing autonomy at the focus of the maternal fetal divide (Van Bogaert and Dhai 2008). Duties are imposed upon institutions to correlate information from all the available sources, not only to protect human dignity but to facilitate autonomous choice. Doctors are aware of such duties, which are fundamental practices within medicine and good practice (General Medical Council 2009b).

6.4.3 Dignity as constraint and the maternal fetal divide

Dignity can constrain action in general, in contrast to our rights, which are specific to furthering our personal goals (Dwyer 2003). Therefore, by choosing to recognize these values and to treat the world accordingly, individuals should accept some constraints on their actions (Bostrom 2008). Therefore, choice is constrained by a seemingly paternalistic bubble whereby those other than the person in question are

making judgements about what is acceptable. The documents appear to recognise such constraints by introducing themes such as risk and the interplay between the individual and the FGT practitioner. However, differences arise between technological and societal constraints, which are external constraints; and self imposed or internal constraints. If the individual was truly paramount within regulation the only external constraint upon their dignity would be technological and financial. If finances were not an issue, then a subjective construction of dignity would be created, which would be conditional upon time and place in relation to technology and therefore unworkable within institutions (McCrudden 2008). Nonetheless, decisions that engage the maternal fetal divide are constrained by more than just risk and genetic manipulation. Removing scientifically orientated constraints such as risk and safety, society emerges as a constraint, which is intertwined with the regulation of science.

By including society as a constraint upon regulation, human dignity recognises the impact of choice beyond the individual. Thus, human dignity examines the implications of this technology within existing and potential patterns of oppression. It requires the examination of specific circumstances, to take into account actual experiences and concerns and to assess the significance of genetic interventions upon personal and social relationships (D'Agincourt-Canning 2001: 236-237). Therefore, human dignity situates individuals in their place within society. Here, thinking in terms of human dignity can, arguably, contribute to understanding people as existing at the heart of complex webs of interrelationships, rather than considering them as isolated persons from the single perspective of their rather abstract individual autonomy (Dupré 2009). However, as the debate surrounding the prohibition upon sex selection has indicated, a ban on social sex selection because of the majority must be recognised for what it is, an attempt to formalise the tyranny of the majority and to institutionalise contempt for the principles of liberal democracy (Harris 2005b). Therefore, calls to constrain choice because of society can be dangerous and must be fully evaluated beyond the barometer questionnaire that is often used.

Constraint does not include 'enforcement of treatment' (apropos abortion see Scott 2002) and in the case of the maternal fetal divide it encompasses far more than a

mere refusal of treatment because there are two entities involved with their own separate rights. Treatment without consent depends on factors such as capacity and informed consent. More importantly for FGT is how the individual is defined. If the individual includes a fetus then a set of competing rights between the mother and fetus arises, which would need resolving.[179] How the individual is defined is important because if the fetus is deemed an individual, a mother's beneficence based obligations to the fetus through practices such as FGT could justifiably constrain (in the broader inclusive sense) her autonomy (Fleischman, Chervenak et al. 1998). Therefore, conflict between the rights of the fetus and the mother cannot be resolved until the relationship between mother and fetus is considered.

6.5 Prioritising the individual over the next unborn generation

Despite the individual emerging as the priority within research and medicine, the problem arises of how the individual is placed in relation to other possible individuals, such as a fetus. With human dignity seemingly flowing ambiguously, it could be seen that outside of the biological connection to the human species a fetus is not 'life'. Therefore, until birth a fetus can be treated without dignity unless that treatment would result in a problem for society or the mother. Within the sample it is the characterisation of a legal individual post birth that creates rights and thus gives one human dignity.

> Except under statute an embryo or foetus in utero cannot be the victim of a crime of violence. In particular, violence to the foetus, which causes its death in utero is not a murder. The foundation authority is the definition by Sir Edward Coke of murder by reference to the killing of "a reasonable creature, in rerum natura:" Co.Inst., Pt. III, ch. 7, p. 50. The proposition was developed by the same writer into examples of prenatal injuries as follows:
>
> > "If a woman be quick with childe, and by a potion or otherwise killeth it in her wombe; or if a man beat her, whereby the child dieth in her body, and she is delivered of a dead childe; this is a great misprision, and no murder [...].[180]

[179] However, one should note incapacity is always a possible avenue for treating a fetus without the consent of the mother.

[180] *Attorney General Reference (No 3 of 1994)* [1998] A.C 245, 254.

Therefore, the human dignity of the next generation is not violated despite the recognition of the maternal fetal divide, because there is no individual upon whom their human dignity can be violated. However, as was seen in the literature review, the relationship between a mother and a fetus, thus the nexus point of the next generation, becomes a regulatory issue. It is case law and policy which illuminates the relationship between generations when pregnancy arises. Legislation does not elaborate upon the nature of the maternal fetal relationship. For example, within the Abortion Act 1967 the rights and interests of the pregnant individual are weighed up against those of the fetus:

> 1 Medical termination of pregnancy
> […] (a)that the pregnancy has not exceeded its twenty-fourth week and that the continuance of the pregnancy would involve risk, greater than if the pregnancy were terminated, of injury to the physical or mental health of the pregnant woman or any existing children of her family; or
> (b) that the termination is necessary to prevent grave permanent injury to the physical or mental health of the pregnant woman; or
> (c) that the continuance of the pregnancy would involve risk to the life of the pregnant woman, greater than if the pregnancy were terminated; or
> (d) that there is a substantial risk that if the child were born it would suffer from such physical or mental abnormalities as to be seriously handicapped.
> (2) In determining whether the continuance of a pregnancy would involve such risk of injury to health as is mentioned in paragraph (*a*) or (*b*) of subsection (1) of this section, account may be taken of the pregnant woman's actual or reasonably foreseeable environment.[181]

Despite abortion being capped at 24 weeks, ultimately it can be done up until birth. It confirms the position that the mother is the most important aspect within pregnancy. Risk, foreseeability and the duty of the physician are important factors, which indicate that the individual needs help to exercise their rights. The statute is silent about fetal interests and rights. However, that does not equate to the fetus having no rights or interests. For example, the limit on abortion to 24 weeks recognises the interests of the fetus in being born after this point. Therefore, to assess whether the fetus has any interests or rights the nature of pregnancy emerged as a theme that could reveal whether, within the climate of scientific progress which

[181] Abortion Act 1967 s.1.

challenges such principles, the next generation could be an exception to the rule. It is evident within the instructional structure that the judicial institution and policy documents emerge as being relevant, rather than the legislative institutions.

6.5.1 The relationship between fetus and mother within pregnancy

Legally, pregnancy is an extension of the mother, thus explaining the intergenerational relation between mother and fetus. Therefore, one can ascertain how the rights and interest of the next generation are weighed up against the rights of the current pregnant mother. Such autonomous rights are closely connected to her right to a private life:

> The commission finds that not every regulation of the termination of unwanted pregnancies constitutes an interference with the right to respect for the private life of the mother. Art 8(1) cannot be interpreted as meaning that pregnancy and its termination are, as a principle, solely a matter of the private life of the mother.[182]

Restricting the scope of pregnancy is particularly important in assessing the competing interests/rights between a mother and those of the next and future generations. However, there is a distinction between the rights of others and the interests of others within the sample. It is clear that the next generation have no exercisable rights until they are born. However, the competing interests within pregnancy results in the prioritisation of the current generation over possible future generations. Speaking specifically about fetal interest:

> Since an unborn child has, ex hypothesi, no existence independent of its mother, the only purpose of extending the jurisdiction to include a foetus is to enable the mother's actions to be controlled. Indeed, [...] in practice:
> "It would mean, for example, that the mother would be unable to leave the jurisdiction without the court's consent. The court being charged to protect the foetus's welfare would surely have to order the mother to stop smoking, imbibing alcohol and indeed any activity, which might be hazardous to the child. Taking it to the extreme were the court to be faced with saving the baby's life or the mother's it would surely have to protect the baby's."
> Another possibility is that the court might be asked to order that the baby be delivered by Caesarean section. [...] it would be intolerable to place a judge in the position of having to make such a decision without any guidance as to the principles upon, which his decision

[182] *Brüggemann and Scheuten v Federal Republic of Germany* (Application No 6959/75) [61].

should be based.[183]

The above extract summarises the competing issues at stake and how institutions should deal with the maternal fetal divide when autonomy, risk and danger are taken into account. Although the maternal fetal divide is recognised by the judiciary it is conceptualised upon the notion of interests. Nonetheless, the interests of another entity, that of the fetus, are not compelling enough to create a right, which can overcome the individual's. Not only is it considered unfair on the individual to enforce such a proposition; but, placing such a burden upon the judiciary without guidance from the legislator is untenable. The emergence of derogation[184] and deference[185] in answering such questions emerge as relevant themes. Because of the institutional structure, when questions of unlegislated moral circumstance with regards to the fetus arise, institutions use 'remit' or the separation of powers to avoid the deeply moral questions.[186] Therefore, within the recognition of the maternal fetal divide the default institutional position is that the individual is paramount, unless otherwise directed.

Prioritising the individual is not surprising considering the institutional emphasis on the individual is based upon autonomy. However, implied from the sample is that the fetus has recognised interests, which themselves are bound up with the interest of the human species and can create correlating duties. Case law provides the interpretation of legislation; thus, can provide information regarding the interface between the individual and the next generation. The only interest the next generation is owed is not to be injured:

> If, as is conceded, any duty is owed to an unborn child, the authority's hospital laboratory and the doctor looking after the mother during her pregnancy undoubtedly owed the child a duty not to injure it, and if she had been injured as a result of lack of reasonable care and skill on their part after birth, she could have sued them, as she is suing the

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[183] *Re F (In Utero)* [1988] 2 W.L.R. 1288, 1301.

[184] A provision that enables a signatory state to avoid the obligations of some, but not all of the substantive provisions of an act (Martin 2001). For example, ECHR Article 15.

[185] Deferring decision making to another body. For example, the judiciary deferring to the legislator as in Lord Bingham, *R. (on the application of Pretty) v DPP* [2001] UKHL 61, [2] & [120]; Lord Hoffman, *R. v Secretary of State for the Home Department Ex p. Simms* [2000] 2 A.C. 115, 131.

[186] The debate surrounding the right for prisoners to vote and those convicted of sexual offences to appeal their naming upon list 99, has shown the problems which can be faced by judicial intervention in such political or 'moral areas' (See The Guardian Editorial 2011).

> doctor, for damages to compensate her for the injury they had caused her in the womb. [...]. But this child has not been injured by either defendant, but by the rubella, which has infected the mother without fault on anybody's part. Her right not to be injured before birth by the carelessness of others has not been infringed by either defendant, any more than it would have been if she had been disabled by disease after birth. [...]. The only right on, which she can rely as having been infringed is a right not to be born deformed or disabled, […]. [However,] the only duty, which either defendant can owe to the unborn child infected with disabling rubella is a duty to abort or kill her or deprive her of that opportunity.[187]

Emphasis within the sample is on the interest of the next generation not to be harmed or injured. Defective genes or physical impairments are considered 'normal', therefore no harm results. In arriving at the current position, there is an increase in international regulatory referencing, as well as influences from scholars. The influence mainly arises from, in no particular order, Canada, the USA and Australia, as well as Europe. However, once that fetus is born the interest of that generation is then taken into account and the rights of others become relevant. Once proximity between mother and child has been broken, then a fictitious act occurs giving that generation rights of action, which in some cases did not exist seconds before. Therefore, with regards to FGT one needs to know what actions lie in respect to the duty of others in relation to the interests that the fetus may have:

> The real question posed for our decision is not whether an action lies in respect of pre-natal injuries but whether a plaintiff born with injuries caused by the pre-natal neglect of the defendant has a cause of action in negligence against him in respect of such injuries. [...]. For the purpose of these proceedings it is to be assumed that the plaintiff's injuries as subsisting at the time of her birth were caused by the act or omission of the defendant in the driving of his car. What creates the difficulty is that such act or omission preceded and was, therefore, separated in point of time from the birth of the plaintiff in her injured condition.[188]

The above example displays the fictitious legal practice that gives a neonate's prenatal interests legal standing. Essentially, interests are only as good as the right that you have, which in the case of the next generations is connected to the nexus point of birth. Ergo, 'life' and therefore the 'individual' are not created until birth within the realm of the institutional reality of FGT. The rights of the next generation

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[187] *McKay v. Essex Area Health Authority* [1982] 1 Q.B. 1166, 1178.
[188] *Burton v Islington Health Authority* [1993] Q.B. 204, 214.

are generated against others, but not the individual pregnant women. As the Congenital Disabilities (Civil Liability) Act 1976 s.1 states:

> (1) If a child is born disabled as the result of such an occurrence before its birth as is mentioned in subsection (2) below, and a person (other than the child's own mother) is under this section answerable to the child in respect of the occurrence, the child's disabilities are to be regarded as damage resulting from the wrongful act of that person and actionable accordingly at the suit of the child.

Therefore, the rights of the next generation are selective and created against FGT practitioners and the mother. Those rights emerge from interests that crystallise into rights upon birth, which is confirmed by the other documents within the legislative and judicial institutions. However, the individual is closely connected with the theme of life; therefore, if the fetus is considered to be a 'life' it may gain more than just interests. Within, *Vo v France*,[189] the theme of life and what is an individual combined to result in a fetus only having interest:

> [The] Court is convinced that it is neither desirable, nor even possible as matters stand, to answer in the abstract the question whether the unborn child is a person for the purposes of Article 2 of the Convention. As to the instant case, it considers it unnecessary to examine whether the abrupt end to the applicant's pregnancy falls within the scope of Article 2, seeing that, even assuming that that provision was applicable, there was no failure on the part of the respondent State to comply with the requirements relating to the preservation of life in the public-health sphere. With regard to that issue, the Court has considered whether the legal protection afforded the applicant by France in respect of the loss of the unborn child she was carrying satisfied the procedural requirements inherent in Article 2 […].[190]

Derogation and deference surrounding the remit of 'life' results in an institutional reluctance to answer the deeply ethical and moral questions. The issue is continually deferred back to the member states that are ultimately silent upon the issue unless an instance arises whereby a question specifically needs the issue of a fetus and if it is a 'life' to be resolved. Until that specific circumstance occurs in case law then such uncertainty will continue. The lack of a clear statement of the interplay of human dignity to the viable fetus has left the question for another day, ensuring continuing confusion for future cases (Goldman 2005).

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[189] *Vo v France* (2005) Application No 53924/00.
[190] *Vo v France* (2005) Application No 53924/00 [85].

6.5.2 Consequence for the maternal fetal divide

Despite the fetus being framed as a distinct and separate being from the mother's body in which it resides (Casper 1998), regulation is clearly based upon dependant moral status (Harris 2000). Clearly, the biological unborn patient that Liley (1972) proposed cannot exist in such a framework. Liley's biologically determined fetal patient being in control of pregnancy cannot be sustained as the mother is in legal control of pregnancy (Liley 1972). Even the fetus as a patient concept proposed by Harrison et al (1984) as well as Chervenak and McCullough (1994) would fail to find full recognition within the institutional framework, because it is accepted that the fetus is not a separate patient, but closely connected to the mother (Chervenak and McCullough 2007). Decisions are viewed as exclusive with regards to the maternal to fetus, but inclusive from the fetus to mother (Harris 2000). Therefore, the maternal fetal divide is strictly one about ostensible individuals. It is the rights of 'actual' persons rather than possible persons that are applicable regardless of the consequences for the next or future generation (Heyd 1994).

Given that informed consent is an integral part of the autonomous decision making process hindsight bias of the 'I've changed my mind' scenario when a mother becomes distressed by a pregnancy is a consequence that mother, child, family, FGT practitioners (to name a few) have to deal with (Brooks and Sullivan 2002). Hindsight bias may become more relevant within FGT because of the vast range of possible certain and uncertain outcomes. Such hindsight bias could result in challenges to established social and legal criteria[191] which medical decisions are judged (Dickenson 2003). Therefore, cases of wrongful birth may become evident especially if FGT and abortion options are not aligned properly.

Nonetheless, hindsight bias is information dependent, which in turn creates social responsibility and accountability within the maternal fetal divide for all practitioners involved. The creation of such responsibility is no different from any other medical or genomic activity; however, the consequences can be profound and thus lead to

[191] See *Bolitho (Deceased) v City and Hackney Health Authority* [1998] AC 232.

elements not being addressed (see 7.6). Uncertainty within medicine can lead to problems within the doctor patient relationship because the time has passed when it was an absolute belief that knowledge of the mechanisms of disease was sufficient to establish correct diagnoses; provide accurate prognoses; and, through application of medical research, produce cures (Giraud 1992).

More importantly, any conflict between the mother and fetus is not relevant for the maternal fetal divide within the framework other than that it exists. The fetus has no 'rights' therefore, there is no conflict between rights holders other than those which are socially constructed. For example, in fetal treatment meetings at one institution, fetuses are routinely referred to as 'the kid,' and 'the baby,' which are all quite human-and gendered-identities (Casper 1994). Nevertheless, in the majority of cases, maternal and fetal interests align and the mother will want to do what is best, no matter what is involved, despite there being no legal or strict ethical obligations (Chervenak and McCullough 2007). However, such beneficence is constrained by human dignity. Therefore, acts which a mother is willing to do, such as sacrificing her own body for the benefit of the fetus, could fall into the dwarf throwing category, whereby using one's own body in the way one sees fit is limited by dignity.[192] Such restrictions upon human dignity are enforced through the regulation of practice and research. Therefore, high risk procedures that would ultimately lead to maternal death, but fetal survival and correction are filtered out by the research process. Therefore, autonomous choice and human dignity within the context of FGT is mitigated by regulators.[193]

Tension emerges between the recognition and appreciation of interests for those who are not 'individuals'. If the interests of the fetus or the public are not capable of overriding the individual then surely the Abortion Act 1967 would be different? Therefore, even if the fetus has no rights and will not be considered life for protection within the regulation of FGT, certain obligations may still be owed that

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[192] See *Council d'Etat* (October 27,1995) req. nos. 136-727 (*Commune de Morsand-sur-Orge* and 143-578 (*Ville d'Aix-en-Provence*) which was confirmed by in the United Nation Human Rights Commission case *Wackenheim v France* CCPR/75/D/854/1999.
[193] See chapters 6 and 7.

entail constraints upon dignity, such as prenatal interventions (Savulescu 2007). However, there does appear to be a ray of light within regulation that takes into account intergenerational interests.

6.6 A ray of light?

Despite the mother being paramount, future generations are taken into consideration and positive action can be taken. Regulation and subsequent case law dictates that they should be taken into account by FGT practitioners, with the interests of the next and future generations being able to influence the decisions of practitioners:

> *Article 16 – Protecting future generations*
> The impact of life sciences on future generations, including on their genetic constitution, should be given due regard.[194]

Therefore, the interests of the next and future generation are important and should become part of the autonomous rational reasoning of the individual. This position is reflected within stem cell research where the dignity of the embryo must be respected.[195] The decision making of the individual should be mitigated not by the interest of others but by the fetus. Within case law from England and Wales several examples emerge, with the below extract being a typical example:

> In my judgment a reasonable medical man or woman carrying out the procedure would take account of the risk of causing injury to the embryo in the womb and the consequent risk of the child being born injured and with abnormalities.[196]

Therefore, the interests of the next and future generations are relevant factors in the practice of FGT practitioners, which regulators would like practitioners to take into consideration. The consultations documents highlight the intrinsic nature of the fetus and how it should be treated with respect and dignity. Nevertheless, intergenerational interests are not the only consideration which limits and guides the practice of FGT practitioners. An example of this is from the highly influential Council of Europe protocol where it states:

> 1. Research on a pregnant woman, which does not have the potential

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[194] United Nations Educational, Scientific, and Cultural Organization Universal Declaration on Bioethics and Human Rights 2005 Article 16.
[195] As seen within Case C-34/10 *Oliver Brüstle v Greenpeace E.V.* [2011] OJ C 362, 10.12.2011, p. 5–6, and the Human Fertilisation and Embryology Act 1990 s.3(3).
[196] *Burton v Islington Health Authority* [1991] 1 Q.B. 638 and upheld on appeal.

> to produce results of direct benefit to her health, or to that of her embryo, foetus or child after birth, may only be undertaken if the following additional conditions are met:
> i. the research has the aim of contributing to the ultimate attainment of results capable of conferring benefit to other women in relation to reproduction or to other embryos, foetuses or children;
> ii. research of comparable effectiveness cannot be carried out on women who are not pregnant;
> iii. the research entails only minimal risk and minimal burden.[197]

However, the above needs elaboration because it could easily be construed that the fetus within this protocol is disposable. Also, the reasons behind the protocol are unclear. The explanatory report goes on to explain:

> [R]esearch [must] be aimed at benefiting other women in relation to reproduction, or other embryos, foetuses or children. The wording "in relation to reproduction" should be understood broadly; for example it would include research relevant to the health of women following pregnancy, or research relevant to women's choice on whether or not to become pregnant. Indent ii requires that research of comparable effectiveness cannot be carried out on women who are not pregnant. Recourse to research on pregnant women, embryos or foetuses must be, scientifically, the sole possibility if it does not produce a significant direct benefit for the participant or her embryo, foetus or child. This provision should not be considered discrimination against the pregnant woman, but protection of her health and that of her embryo, foetus or child (Council of Europe 2005: [103]).

It is evident from the explanatory report that the treatment of future generation will not be discriminatory if based on objective reasoning. It should be noted that the language used is future' rather than 'next' generation. Future generations encompass a far wider remit than next generations because future generations include any results that affect the germ line. Despite the above quote explicitly mentioning embryos and fetuses; it is the relevant provision in terms of reference to the benefit of other fetuses, embryos and children that encompass the next generation, and implicitly future generations. Despite terms such as 'future' being used, the above quotes typify that in practice, when legislating, the next generation has a relevant interest in conjunction with the individual. Therefore, the tension and conflict appears to emerge from how others, such as third parties, view how a mother should exercise

[197] Council of Europe Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research 2005 Article 18.

her autonomy, but also how that autonomy is balanced against the next generation (Scott 2002). So what does that mean for the maternal fetal divide within FGT?

6.6.1 Consequence for the maternal fetal divide

By implying that fetal interests have the ability to constrain certain practices, human dignity as a constraint must also be considered in areas such as enforcement of treatment. Fetal interests appear to be recognised, even within regulatory institutions where the fetus is not a legal 'life'. However, due to fetal interests crystallising postnatally one does not need to engage with questions of personhood or agency because the focus can be on the next generation's wish not to suffer harm (Buchanan, Brock et al. 2000). Therefore, as long as children are being forced to receive treatment against their own or parental wishes,[198] the enforced treatment of pregnant women is possibly tenable (Purdy 1990). Because of the institutional recognition of the maternal fetal divide and 'the nature of pregnancy', the next generation can be considered, due to the 'best interests' of the current individual. FGT technology will be targeted at conditions whereby 'life' is highly likely not to occur or where 'life' will occur, but with severe disabilities and where there is no postnatal cure (Gene Therapy Advisory Committee 1998). Therefore, in assessing responsibilities towards a fetus, an alternative perspective is needed to understand the relationship between the mother and the next generation (Groves 2006). The introduction of fetal interests creates a responsibility for rights holders to consider the interests of others. Consequently, one has to separate life saving and therapeutic treatment from life enhancing therapy. Surely the state has a legitimate interest in protecting the health of the next and possible future generations from conditions that lead to neonatal death?

Empirically, reproductive choices that affect future generations affect 'actual' persons because they can restrict choice (Heyd 1994). The inclusion of future interests within the regulation of FGT appears to signify this because of the emphasis on safety (see chapter 7). Furthermore, it would appear that the function of FGT

[198] See *Re R (A Minor) (Wardship: Consent to Treatment)* [1992] Fam 11 CA; *Re E (A Minor) (Wardship: Medical Treatment)* [1993] 1 FLR 386.

within its narrow remit of applicable conditions should be preferential on a regulatory level than the alternatives of abortion or no action at all. Ultimately, however, independent physical persons are more important than the future 'actual' persons within regulation once implantation occurs. By focusing upon actual persons, the maternal fetal divide does not take into account the difference between life saving and life enhancing treatment (Savulescu 2007). The sample does not appear to engage with the possibility that these conditions can only be treated in utero. As a result, harm to the next generation within the maternal fetal divide can only be mitigated by the choice of the mother. As it will be shown in chapter 7, these issues are compounded further. Therefore, despite the benefit to society in preventing disease propagation the state cannot act to secure the protection of future generations within the clinical context.

6.7 Conclusion

Human dignity appears as an explicit overarching principle for the future use of FGT. However, human dignity is facilitated by autonomy which ultimately raises the individual above all else within the clinic since without individual consent science cannot legitimately proceed. There is a ray of light for the protection of future generations within the regulation of future FGT because the dignity of the embryo is to be respected in stem cell research, and the status of the fetus must be taken into account in the decision making process. However, a fetus is not considered an individual, therefore maternal choice within the clinic trumps fetal interests. In addition there are precedents in restricting choice within the clinic due to society and governmental will. Nevertheless, autonomy within the clinic appears unrestricted because of the narrowness of present choices.

In adopting a consistent approach to autonomy, society avoids problems such as deterring women from seeking medical care; burdening women and often minority groups disproportionately with these interventions; and highlighting the uncertainty of medical predictions of harm (Annas 1986, Purdy 1990). Importantly, by liberalising the rules on pregnancy such rules are considered as not casting a social function upon pregnant women to be merely fetal containers. However, the fetus as a patient concept is shaped and formed by the relationship between the mother and

the clinician (Casper 1998). Yet that social relationship does not have any weight within regulation, despite having consequences for engaging further social relationships between the mother, child and third parties. Such a position shows a flagrant disregard for the harm that could be suffered as the relationship between mother and fetus matures and crystallises postnatally. It focuses upon fetal harm, rather than upon the future child (Buchanan, Brock et al. 2000); thereby guaranteeing postnatal harm because only palliative postnatal treatment would be available. This would be an injustice contrary to the prevention of harm to future individuals (Savulescu 2007).

The law crystallises rights upon birth, which within the confines of FGT creates a legal tension. Two elements arise that settle the regulatory and practical implications of such crystallising rights, namely: a mother cannot be held liable for negligent acts towards her own fetus (Jackson 2009);[199] and, such action would be an omission which does not increase the harm suffered by the fetus and is not within the remit of sanctionable omissions in tort (Markesinis, Deakin et al. 2003). However, such general principles appear to mask over the need to evaluate the moral implications of such unique practices and the possible moral, societal and political implications.

Despite recognition of the impact of biotechnologies, it is possible to discriminate against the interest of the fetus if it is deemed objective with a legitimate aim. Thus the interest of the next generation can still be overridden ultimately by the individual. Therefore, despite the ray of light offered in 6.6 for the protection of the interests of the next and future generations, ultimately, where autonomous choice is allowed, future generations are at the mercy of the current individual. Nevertheless, the importance of future generations' interests in conjunction with the interests of others within FGT means that the scientific progress of research must be examined more intently to discover the ways in which FGT progress impacts upon current thinking.

[199] Congenital Disabilities (Civil Liability) Act 1976.

7 Documentary Data: Scientific Progress

7.1 Introduction

Having seen that human dignity has played an implicit role in the clinic before choice can be exercised within the clinic certain research protocols have to be followed. Given the purported importance of human dignity seen within the first half of the documentary analysis in chapter 6, this chapter will analyse the regulation of the FGT and the way in which it impacts not only upon the progress of FGT but also on the maternal fetal divide. This chapter will show how the progress of FGT is controlled through creating a set of research parameters prescribing limits within which a FGT practitioner can operate. The limits emerge from risk and safety assessments which have elements of fear within them. The consequence is that scientific progress has many hoops to jump through which impacts upon choice within the clinic and creates a paternalistic bubble within which FGT proceeds. The creation of this bubble protects future generations and, therefore, intergenerational interests but effectively regulates the scientific progress of FGT and restricts maternal choice.

In section 7.2 the remit of FGT will be outlined in order to identify whether 'choice' is restricted and if there is any effect upon the maternal fetal divide. Section 7.3 explores the research procedures to see if there was any influence of rights and dignity within the process or whether dignity is just a feature found within the clinic. It emerges that through safety and risk assessments dignity and protection of future generations are being taken into consideration. However, within section 7.4 these principles appear to stifle the progress of FGT because human dignity appears to be one of the driving principles behind the research restrictions. In section 7.5 it emerges that this leads to limitations such as the prohibition on germ line interventions. Therefore, human dignity within the research process ultimately restricts the areas FGT practitioners can pursue and hence what patients will be able to choose. Finally, in section 7.6 missing issues are identified from the documentary analysis in order to provide some contrast and guidance for analysis of the interview data in chapter 9.

7.2 Remit of fetal gene therapy: disease selection

It is often argued that scientists have freedom to research whatever they like. Within humans this is not the case because the interaction of that freedom to research and the rights of others often intersect:

> […] "*scientific research in the field of biology and medicine shall be carried out freely, subject to the provisions of this Convention and the other legal provisions ensuring the protection of the human being*." As mentioned in the Explanatory Report in relation to the latter, if *"freedom of scientific research is justified not only by humanity's right to knowledge, but also by the considerable progress its results may bring in terms of health and well being of patients*", it is "*not absolute. It is limited by the fundamental rights of individuals, which protect the human being*"(Working Party on the Protection of the Human Embryo and Fetus 2003: 22).

Therefore, a FGT practitioner does not have complete freedom in research as their choices are not only restricted by regulation, but also by fundamental rights. Therefore, as highlighted in chapter 6, these rights include the right to life, the right to private life, autonomy and human dignity. These rights tell us little about what diseases FGT practitioners can investigate and develop treatments for. However, it is clear that only specific diseases can be researched:

> The disorder or disease treated would need to be life threatening, or associated with severe disability, and for, which no suitable treatment is available after birth, in order to justify intervention in utero (Gene Therapy Advisory Committee 1998: [27(c)]).

Therefore, harm must occur before birth and be irreversible, assuming the phrase 'no suitable treatment' means 'a treatment that is unsuccessful in curing or alleviating a condition' as the report implies. Essentially, conditions that violate the right to life and autonomy of the next generation include conditions such as cystic fibrous and Duchenne muscular dystrophy,[200] but what about future generations?

It is clear from the documents that future generations are protected from further harm through the prohibition of certain practices. It is only somatic treatments that are

[200] A severe progressive form of muscular dystrophy of males that appears in early childhood, affects the muscles of the legs before those of the arms and the proximal muscles of the limbs before the distal ones, is inherited as an X-linked recessive trait, is characterized by complete absence of the protein dystrophin, and usually has a fatal outcome by age 20 (National Institute of Health 2011).

permissible because germ line interventions are prohibited. The practice is prohibited such that a clinic trial licence cannot even be applied for:

> The licensing authority shall not authorise a clinical trial involving products for gene therapy if the use of those products in that trial would result in modifications to any subject's germ line genetic identity.[201]

Therefore, a divide is created between somatic and germ line genetics. A child born as a result of successful treatment will have two different genetic constitutions. Furthermore, the issue of germ line transmission and treatment within FGT has lead to a narrowing of the point of permissible intervention once pregnancy has occurred.

> In utero gene therapy heightens concerns about the risk of germline transmission. Until compartmentalisation of the primordial germ cells in the gonads, which is completed in humans by the 7th week of gestation, cells are unprotected and mitotically active, allowing viral vector infection. This must be taken into account, and in utero gene therapy should preferentially be conducted after this time-point in order to minimise the risk of germline transmission. In addition, this risk should be considered also for other types of gene therapy in fertile women (European Medicines Agency 2006: 5).

The consequence of the explicit prohibition on any germ line interference is that regulation reflects this position through reinforcing safety procedures. Therefore, precaution must be taken in research that could inadvertently affect the fetal or maternal germ line:

> Reproductive and developmental toxicity: Studies on the effects on fertility and general reproductive function shall be provided. Embryo-foetal and perinatal toxicity studies and germline transmission studies shall be provided, unless otherwise duly justified in the application on the basis of the type of product concerned.[202]

Therefore, a separation is made between in vitro embryo genome alterations and fetal alterations. It is here that FGT must tread with caution, because treatment would be in danger of no longer being fetal treatment but embryo treatment and therefore prohibited.[203] Yet, it is the distinction between fetal and embryo research that has an effect upon the maternal fetal divide.

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[201] The Medicines for Human Use (Clinical Trials) Regulations 2004 s.19(3).
[202] Directive 2009/120/EC Annex 1 s.4.2.3.
[203] See Human Fertilisation and Embryology Act 1990 s.3(3) whereby embryo research is prohibited to embryos that are below 14 days of development and have not developed a primate streak. Also any

7.2.1 Effect for maternal fetal divide

It is evident that the management of a condition is being driven by two ethical considerations. The avoidance of treatment in utero where possible; and secondly, the risk of germ line transmissions. Consequently, the maternal choice identified within chapter 6 is restricted in favour of human dignity and choice is made within the confines of the paternalistic bubble. The restrictive and precautionary range of diseases that can be researched once again affects reproductive choice (Heyd 1994). Nevertheless, where prospective parents have knowledge of their genome they can still choose to exercise limited choice over which embryo, sperm or oocyte are used. Therefore, through negative selection of specific genetic constitutions, prospective parents are exercising intergenerational choices (Buchanan, Brock et al. 2000). However, these intergenerational choices are not exercised through alteration, but selection. The consequence is that the maternal fetal divide will become relevant only for those who do not have genetic information before conception or implantation and those cases where mutation occurs. Therefore, the restriction upon the development of in utero treatments will make certain conditions principally about termination or birth, rather than termination, birth or treatment. Where a condition falls into the former category, then emphasis will be placed upon pre-implantation reproductive choice; therefore moving the debate away from the maternal fetal divide. For those conditions, choice does not have to be weighed up against actual future persons, merely future potential persons (Savulescu 2007); therefore, there is no maternal fetal or maternal embryo conflict.

However, it is clear that even where a condition is treatable one has to consider the duties of parents towards their children. Due to only somatic interventions being pursued, any future offspring of the treated child would have a chance of inheriting the treated child's genetic condition, because the treated child's germ line will not have been altered. As a result, future interests remain relevant within the disease selection model, because of the possible effect upon treated child's reproductive future. However, the debate surrounding the informing of offspring and the

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embryo that has been researched upon must not be implanted within a woman, Human Fertilisation and Embryology Act 1990 s.3(2).

offspring's reproductive choices moves the debate away from the maternal fetal divide. Yet, once conditions have been identified for which treatments can be developed, it is clear that certain research procedures must be followed.

7.3 Research procedure

Legislation, accompanied by codes of practice, are the principle documents for governing research procedure. There was little, if any, mention of research procedure within the cases analysed because the 'procedure' was not the substantive issue in question. However, within the regulatory documents the themes of procedure and good practice are evidently paramount to scientific research. Within those documents the procedural requirements of FGT includes: specific information needed for a research application; having an emergency protocol to reduce adverse reactions; what laboratory procedures should be followed as well as outlining good clinical practice and practical procedures. Good clinical practice is a set of internationally recognised ethical and scientific quality requirements which must be observed in designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.[204] These principles include obtaining informed consent, conducting risk-benefit calculations and trials that are scientifically sound.[205] Within good clinical practice 'clarified guidance' emerges as a key theme. Within the theme, protection, due process and uniformity/standardisation appear as strong themes from the documents that govern the current regulation of gene therapy. It would appear that FGT practitioners must adhere to these in order to merely operate:

> Standard procedure
> 1. […] a competent authority or the Commission may ask for further information, make comments or present reasoned objections to the placing on the market of the GMO(s) in question within a period of 60 days from the date of circulation of the assessment report.
> [...]
> The competent authorities and the Commission may discuss any outstanding issues with the aim of arriving at an agreement within 105 days from the date of circulation of the assessment report.
> Any periods of time during, which further information from the

[204] Directive 2001/20/EC, Article 1(2).
[205] The Medicines for Human Use (Clinical Trials) Regulations 2004 Schedule 1.

> notifier is awaited shall not be taken into account for the purpose of calculating the final 45 day period for arriving at an agreement. Reasons shall be stated in any request for further information.[206]

This quote typifies the due process nature of an application and the clarification needed to guide FGT practitioners. It also makes scientific progress based on a uniform process so that ideas can be disseminated across not only the UK, but across the European Economic Area. Specifically to UK, FGT practitioners, an example of a structured process can be seen within Appendix E. It should be noted that by utilising a clarified application process with due process embedded within it, the research procedure outlines duties and rights that research should follow. Within these duties, obligations arise for FGT practitioners to obtain informed consent from individuals before they can conduct research. Therefore, the individual becomes a prominent and important part of research. The 'individual' theme will be returned to below, as the main thrust of the research procedure from the institutional documents is to guide FGT practitioners through the process and attain good clinical practice. It is clear from the titles of regulatory documents that good practice is key.[207] In attaining good clinical practice certain technocratic criteria emerge:

> 5.2. **Specific requirements for gene therapy medicinal products**
>
> 1. *Human pharmacokinetic studies*
>
> Human pharmacokinetic studies shall include the following aspects:
>
> (a) shedding studies to address the excretion of the gene therapy medicinal products;
>
> (b) biodistribution studies;
>
> (c) pharmacokinetic studies of the medicinal product and the gene expression moieties (e.g. expressed proteins or genomic signatures).
>
> 2. *Human pharmacodynamic studies*
>
> Human pharmacodynamic studies shall address the expression and function of the nucleic acid sequence following administration of the gene therapy medicinal product.
>
> 3. *Safety studies*
>
> Safety studies shall address the following aspects:
>
> (d) emergence of replication competent vector;
>
> (e) emergence of new strains;
>
> (f) reassortment of existing genomic sequences;

[206] Directive 2001/18/EC Article 15.
[207] See Appendix F - List of Analysed Documents.

(g) neoplastic proliferation due to insertional mutagenicity.[208]

This is just one example of the clarification and remit of FGT that emanate as typical themes in relation to guiding research within the area. Information is communicated in technocratic language unlike the documents that generally outline principles. The voluntary code of practice, the Health and Safety Executive (HSE), is heavily loaded with technocratic language thus making the document opaque to all readers other than trained expert readers. However, the technocratic style informs the researcher of important criteria they must cover and in some cases how to do it. For example, it goes as far as to prescribe how to label samples and products for manufacture to ensure uniformity between FGT practitioners.[209] The techno-scientific script, in relation to clinical trial applications through to emergency procedures, crystallises multiples trajectories of medical practice through protocols and regulation (Timmermans and Berg 1997). Therefore, the standardisation of procedure traverses all practice of gene therapy. In standardising the practice of FGT in accordance with the rest of Europe, data becomes more reliable and transparent, thus increasing the objectivity and understanding of results within the european scientific community. As a result of this standardisation 'biomedicalisation'[210] of science within the UK emerges due to inclusion of conceptual and clinical expansions through the commoditisation of health, the elaboration of risk and surveillance, and innovative clinical applications of drugs, diagnostic tests, and treatment procedures (Clarke, Shim et al. 2003). Therefore, through technocratic language, risk is quantifiable and provides assurance about the safety of FGT.

7.3.1 Safety first through risk assessments

Safety emerges as a key concept that FGT practitioners must observe. The standards they are expected to attain are communicated in a technocratic way. Procedural duties are in line with the conformity of research and the practice of good clinical practice. Procedural safety and informed consent also fall within the good clinical

[208] Directive 2009/120/EC Annex 1 s.5.2.
[209] For example see Directive 2001/20/EC.
[210] As defined by Clarke et al (2003: 163) as the increasingly complex, multisited, multidirectional processes of medicalisation that today are being both extended and reconstituted through the emergent social forms of a highly and increasingly technoscientific biomedicine.

practice of FGT practitioners and are present throughout the work. Where the themes of safety and procedure are raised it is evident that they are based upon scientific practice. Therefore, as will be shown below, scientific evidence and progress are helping to inform both the individual persons and the safety protocols that are made. In order to conduct risk assessments and facilitate the action of FGT practitioners, procedural requirements emerge based around risk avoidance:

> **2.4 Bacterial vaccines and gene delivery systems**
> Overview 53
> Risk assessment for human health 54
> Hazards associated with the recipient strain 54
> Examples of bacterial gene delivery systems 55
> Hazards associated with genetic inserts 60
> Alteration of phenotype 61
> Genetic stability and sequence mobilisation 62
> Risk assessment for the environment 63
> Survivability and stability 63
> Hazards posed by the genetic insert 64
> Alteration of phenotypic and pathogenic traits 64
> Procedures and control measures 65
> Operational considerations 65
>
> (Health and Safety Executive 2007: 2)

The risk assessment is for the benefit of the research subject, as well as for the environment and society in general. From the contents pages of the Health and Safety Executive (HSE) voluntary code of practice this is a visible consideration. In fact, the guidance from the HSE is principally about risk assessment within clinical trials. Risk assessment and informed consent are all part of the general theme of good practice. The Medical Research Council (MRC) good practice guidance indicates the same reliance upon risk for good management in their construction of what amounts to good practice in the below extract:

> Conducting the research
> 4.1 Information and organisation
> 4.2 Use, calibration, and maintenance of equipment
> 4.3 Risks of research misuse
> 4.4 Hazardous processes and materials
> 4.5 Standard operating procedures
>
> (Medical Research Council 2005: 1)

Risk assessment is not only communicated in a technocratic manner, but in order to facilitate good clinical practice through principles such as informed consent, further procedural tick lists are obligatory. Communication of those risks that must be made

clear to the patient appear to be simplified into layman's terms. For example, Directive 2006/17/EC highlights that patients:

> [M]ust be selected on the basis of their age, health and medical history, provided on a questionnaire and through a personal interview performed by a qualified and trained healthcare professional. This assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, such as the possibility of transmitting diseases (such as sexually transmitted infections), or health risks to themselves (e.g. superovulation, sedation or the risks associated with the egg collection procedure or the psychological consequences of being a donor).[211]

Because information has to be communicated to the patient whom may not have the expertise or experience in the field (based on scientific qualifications), the language appears simplified. It is noteworthy that post 2005 there is a marked shift in amending directives, which clarify and extend the risk calculation of tissue and Genetically Modified Organisms (GMOs) that are within the ambit of Directive 2004/23/EC. No doubt the increase in risk assessment is connected to the French X-SCID gene therapy trial upon children where, in 2005, it could be considered that the previous risk calculations were not adequate to take into account the risks within human patients. The introduction of Regulation 1394/2007/EC is a clear indication of the practice of FGT adjusting what is included within the risk assessment. Therefore, risk is an important factor within research, with risk predictability emerging as a key component regardless of whether its effect is environmental or medical:

> The use of tissues and cells for human application carries a risk of disease transmission and other potential adverse effects in recipients. In order to monitor and reduce these effects, specific requirements for traceability and a Community procedure for notifying serious adverse reactions and events should be set out.[212]

Therefore, risk calculation indicates monitoring is also an important process and includes the monitoring of premises so that they comply with enforceable standards. There is the specific requirement for long term monitoring of the engraftment of a biomolecule, thus the prospective nature of gene therapy is a consideration.

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[211] Directive 2006/17/EC Annex 1 s.2.2.1.
[212] Directive 2006/86/EC Preamble.

However, within the documents it appears vague as to how long 'long term monitoring' is, as indicated in Regulation 1394/2007/EC. EMA guidance indicates that it could be days, months or years, but does not explicitly reference looking at the next generation (Committee for Medical Products for Human Use 2009). The next generation may implicitly be included, but it is not clear that this is the case. To facilitate the monitoring of research it has to be traceable. Therefore, further duties are imposed upon FGT practitioners to create research trials not only for their own science, but also for safety protocols which can be followed in cases of emergency. Therefore, with monitoring comes compliance, which is monitored by regulators. Whether procedural guidance is considered red tape is another issue, but it is a uniform process that appears to be constrained by fear and safety concerns.

It is clear that the focus of regulation is to: deal with scientific uncertainty (risk) and; apply ethical principles for the protection of present and future generations; offer special guarantees that secure the legitimacy of genetic governance through public participation and transparency in a globalized world; and finally employ a variety of different instruments for the regulation of extremely diverse applications of biotechnology, all of which function in the shadow of biotech patents (Somsen 2005). The main focus is upon the first and last points. The final point is clearly demonstrated through the operational focus of bodies such as the HSE, GTAC, MHRA and DOH. Risk being prevalent within the regulation of FGT is not ground breaking. Due to the uncertain elements of novel technologies the state through regulation should guide the size and direction of biotechnologies (Somsen 2005). The preoccupation follows the increasing focus of proactive risk regulation of biotechnologies because of the uncertainties inherent in their release (Tait and Levidow 1992). However, the documents appears to understate the inherent uncertainty of gene therapy with rigorous good practice, risk assessments and long term follow-up providing adequate measures that ensure certainty and thus do not violate human dignity.

7.3.2 Consequence of risk assessment on scientific progress and the maternal fetal divide

Risk within the sample is based upon expert scientific models of risk rather than lay perceptions of risk (Somsen 2005). The risk is balanced relatively to risk-benefit criteria (Van Ness 2001). Therefore, risk is framed by technocratic calculations of 'risk-benefit' and communicated by technocratic language. In doing so, the apparent objectivity of scientific discourse can be shown often to be presenting 'highly contentious' statements as 'uncontentious', indeed, as fact (McKenna and Graham 2000). The lack of animal models for evaluating the effects of biological products are much less well developed than their counterparts in traditional toxicology because of a lack of prenatal research in general (Office of Recombinant DNA Activities 1999). Therefore, the above mentioned safety models may not be appropriate or adequate to foresee dangers despite the certainty that such models should maintain safety within FGT. The technocratic language appears to the lay person to provide certainty within an area which is 'experimental' and thus always containing uncertainty within it. The uncertainty of such practice is evident within the evolution of medical practice, none more so than within gene therapy (Henry 2006). Given the relationship between the patient and physician, communication of risk and uncertainty must occur in order to achieve informed consent and maintain human dignity within the maternal fetal divide. By communicating this risk it also seeks to identify uncertain future harms to future generations that may not have been already considered within the maternal decision making process.

Yet even the most successful trials of gene transfer have engendered questions about its prospects, which was evident in the haemophilia B trial raising concerns about germ line modifications (Marshall 2001). The results of the X linked, severe, combined immunodeficiency trial were offset by unexpected, vector induced leukaemia in two participants (Kimmelman 2005). Therefore, 'risk' is based on perceived as well as known risks from previous scientific knowledge (Williams 2001). Further examples of such uncertainty surrounding in utero damage are the thalidomide and Epilim cases. These two examples highlight two different issues relating to the culpability of FGT practitioners and drug companies involved in novel

drugs. Importantly, both highlight the intense and emotional effect of damage to the next generation, and how unforeseeable certain acts can occur within the framework of certainty and risk management (BBC 2002, Hirsch 2011). Such examples highlight the difficult nature or regulation within FGT.

Despite the certainty presented by risk management, precautionary reasoning is evident within regulatory bodies. As was the case with thalidomide, Epilim and other known drugs, uncertainty, although statistically low due to the proactive approach, was still a possibility, as within any clinical trial. Therefore, precautionary reasoning through monitoring and strict risk management is the best that can done and addresses some of the ethical concerns regarding the next and future generation (Somsen 2005). Yet, a focus on risk management can lead to stifled scientific progress (Rostein, Irving et al. 2006), or at least significantly hindered scientific progress. However, that restriction on progress may be legitimate where the reasons are justified. Those reasons appear to be because of fear and safety concerns, which appear to stem from the application of human dignity. The resulting effect upon the maternal fetal divide is that, rather than allowing mothers to assess risk themselves, the choice is once again restricted by paternalism, by society and by humankind in general.

7.4 Scientific progress stifled by fear and safety concerns

In considering future generations it appears that in terms of germ line technology the current regulatory system is contradictory because of the stifling fear and safety concerns. On the one hand regulation is pro scientific progress. On a policy document level pride emanates about the achievements of genomics and scientific progress.

> Here in Britain we start with a great advantage. We have in this country some of the best scientists, academics and universities. A great deal of the research and innovation into genetics is happening here – in both our pharmaceutical and biotechnology industries as well as in the public sector. Our NHS genetic services are admired throughout the world. We are well placed to lead the world in the discovery and realisation of the maximum benefits of genetics in healthcare (Department of Health 2003: [1.4]).

Scientific progress within the UK is seen as something to be proud of. Scientific

progress is important not only for science itself but for the public good. It emerges that good clinical practice as identified in section 7.3 (such as scientifically sound trials and informed consent) is built upon the previously mentioned procedural requirements. It is from these procedural requirements that science is reinforced by its own findings in order to progress. At the European level, it is clear to see:

> The principles of good clinical practice and detailed guidelines in line with those principles shall be adopted and, if necessary, revised to take account of technical and scientific progress […].[213]

It continues by stating:

> **Adaptation to scientific and technical progress**
>
> This Directive shall be adapted to take account of scientific and technical progress in accordance with the procedure referred to in Article 21(2).[214]

In fact, regulation is actively striving to maintain a grip upon research, which can be seen in the extract below. Research informs the regulators, who in turn inform the legislators, who then govern the practice of science, which then develops further within those confines thus needing further regulation:

> Due to scientific and technical progress in the field of advanced therapies, as reflected in Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, it is appropriate to adapt Annex I. The definitions and detailed scientific and technical requirements for gene therapy medicinal products and somatic cell therapy medicinal products should be updated. Moreover, detailed scientific and technical requirements should be established for tissue engineered products, as well as for advanced therapy medicinal product containing devices and combined advanced therapy medicinal products.[215]

The influencing nature of scientific progress within areas such as FGT, which seeks to challenge our understanding of not just humanity but language, is an important, visible concept. However, in relying upon science to guide and direct regulation, one must look at the consequences and possible restrictions upon the progress of FGT. In terms of intergenerational issues, in order not to violate human dignity research within pregnancy is severely restricted. With images of Frankenstein

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[213] Directive 2001/20/EC Article 1(3). Another example is Directive 2005/28/EC Article 13.
[214] Directive 2001/20/EC Article 20.
[215] Directive 2009/120/EC, Preamble.

monsters and deformed thalidomide babies fresh in the minds of those who conduct research, and the fear of reoccurrence, restrictions upon FGT can be seen:

> An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.[216]

Therefore, a reiteration of the disease model above is seen. However, with scientific progress reinforcing itself with continuing research it ends in a contradictory position. It is clearly stated within Directive 2001/20/EC, which is transposed directly into the Medicines for Human Use (Clinical Trials) Regulations 2004:

> The licensing authority shall not authorise a clinical trial involving products for gene therapy if the use of those products in that trial would result in modifications to any subject's germ line genetic identity.[217]

The position of a complete ban on germ line interventions is reiterated within the policy documents analysed. The regulation goes further to explain why germ line interventions are prohibited:

> The UK Clinical Trials Regulations 2004 prohibit gene therapy on reproductive (germ line) cells; it can only be carried out on non-reproductive (somatic) cells. Germ line gene therapy can potentially cause changes in a patient, including harmful effects that could be passed on to future generations. It is therefore currently considered unacceptable for both ethical and safety reasons (Parliamentary Office of Science and Technology 2005: 1).

Therefore, biological intergenerational aspects are an explicit consideration. The interests of future generations are enough to prohibit the research freedom and practices of FGT practitioners on human beings. However, how can one overcome safety fears when all clinical trials that would seek to alter the genome on humans are prohibited? If one assumes that within the normal model of clinical trials in other sections of experimental medicine, once animal models have been properly conducted then safety concerns should only be fixed to current contemporary knowledge. Therefore, another reason must emerge as to why certain practices are prohibited, if regulation wishes to be progressive rather than reactionary.

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[216] Council of Europe Convention on Human Rights and Biomedicine 1997 Article 13.
[217] The Medicines for Human Use (Clinical Trials) Regulations 2004 s.19(3).

7.5 Fear stemming from human dignity?

With the individual embedded as a paramount consideration within good clinical practice of research, human dignity arises as an element which can be used to hinder scientific research. Therefore, within FGT carte blanche prohibitions emerge because of human dignity:

> The International Bioethics Committee of UNESCO should contribute to the dissemination of the principles set out [...] and give advice concerning the follow-up of this Declaration, in particular regarding the identification of practices that could be contrary to human dignity, such as germ-line interventions.[218]

It emerges that germ line alterations could be contrary to human dignity. Although the contingency of 'could' is used within the above quote, it is clear from reading other international explanatory reports that it is the fear of the effect of germ line alterations producing individuals or entire groups endowed with particular characteristics and required qualities (Council of Europe 1997), which would intuitively violate human dignity. Such intuitive violations of the abstract notion of human dignity should never be allowed, because to do so would devalue and disrespect humanity. However, further investigation into the prohibition reveals that:

> Because little is known about the possible consequences and hazards, and any harm to future generations would take a long time to discover and deal with, this application of gene therapy needs to be considered quite separately from somatic cell gene therapy (Clothier 1993: [2.26]).

However, carte blanche statements such as safety are time limited; whereas calls to human dignity are indeterminate in length. By prohibiting germ line technology, even for therapeutic and preventive purposes, regulation does not recognize an interest in inheriting a genetic patrimony made better through the eradication of genes causing diseases (Mori and Neri 2001). A distinction between the next generation and future subsequent generations is emphasised by a prohibition on germ line technologies. Restriction due to human dignity being violated could be considered valid on safety reasons because of the underlying themes that guide research. The foreseeability of scientific research emerges as a possible reason why

[218] United Nations Educational, Scientific, and Cultural Organization Declaration on the Human Genome and Human Rights 1997, Article 24.

human dignity is violated by not just the intervention on the genome, but by safety concerns. The best example of the importance of foreseeable consequences is from GMO regulation. When emergencies occur FGT practitioners must be prepared for foreseeable incidents with, once again, procedural process being key:

> (1) Where an assessment carried out pursuant to regulation 6(1) shows that, as a result of any reasonably foreseeable accident –
>
> (a) the health or safety of persons outside the premises in, which an activity involving genetic modification is carried on is liable to be seriously affected; or
>
> (b) there is a risk of serious damage to the environment, [...].
>
> (2) Where an assessment carried out pursuant to regulation 7(1) shows that, as a result of any reasonably foreseeable accident, the health or safety of persons outside the premises in, which an activity involving genetic modification is undertaken is liable to be seriously affected, the person undertaking that activity shall ensure that, before the activity to, which the assessment relates begins, a suitable plan is prepared with a view to securing the health and safety of those persons.[219]

Evident within the uniformly structured risk calculation, is that the foreseeability of risk is important. Foreseeability within risk assessment links back to the circular reinforcement of scientific progress by scientific practice dependent upon regulation. In doing so, reasonably foreseeable accidents become part of the mechanism of safety. The intended primary benefit of a clinical trial is the attainment of generalizable knowledge, because clinical trials are directed towards attaining medical and clinical knowledge (Van Ness 2011). Furthermore, that knowledge will empower the effective treatment of the population of patients that the experimental subjects statistically represent (Van Ness 2001). However, with indefinite changes to a genome, the foreseeability of germ line interventions becomes unforeseeable. Such unforeseeability is no different from other forms of clinical practice, such as inadvertent germ line transmission by chemotherapy (Laurema, Heikkila et al. 2003). However, in general, the outcomes of scientific knowledge are rarely amenable to previous knowledge, therefore, science has an inverse relationship with the capacity to know scientific consequences (Adam and Groves 2006). Since the effect of altering a genome can never be fully known, one can understand where safety

[219] Genetically Modified Organisms (Contained Use) Regulations 2000 s.20.

concerns about violations of human dignity related to future generations and humanity arise.

7.5.1 Foreseeable fetal gene therapy?

The foreseeability of future research is stifled by the inherent contradiction within the institutional reality of in utero germ line therapy. Regulation is kept up to date and altered by further scientific knowledge. Well designed clinical studies are the best available means of addressing uncertain gene therapy risks in human patients whether that be for somatic or germ line interventions (Deakin, Alexander et al. 2009). These technologies require investigation into the 'risk', which poses challenges for both the informed consent process and the conduct of clinical research more generally (Deakin, Alexander et al. 2009). Therefore, an inherent contradiction emerges that stifles the progress of germ line interventions and consequently overrides the interests of future generations in not having debilitating genetic conditions eradicated, without the need of further intervention, such as PGD. Therefore, the current prohibition upon germ line therapy is based upon risk to human dignity, due to causing more harm than cure (Pattinson 2002). Nevertheless, if those factors are important enough to stop germ line research, given the lack of knowledge about somatic interventions, should they also be prohibited? Clearly the extent of the lack of scientific knowledge is key in the distinction, but it could lead to the stifling of technological innovation if all procedures are banned where the risk of a therapy was not 100% known (Van Ness 2001).

One has to assume that it is the resulting safety concerns of direct physical gene manipulation that violates human dignity, rather than the notion of gene pool altering, because germ line choices already occur within embryo selection in assisted reproductive technologies (Nielsen 1997). However, in the distant future (and not as we understand FGT today) gene editing (See Disterer, Simons et al. 2009, Ledord 2011)[220] could be conducted in utero, thus making in utero germ line editing akin to negative selection, yet contrary to human dignity. Nevertheless, the possible positive

[220] A gene therapy method that specifically disrupts a single gene without the need to introduce 'foreign' material into the genome (Ledford 2011).

effects do not violate human dignity because somatic gene therapy is permitted and this practice is akin to somatic gene therapy (See Suziki and Knudtson 1989). One has to assume that the choice itself does not violate human dignity, but rather the unknown consequences through future generations that distinguish germ line and somatic alterations. The ability not to be able to contain and control medical problems to the current and/or the next generation is what appears to give rise to the violation of human dignity. Yet, current treatments such as chemotherapy and radiation therapies possess significant risks to ovaries and germ line cells (Laurema, Heikkila et al. 2003). However, these treatments are not considered to violate human dignity. Therefore, despite regulation not distinguishing between deliberate or inadvertent germ line alterations, it could be assumed that somatic FGT would still be acceptable but whether it would continue to be licensed is another issue. No doubt those such as Habermas would identify that imposing a genetic preference upon a potential person does not treat that potential person as an autonomous individual because a positive response to therapy cannot be guaranteed (Habermas 2003). However, it is still unclear how dignity is violated by gene therapy within the sample other than by invoking the notion of 'playing God'. This is currently occurring within assisted reproductive technologies but in a less intrusive manner because PGD is seen as an acceptable form of intervention despite the implicit picture it paints of society.

7.6 Missing key issues surrounding fetal gene therapy

In terms of framing the intergenerational issues that affect FGT there appears to be a big gap within the documents analysed. The regulatory documents frame the intergenerational aspect of their work in terms of inheritance or germ line issues. However, there are exceptions which include information about the effect of somatic gene therapy in general. The issue is recognised and taken into account; but the absence of recognition that somatic gene therapy indicates a change to the next generation merely shifts connected issues to future generations. The lack of recognition creates a difference between biological intergenerational issues (germ line) and intergenerational issues *per se* (future reproductive choice, the environment etc). There is scientific recognition of the difference between germ line and somatic technology which appears to drive the distinction between issues which are

intergenerational and those which are not. In a sense the documents appear to consider future generations connected to direct germ line interferences, thus in an inheritance or biological way, rather than viewing intergenerational issues. It is the silence within the documents relating intergenerational issues to somatic gene therapy that leads to this conclusion. Without explicitly stating this is not the case, and with such an explicit divide between germ line and somatic regulation, one has to come to this conclusion. However, the wider intergenerational aspects of somatic gene therapy are recognised.

> There is a duty to identify and assess promptly any adverse consequence of gene therapy for the patient, both in the aftermath of treatment and in the long term. This duty does not end with the death of the patient. To verify that therapy has not inadvertently affected offspring and successive generations monitoring should extend at least into the next generation. Indeed, insofar as it is possible, monitoring should continue over several generations. Therefore, those conducting such research have a duty not only to maintain adequate records but also to ensure that an effective monitoring system is in place. It will require that a register be setup, and carefully maintained, with safeguards to protect confidentiality (Clothier 1993: [4.9]).

In highlighting that the possible effect of somatic gene therapy is perceivably unknown; the Clothier Committee rightly acknowledges that intergenerational issues are relevant. However, another inherent contradiction within the perceived practice of FGT emerges. If the carte blanche ban on germ line practices is because of the themes of unknown risk and ethical issues, then, as the Clothier Committee highlights, potentially somatic gene therapy engages the same issues. In terms of somatic FGT it should be just as important because of the stage of development. Within the Clothier report the theme of confidentiality emerges and is linked to issues relating to the right to know, thus engaging the patients and their human rights such as the ECHR Article 8. However, it is evident that long term studies should be done, possibly over many generations, if evidence of germ line transmission occurs. If that is to be done then confidentiality, the right not to know and informed consent cannot be fully attained. The choice must therefore be between safety/human dignity and these concepts. If safety is a paramount consideration then enforcement of follow-up on patients and future children must occur to fulfil this criterion regardless

of other criteria. Clearly, it is the current generation that is more important when practicing human dignity.

7.6.1 Consequence of rights crystallising after birth for practice

It is evident that interests within pregnancy can accrue into rights upon birth (Jackson 2009). The sample indicates that the 'life' of a fetus is intimately connected with, and cannot be regarded in isolation from, the life of the pregnant woman.[221] Therefore, it could be submitted that any genetic intervention is an intervention on both mother and fetus. That does not mean a fetus has a right to that intervention, but it does presuppose that the intervention creates an interest which the fetus is party to, just as children have an interest in familial genetic information (Clothier 1993). Therefore, it could be submitted that regardless of whether the intervention is deemed to be legally solely on the mother, that the fetus maintains an interest, as a child would, in this information which crystallises upon birth.[222] Therefore, the issues no longer concerns confidentiality between fetal therapist and mother, but it includes whether it would be in the best interest or welfare of the child[223] to know the information about their genetic constitution against parental wishes, given that there would be a disparity between their somatic and germ line genetic constitution.

Such a dilemma highlights the difference between knowing about your genetic heritage and it being medically recorded. The difference between the two has lead to the introduction of ghost records as patients within the USA wish to avoid such issues for themselves by choosing not to have genetic information placed upon their medical records (Klitzman 2010). Therefore, further issues surround FGT such as do insurers have a case for requesting genetic information for prenatal therapy if the child does not know about that genetic information (Ashscroft 2007)? Who is in control and legally entitled to prenatal gene therapy information? What effect would

[221] *Paton v UK* [1980] 3 EHRR 408, *Vo v France* (Application no. 53924/00) (2004) 79 BMLR 71.
[222] *C v S* [1987] 1 All ER 1230; *Re C (HIV testing)* [1999] 2 F.L.R. 1004.
[223] Children Act 1989.

this have on antenatal care? [224] Does privacy need to be rethought and reconstructed relevant to generations for all genomic information (Chadwick 2010)? For all the positives in mitigating the differences between biological and social intergenerational issues, it does not offer a conclusive account of intergenerational issues. It may be a question of remit, which is an important concept for the institutional documents, but the guidance and code of practices do not appear to fully address the issue.

Given the silence within the sample about liability other than a reference to 'good clinical practice', if the unknown 'unknown' occurs claimants would have to seek restitution by claiming under the Consumer Protection Act 1987. However, a successful action under the Consumer Protection Act 1987 might be made difficult by the controversial 'development risks defence.'[225] Under that defence producers will not be liable if they show that, at the relevant time, the state of scientific and technical knowledge was not such that they could be expected to discover the defect (Corrigan, Liddell et al. 2006).[226] However, it is unclear how to compensate parents where the child in question would die within a short period of time, or would have debilitating condition regardless of the genetic intervention. Without insurance payouts or preordained out of court settlements via contract, financially supporting a case would be astronomic. The Epilim case classically illustrates several key ethical considerations, which are intertwined with political decisions which ultimately decide if justice is done, but is most notably on the side of Goliath (Hirsch 2011). Given the unique nature of FGT such an omission for redress to cover the unknown 'unknowns' through insurance is potentially contrary to human dignity.

It is also clear that the regulations paint an ideal model which has not taken into consideration, for example, the financial implications on issues such as long term

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[224] Elbourne et al claim that women holding their full records were significantly more likely to feel in control of their antenatal care (rate ratio 1.45; 95% confidence interval 1.08-1.95) and to feel it was easier to talk to doctors and midwives (rate ratio 1.73; 95% confidence interval 1-1&2-59). Elbourne, D., Richardson, M. *et al.* (1987). The New bury Maternity Care Study: a randomized controlled trial to assess a policy of women holding their own obstetric records. *An International Journal of Obstetrics and Gynaecology* 94(7), pp. 612-615.

[225] Consumer Protection Act 1987 s.4.

[226] Consumer Protection Act 1987 s.4(1)(e).

follow-up. It is clear that the documents analysed in this chapter are not giving a true reflection of practice, and therefore the barriers to the progress of FGT must be explored within the interview data. Issues regarding the usefulness of human dignity within practice, and implications for future generations must be more fully explored within the interview data.

7.7 Conclusion

In conclusion, with the rapid evolution of biomedical techniques new threats to human dignity may arise, which regulators are under a duty to prevent through clear and precise regulation.[227] The guiding principle for FGT practitioners is human dignity, which initially appears vague and lacking in substance. However, through the examination of the documents human dignity has been fleshed out into principles that are commonly seen from the basis that the individual is paramount. From the concept of human dignity the emphasis is placed on the individual as being paramount within research. Autonomy is the key concept. From autonomy, the individual is empowered to make their own decisions on their own terms. Individual rights make the rights of others, such as the right of the father or fetus, mere considerations with no overriding authority. However, for the next and future generations there is a stark difference between rights and interests. It is the difference between rights and interest that appears to give future generations a voice. The next generations' interests are taken into account, but their interests appear to be overruled by the individual within the clinic. Interests manifest themselves into rights only after birth. The interest of future generations also appears within the regulation of scientific progress. However, those interests are not always a straightforward balancing exercise. Protection of future generation interests are afforded through risk and assessment procedures that have to be strictly adhered to in any research carried out in FGT. However it has been shown that the notion of human dignity that underpins the research protocols ultimately restricts the areas of permissible research. Fear of outcomes, for example germ-line transmissions, and inherent uncertain consequences for future generations emerge as hindrances to scientific progress, seen in the current prohibition on germ-line research and

[227] *Cyprus v Turkey* [2001] 35 EHRR 30.

intervention. The same fear acts as a procedural restriction upon the research autonomy of FGT practitioners. It appears that the intergenerational aspects of FGT are framed around germ line interventions, ergo permanent interventions to the human heritage rather than looking at intergenerational issues that encompass more than just germ line interventions. As stated above, it may be a question of remit rather than a failure to be explicit within the sample, but it is clear that the issue of confidentiality and of the right to know after birth is not adequately represented within the immediate regulation of FGT.

However, there are inherent contradictions within the sample documents. For example, the institutional principle of the individual being paramount is not based on the individual's own thought or choice. The individual is only paramount within a framework of what the institutions allow and consider ethical, safe or appropriate for society at large. The current generations' rights prevail over the interests of the next generation but for FGT practitioners the interests of future generations override their work in the name of dignity. Yet the same interest is not enough to override the autonomy of the individual once a choice is made available. Therefore, a paternalistic bubble in which choice can be made is in operation. There are still further issues relating to the remit of the sample, and the deference about questions concerning viability of fetus' and treatments which are purely of fetal benefit. In addition how such technologies are accessed has to be taken into account since they may simply resolve individual problems whilst leaving social problems intact (Rothman 1985). However, the analysis presented in this chapter may not have given a true representation of the guiding principles within FGT or the potential impact of scientific progress upon future interests and FGT practitioners. There could be other more important issues that the documentary data cannot reveal. Chapters 8 and 9 set out to explore further the impacts of scientific progress through the interview data.

8 Interview Data: Human Dignity in Practice

8.1 Introduction

Having conducted the literature review and documentary analysis the next step was to conduct interviews with those who would be at the forefront of FGT within the UK. The prospective interviewees were identified through purposive sampling and led to a total of 13 interviews being conducted between November 2010 and May 2011. These interviews supplement as well as challenge the conclusions found within chapters 6 and 7, such as: human dignity is not a useful concept within the clinic; autonomy is paramount; and, intergenerational interests are taken into account within the research process. In order to do this, the interviews were conducted in a semi structured way following the outline in Appendix B - Interview Question Schedule. Therefore, the interview data acts as the glue which binds the thesis together, and ultimately helps answer the research questions, because FGT is now progressing into the clinic. Therefore any concerns regarding regulation as well as missing issues not highlighted within the documentary analysis can be revealed. The revelations from the interview data presented within chapter 8 and 9 include: human dignity is not explicitly used by FGT practitioners; maternal rights trump intergenerational ones only within the clinic; there is a potential conflict between FGT, abortion and ethics; and, collaboration as well as being a convincing argument in itself can mediate the uncertainty of scientific progress.

As mentioned within the methodology chapter, the interview chapters will mirror the documentary chapters in order to make comparison easier. This chapter will focus upon the theme of human dignity and therefore correlates with chapter 6. Section 8.2 starts by identifying that human dignity is not a concept readily used by FGT practitioners, and the logical conclusion from the deconstruction of the concept leads to the idea that certain practices are not contrary to human dignity (see section 8.2.1). It will then show that human dignity is implicitly upheld by FGT practitioners by autonomy and informed consent. As with the documentary data, some themes were identified initially, such as human dignity and autonomy, and eventually other concepts, such as ‘do no harm’, were identified as being connected to human dignity. The analysis in section 8.3 then followed the concept of autonomy within the clinic

and shows how autonomy leads to the mother being paramount. However, the effect on the next generation was still a pertinent theme connected to autonomy within the clinic and subsequently examined. Ultimately, in the view of FGT practitioners, the autonomy of the mother trumps all others, including the fetus. Therefore, despite 'a step further' being identified in section 8.3.3 which potentially could see fetal interest within the clinic mediating maternal autonomy, this was a minority view which defaulted back to maternal autonomy in section 8.4. The chapter will then conclude in section 8.5. Each section will be contrasted with the documentary analysis and will also indicate the effect upon the maternal fetal divide. The chapter will then conclude whether or not human dignity is relevant within FGT.

Because of the subsequent deconstruction of human dignity it was evident to the interviewees that germ line therapy should be currently banned but not because of human dignity. Rather it should be banned because of safety concerns and the lack of scientific knowledge upon gene therapy in general. Although prohibition of germ line technologies was discussed within the research procedure of the documentary analysis; within the interview data it appeared in the general discussion about human dignity. Therefore, the prohibition will be explained in relation to the context in which it arose.

8.2 Human dignity: what do you mean?

In the view of FGT practitioners it was evident that raising the idea of human dignity as a central concept leads to definitional issues and was not a concept readily used by FGT practitioners.

> RC [O]ne of the things that comes in the literature is this concept of human dignity, which being situated in the UK is not necessarily something you've come across. It has been argued that there is role for human dignity within the work that you do from an international documents especially given the international nature of what you do. Is it something that you've ever considered?
> IE11 What do you mean by human dignity?

Another interviewee responded:

> The phrase human dignity is not one I've encountered or come across before to be honest. IE12

The above extracts demonstrate how the term 'human dignity' is not readily used. The frequent response to the concept of human dignity was one of seeking clarification about it [IE1-3,5,7-9,11-13]. Seeking clarification was more prevalent within the basic scientists than the clinicians. A minority appeared to formulate human dignity in an abstract way, which went beyond autonomy [IE1, 4, 6, 10] (see 8.3.3). In general, these were the interviewees with 20 years of experience within genetics. However, the explicit notion of human dignity is not one that is prevalent within the practice of FGT practitioners. Where the response was not initially one that asked for clarification about human dignity, the result was still one dismissing the explicit utilisation of human dignity:

> [Do I use human dignity?] Not explicitly. I think parents and medical professions would consider it under their list of essential ingredients for a healthy life. So, parents trying to decide if to have a termination or not; or me trying to decide if it would be appropriate to do a termination at 32 weeks would undoubtedly take human dignity into the equation. So yes it would be a concept that you would be familiar with in trying to quantify or decamp what it decreases from a dignified existence. But I don't think I've heard it discussed more explicitly than that. IE6

Therefore, human dignity may not be an explicit concept utilised within the laboratory or clinic, where they are guided by other principles. There was a recognition of the term 'dignity' as one might associate it with dignity in dying [IE10] rather than human dignity in the immediate Kantian sense (See Tadd 2006). Only a minority of the interviewees recognised that they used human dignity explicitly within their work [IE1,4,9]. Given their own unique professional, academic and cultural upbringing it could be expected that they would fall outside what one might expect from medical practitioners within England and Wales. However, due to confidentiality these unique features cannot be revealed, since it would lead to the interviewees being identified. What is intriguing is that their unique circumstances (which differ between the three interviewees) would lead to the idea that human dignity would be a concept that they are aware of and fully use. Therefore, human dignity within the practice of FGT was introduced through the ideas that the document analysis revealed.

> I think that the principle of human dignity in medical therapy encompasses an obligation to respect the individual's autonomy and a duty to ensure safety and predictability of the intervention. The issue

> is that there is often a conflict between the interests of the parents and those of the fetus. IE9

The interviewees all recognised concepts that have been attributed to human dignity such as autonomy, informed consent and respect for decisions (Beyleveld and Brownsword 2001). In identifying the implicit nature of human dignity, professional standards shape practice and, as seen within the documentary analysis, implicitly carry human dignity into practice:

> In medicine, you are always guided by the principle 'do no harm'; and that is particularly important in pregnancy where you have a mother and fetus and interventions that affect the mother can affect the fetus, and we are very often guided by we know that treating the mother that it would do harm to the fetus, but the overriding principle is that the mother take priority, especially in the UK. I think it becomes more of a problem in other countries where there isn't such a cut and dry basis to stand on. So yeah I think human dignity does shape what we do as do no harm basically means that, preserving the human state or trying to improve it by not making it worse. But I've not really come across it. IE2

The very essence of treating illness is human dignity in action. Yet, the documents and ethical sources that were identified by the interviewees were not documents that explicitly use the term human dignity. The Hippocratic Oath was referred through the principle of 'do no harm' by the clinically trained interviewees [IE2,4-6,8,10], which does not contain explicitly human dignity, but focuses upon the patient (See Mason, McCall Smith et al. 2006). Therefore, unlike the document analysis which explicitly states human dignity as the principle that is utilised, it is the resulting concepts such as autonomy and 'do no harm', which guide the practice of FGT practitioners. It is clear that these concepts implicitly put human dignity into action. However, concepts such as 'do no harm' are not reliant upon human dignity being explicitly mentioned or referred to, in order to be actionable. The interviewees' references to governing body protocols such as the professional codes of practice (for example GTAC), which do not explicitly mention human dignity, appears to have more prevalence within the ethical tools of FGT practitioners. Therefore, within the practice of FGT the explicit term human dignity appears a useless concept that does not add anything to the debate or the practice of FGT and can add inconsistency (Gewirth 1983, Macklin 2003, Melo-Martin 2011, Salvi 2001). This inconsistency of its application is elaborated upon by the interviewees' view upon

the prohibition of germ line technologies, which should be prohibited but not for the reason stated by the documents.

8.2.1 Germ line alterations are not inherently contrary to human dignity

It followed that because human dignity is a vague concept, where it had been cited as a reason why certain scientific practices are banned, the interviewees questioned whether germ line technologies infringed human dignity:

> I'm not against germ line gene therapy provided it's safe and it's in the interest of human dignity and not to do with weird things, which is more science fiction and popular press speculation, but that's why we have GTAC and other bodies. But in principle the reason not to do germ line therapy is that we know so little about these things that it's not acceptable. And the other hand there are only very few exotic cases where it would be beneficial. Most things that you can do that you would like to apply it for you can do it other ways, like abortion and embryo selection things like that, so it's not really necessary. It may get to a time where altering the genome of people would be of general benefit like if you could reduce the occurrence of cancer, we don't know. I wouldn't close the door on research in that area but I don't think it's anything that we should aim for by clinical application. IE1

Therefore, human dignity *per se* is not the direct reason why one should not pursue germ line alterations for the benefit of future generations (Beyleveld and Brownsword 2001). It is the current state of scientific knowledge and safety concerns that is the reason why germ line alterations should not currently be carried out. This appeared to be the prevailing opinion with the exemption of one interviewee who appeared to advocate a carte blanche ban on germ line technologies, because 'it still maybe unethical even if safe' [IE7]. However, the interviewees all agreed with the current ban on germ line technologies. Despite this the question still remains about germ line interventions because gene therapy is progressing at a remarkable pace:

> [T]he thing is, the question is now gene therapy is looking at gene editing, and there is a paper out in the American Society of Haematology, which came out a couple of months ago where they have shown efficient gene editing for haemophilia in a mouse model, which means you're not putting a gene in, but you're correcting a mutation. So the thing is, well, what would be bad about germ line mutation with that? Surely you'd want that? Then you're not getting

> into the fetus and you're correcting a severe genetic disorder and their kids would be cured. Well you could argue that gene therapy is unethical because you're curing people who would then go on to reproduce and have a greater chance of having kids together who are carrying the mutation. Disease propagation for the next generation, so surely you'd want to stop that? So there's a heck of a lot of stuff that you can discuss. IE3

Therefore, ultimately germ line therapies should not be ruled out in the future for a few specific conditions. The example of gene editing highlights that technology is progressing at such a pace that current prohibitions are constantly being challenged. Despite the pace of scientific progress, the violation of human dignity appears to come from the purpose behind the intervention.

> I think it depends it comes down to issues of regulation. I don't think anyone would think that arranging some sort of DNA to prevent a child having cystic fibrosis or its offspring could be considered to be against human dignity. Whereas I suppose if we need loads of tough people to Shot Putt in the Olympics, or something so we wanted to put in genes that made your muscles big because we as a nation decided that was important, then that would be tinkering with human dignity because our interest would be socially driven rather than in their interest of the individual. IE2

Therefore, where the documents express a carte blanche ban on germ line technologies the interview data suggests that using 'human dignity' as the reason for prohibition is misleading, unless the prohibition is connected to the safety concerns of current scientific knowledge. Therefore, human dignity is being supported indirectly through the application of scientific safety. However, the current scientific criterion for safety has uncertainty rooted within it. Therefore, how much uncertainty someone is willing to accept will be a key area of debate if/when germ line technologies occur in the future. Several interviewees highlighted that germ line alterations are currently occurring within medical practices such as radiotherapy [IE1-3,5,6,10-12] (Schneider and Coutelle 1999). Several went further to postulate what if current somatic intervention inadvertently caused a germ line intervention that benefited the patient, would that then be a violation of human dignity [IE1,3,10]?

As highlighted above, human dignity could, in theory, be abandoned within the regulation of germ line technologies if they were safe [1-6,9-13]. However, the

indirect violation of human dignity differs from the direct prohibition of germ line therapy within the documents, which is key if scientific progress and ethics are to be balanced. The fundamental difference is that the interviewees reasoning behind a current prohibition is based upon the contingency of current scientific knowledge. Once the contingency of sufficient knowledge is surpassed then germ line therapies will not be contrary to human dignity in the minds of therapists. Therefore, the prohibition forwarded by the interviewees is time and place dependant whereas the prohibition within the documents transcends time and place because of the intrinsic notion of human dignity. Therefore, as science progresses, the ban formulated by the interviews must be constantly reviewed to ascertain if the ban is still justified. It may become a question of efficacy of treatment between somatic or germ line treatment, and whether a condition mutates, to ascertain whether human dignity is maintained (Pattinson 2002). The proviso of safety still applies, but that is markedly different from a definitive ban, which the documents advocate (Pattinson 2002). Yet, if the documentary analysis is correct in indicating that the germ line ban is a timeless ban, a debate surrounding the prohibition would not occur, because once a technology is considered contrary to human dignity, then it will always be so. The difference between the two approaches is a reminder of the tension between therapy and those who practice science.

8.2.2 Consequence for the maternal fetal divide

Human dignity may appear as the overreaching principle of biolaw (Andorno 2009) and human rights,[228] but it is certainly not explicitly the overreaching principle of FGT practitioners. Implicitly, through other principles such as autonomy and safety it is up held but the term 'human dignity' does not substantially add to the practice of FGT practitioners. It is the intrinsic worth of people that is implicitly recognized and respected by others; thus, requiring some forms of treatment by others are

[228] See the Charter of Fundamental Rights 2007 Article 1 as incorporated by the Treaty on European Union 1992 Article 6 and the Treaty of Lisbon 2007. However under Protocol 7 Article 1 The Charter does not extend the ability of the Court of Justice of the European Union, or any court or tribunal of Poland or of the UK, to find that the laws, regulations or administrative provisions, practices or action of Poland or of the UK are inconsistent with the fundamental rights, freedoms and principles that it reaffirms; and 2. In particular, nothing in Title IV of the Charter creates justifiable rights applicable to the UK except in so far the UK has provided for such rights in national law.

inconsistent with, or required by, respect for this intrinsic worth (McCrudden 2008). Therefore, one has to question the use of the term within regulation at the international level (Kuhse 2000, Macklin 2003, Melo-Martin 2011). If a principle merely collapses into other principles which are utilised by practitioners, then why even use the term 'human dignity' where it could be substituted for 'medical ethics' and reach the same conclusion? The referral to 'do no harm' and the lack of consistent abstract definition by the FGT practitioners suggests that the concept of human dignity *per se* is not important and is certainly not explicitly the foundation for the work of FGT practitioner. Therefore, the interview data indicates that, despite the documents professing that 'human dignity' is a fundamental principle within genetic technology, it explicitly is not for FGT practitioners. Therefore, the deciding factors on the outcome of the maternal fetal divide rests with other principles such as autonomy and informed consent.

The FGT practitioners also indicated that the prohibition upon germ line technologies is because of principles such as safety and scientific knowledge rather than human dignity *per se.* It is this current clinical risk that would have to be overcome (Elias and Annas 1992). The risk-benefit ratio may still be too high to warrant germ line interventions but it is the scientific consideration that appears prevalent (Anderson 1990, Elias and Annas 1992). The moral distinction between the purposes behind germ line intervention is a permissible line to draw because inserting a gene to restore normal function is different to enhancing 'normal' functioning genes (Anderson 1989, Beyleveld and Brownsword 2001, Buchanan, Brock et al. 2000). However, the documentary analysis does not make the above distinctions. It rests solely upon human dignity and appears to rest upon crossing a symbolic barrier that biotechnologies should not cross (Elias and Annas 1992).

The interviews confirm the documentary analysis by indicating that human dignity needs unpacking from the data. Therefore, it is the utilisation and implementation of other principles that are paramount for the working of practitioners and regulators within England and Wales. Autonomy emerges as a key principle in the unpacking of human dignity. Importantly, it is the mother's autonomy that is considered the paramount concept within the clinic. Therefore, the next section will expand on this

and it will be seen that it follows from autonomy that informed consent is important, and that other parties such as the father and other medical professionals should also be considered.

8.3 Mother's autonomy paramount

Within the interview sample the mother's autonomy within the period of pregnancy appears paramount, thus supporting the documentary analysis.

> It is the mother that has to undergo the surgery, so we would need to explain to her what we would be doing to her, but it's for the benefit of the fetus. […] I personally think it's the patient's choice, whether she is willing to undergo, whether she will give her consent or if she's happy to undergo this procedure or not rather than the doctors in the clinic. IE7

The introduction of FGT as another treatment option does not fundamentally alter the position of autonomy. It is the patient's choice whether to use the technology.

> I think it's important that they're not forced even if it does show that having this therapy is better than having no therapy at all. You can't force someone to take chemotherapy if they're dying of cancer. It's completely their responsibility unless they're mentally impaired and not able to make a decision. But the same should apply for any kind of fetal therapy. IE8

Autonomy appears as the main principle to apply despite the direct beneficiary of treatment not being the mother. Given that within England and Wales autonomy is the foundation for the patient's right to choose, in both a legal and medical context,[229] it is unsurprising that autonomy emanates throughout the sample. Therefore, the default position is an individually focussed approach regardless of the interviewee's position or experience. The position of autonomy being paramount confirms the documentary analysis.

> In the end the mother, and in the broader sense the family, should have the say as you can't ask the fetus. IE1
> I think that you should take everything into consideration in a family environment and it should be a family decision except in the situation where there is disagreement and of course it's the mother's body that suffers, so she takes priority. IE5

Therefore, the wider social decision of the mother is not to be ignored, but ultimately

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[229] *Re C (Adult: Refusal of Medical Treatment* [1994] 1WLR 290; *Re MB (Caesarean Section)* [1997] 2 FLR 426.

it is the mother's decision, because she is the site of intervention and not just an innocent bystander. To facilitate maternal autonomy, informed consent was highly relevant for both clinicians and basic scientists. By utilising informed consent it provides the conditions necessary for autonomy. However, the FGT practitioners highlighted several difficulties surrounding the assessment of what information may be important, how much information should be given to patients and issues relating to a patient's retention, understanding and use of that information:

> I think one of the most difficult things to do is to make sure that what you've said gets through and it's absolutely clear they've understood. I think that it's a very very important thing, but also a very difficult thing because you have very different levels of basic knowledge and understanding. Some people you give them a percentage they don't know what you're talking about. So making sure that the message that you are conveying is received and can be reproduced in a discussion, that they tell you what and why a certain therapy is proposed is a very important part of the consent process. IE1

Therefore, the complexity of the information to be understood is important, but also how it is communicated:

> If the patient needs more information or would benefit from counselling from not just the obstetrician but the fetal medicine expert about what the risks are, the procedure, to talk to the geneticist about accuracy of the diagnosis, to talk to the paediatrician about the alternative outcomes, what are the chances of the child having a normal life if nothing is done? What are the chances of the child surviving the intervention? […] That hasn't even touched on explaining the uncertainties involved because there are lots of uncertainties from the point of intervention to what happens after the child is born. […] So we have to explain to her in a frank and open way as possible what the uncertainties are, that she would have to be monitored as well despite she would not be getting the intervention *per se*, that this is going to go on for a long time […] and we'd have to stress the importance of a long term follow-up for her as well as the child. So there are lots of issues to discuss. IE13

Therefore, being open, honest and frank about the information involved should help facilitate the informed consent process. However, several interviewees [IE1,2,5,6,8,10] highlighted the importance of having sufficient time to consider what is being proposed because of the amount of information that needed to be digested. The basic scientists implicitly identified time to consider the options in front of them, but the clinical interviewees were more explicit about the issue, drawing upon past clinical experience as examples.

> It's very easy to only take in half the information or a tenth of the information a clinician is telling you so it's not something that is rushed into quickly. I find, in my experience, that often in pregnancy that everything is meant to be normal. People are often very shocked or horrified when something deviates. And what you find is that lots of women that have had miscarriages, ectopic pregnancies, fetal abnormalities want to make a decision right there and then and I think in the clinical setting that wouldn't be an appropriate thing. So it wouldn't be appropriate to discuss it initially. It would be important to give more information and let people fully absorb everything before making a decision. IE5

Therefore, it is important for a mother not a have an impulsive reaction when receiving information, even if her decision has been preconceived through her past experience. Interestingly, despite the mother's decision being paramount, it was contextualised around other important parties and considerations. Therefore, informed consent also included consultation with the father and broader family unit as well as other medical professionals. Therefore, despite maternal autonomy being paramount, reference was made to 'the parents' and making the decision in the context of the immediate family. It included considering the possible consequences upon those family members.

> Well you know if a couple came in and the mother came in and said she wanted therapy but the father said no. I think you'd have to say them you've got to go and decide. But that's for whatever kind of therapy you do, I mean we hit that all the time with caesarean sections. We have husbands saying that their wife isn't going to have caesarean section and you have to put them out the room and say they've got nothing to do with it. IE2

In other words, the interviewees referred to differing parties which the mother should consult before making her decision, and the importance of their role in the decision making process. These parties included the future father, clinical staff members such as genetic counsellors and the broader family. Therefore, the mother's decision is not an isolated medical decision but a social decision as well and part of an autonomous decision making unit (Rapp 2000). In other words, a mother's decision is where multiple interests of other parties intersect before a decision is reached. However, as demonstrated above, the interviewees stressed the importance of it being the mother's choice even if it is contrary to the wishes of the 'family unit'. Therefore, maternal rights to informed consent and the right to refuse were strong themes throughout the interview data when clinical choices were made.

8.3.1 Consequence for the maternal fetal divide

Regardless of interviewee attributes, the interviewees confirmed the position identified within the document analysis that autonomy is realised through informed consent. Given the huge amounts of guidance and focus upon consent within medicine (See General Medical Council 2009b) as a general rule informed consent is not a new or exciting find. Nonetheless, there are already ethical issues surrounding informed consent for gene therapy (Kahn 2008), gene therapy for young children (Lowenstein 2008) and general prenatal decisions (Rapp 2000). In fact, the adverse reactions that have occurred within gene therapy have called into question the informed consent process (Caplan 2007, Kahn 2008). Questions were raised by several interviewees, in particular relating to the uncertainty of knowing what a mother would want to know in the informed consent process [IE1-4,6,10-12]. As stated above open, honest and frank conversations with the patients about the options and the consequences of their action or inaction were important factors in ensuring that the informed consent process is adhered to fully. In doing so, FGT practitioners are ensuring that the safety of patients is protected, while also enabling research to develop better treatments for patients (Deakin, Alexander et al. 2009).

Time is an important concept for the fulfilment of informed consent, thus human dignity. For some patients that amount of time maybe more than adequate in deciding between nature, intervention or termination; but, for others it may not be so as they could be suffering from post traumatic stress (European Critical Care Foundation 2010). Some may find themselves with insufficient time to decide due to difficulties in arranging meetings with genetic counsellors or because of the enormity of the decision at hand. They will have to weigh up the decrease in likelihood of successful treatment by a delay in their decision making, but still come to their right decision. Therefore, as alluded to within the documentary analysis, hindsight bias becomes even more a issue (Brooks and Sullivan 2002). However, a mother must be allowed the time to come to the decision that she feels is right.

Therefore, on initial inspection the general rule is that autonomy is paramount. The FGT practitioners are focused upon individual choice within the clinic. Yet, the

admission that other parties should be consulted allows a mother to consider the implications of the genetic intervention and recognises that medical decisions have wider implications. However, outside of the mother and the clinician these 'other parties', which include the fetus, father, and society at large are ultimately only considerations. Therefore, despite fathers being increasingly included within pregnancy, the medical technology of FGT is further transforming choice at an individual level for the mother (Rapp 2000).[230]

However, what differentiates these interviewees from the rest of the medical profession is that they work specifically with the fetus. Therefore, the fetus as a patient may implicitly emerge within data. If it does emerge then it may have implications about the explicit stance initially forwarded by the interviewees. Within the next section the next generation is recognised through identifying that the fetus has some form of status. Therefore, ethical questions are raised not only about what is ethical but about the status of the fetus.

8.3.2 Next generation interests

Despite the autonomy of the mother being paramount, the fetus appeared as an important party within FGT. It emerged that the fetus is important because of the debate it sparks and whether it should be treated as a patient.

> […] because we do a lot of stuff that is, I wouldn't say ethically challenging as that would make it sound too dramatic, but because it involves the fetus, is the fetus its own person? Is it separate to the mum? Who is more important in terms of anything you treat a fetus with the mother is going to get affected. Does that mother then have the right to choose not to have that therapy even though she knows that her unborn baby is sick? IE11

The above quote symbolises the tensions within FGT because the fetus is sole beneficiary of treatment. The recognition of site of intervention or benefit means that the fetus cannot be ignored. But does being a beneficiary make you a patient? If so what are the consequences of having patient status?

The first thing is about rights of the fetus I suppose and whether you

[230] Whether choice within a medical context is fictional or not will be discussed in relation to abortion in 9.3.4.

> consider the fetus a patient or not. It's something that is central to fetal medicine and hence why it's a fairly new concept is that up until recent decades the fetus was not considered a major priority. And of course there is the legal side of things that the fetus does not have any legal rights until it's born as you know. And so I think it's variable how much autonomy or moral status people bestow upon the fetus and it's very patient dependant. Doctors also have varying feelings about it; I suppose it's gestation dependant. And so the very concept of performing a procedure on a fetus that can't consent is slightly controversial. But, I suppose with the principle of medical ethics of preventing harm and do the best for your patient and as an obstetrician you are considering both, you want the best outcome for the fetus specifically but taking into account the mother's wishes. And so you would in most circumstances you would try and act in the fetuses interests as potentially it's a born child and that born child will have rights at that stage. IE5

It emerges within the data that the fetus has to be a consideration even if "the fetus as a patient does not exist […] [because a fetus] is more than a series of organs" [IE10]. It has to be of consideration because the *modus operandi* is to treat the next generation, which is the fetus. The recognition that the fetus is more than a series of organs means it is in the thoughts of FGT practitioners. The question emerged: How much weight should be given to the fetus purely as an individual?

> I would like to think about the fetus as a patient, as a being that needs protection. What applies to an infant should theoretically apply to the fetus. But, reproduction is an inefficient process and reproductive loss is a way to ensure that only those fetuses that are fit enough will be born and survive. Are we intervening where we should not? This is a possibility. IE9

Therefore, by giving the fetus a status that overrides biology and the mother's autonomy, FGT could raise further questions about what should be done to the 'patient.' The focus upon not just fetal benefit, but the corresponding effect upon the future child makes the next generation the patient that needs consideration. However, due to the movement of FGT to indirect FGT,[231] understanding who is the patient is a blurred concept

> We injecting […] into the mother […], which in turn increase the supply of substrates and oxygen to the fetus. So the gene therapy is not a fetal issue but a maternal issue. […] The patient is the mother but the beneficiary is the fetus.IE7

[231] Gene therapy upon a mother for fetal benefit which has been referred to as prenatal gene therapy.

Because of the blurred patient status further questions are raised regarding whether the fetus can be prioritised over the mother by the mother's autonomous decision.

> [I]f gene therapy improves XXXX people are still concerned that for the sake of the fetus are you going to inject a large dose of viruses into the mother can you prioritise the benefit of the fetus over the mother? What if the vector does some benefit for the fetus but in turn harms the mother. Can you actually do that? IE7

Therefore, fetal interests appear within the work within the duties of the FGT practitioners. They actively think about the fetus and understand that their work is about benefiting the fetus. The area is connected to the research procedure and will be elaborated upon within chapter 9. Yet, forwarding fetal beneficial treatment in the clinic highlights the fetus as an independent being that needs help. Its independence is not drawn from its status within pregnancy but from its status as a future child.

The interviewees that raised the 'fetus as a patient' concept knew that it depended on the viability of the fetus and the acknowledgement of the mother to continue a viable fetus to term, thus implicitly forming the same criteria as Chervenak et al (2007). The concept appears more pertinent within the clinically educated interviewees. The basic science interviewees had more autonomy focused answers, but there were still elements of the fetal benefit within their accounts. All the clinically based interviewees had a version of the fetus as a patient within their account, which confirmed fetal patient status within the UK is dependent upon maternal autonomy. Interestingly, the more experienced the FGT practitioner the more intrinsic and in depth the exploration of the concept was. The result of a more in depth analysis was to pose more hypothetical questions. As one interviewee put it "[some] have more time to ponder in depth than those still currently working in the field" [IE9]. The fellow clinical interviewees were just as insightful about the ethical dilemma that such a concept could produce. Given the dilemmas that could evolve from fetal therapy there was an avoidance of prioritising the fetus over the mother. That included the prioritisation of those acting on behalf of the fetus. In doing so, the

majority confirmed the case law concerning fetal medicine.[232] Therefore, the emphasis is firmly upon the mother and her rights within the clinic. However, preclinical decisions directly affect the choices that can occur as well as choice in general (see chapter 6). The question that flows from indentifying the fetus as a being that needs help is whether that can override the autonomy framework that is engrained within the practice of medicine?

8.3.3 A step further?

The majority of the interviewees closely followed the autonomy framework currently in action with England and Wales. However, there was recognition of a possible step further for the practice of FGT. The recognition took two forms. For the majority there was recognition of deviating from the current autonomy framework because of the site of intervention, but it was no more than that. The problems caused by such action in the USA caused the majority to reaffirm the autonomous decision making of the mother [IE1,3-6,10,11,13].[233] Then there was the recognition by two interviewees [IE4,9] that because of the site of intervention one should ask further questions about the status of the fetus, which should lead one to the conclusion that it may be permissible to act against the interest of the mother in favour of the fetus:

> I think human dignity is caused by human beings ability to have abstract thought. [...]. I think there is a human soul and that gives human dignity. Now monkeys have 99.9999% DNA the same as us. I think the DNA is irrelevant; it comes from activity and the ability to take two ideas put them together, come out with a third, which is unlike the previous two, like music and poetry. The second concept is, is that applicable to all human beings? So a child with Down's syndrome is that a human being? The vegetative human after a car crash, is that a human being? Going back to Aristotle I don't know, but it's more important not to deny human dignity to those who should have it than to give it to those who might not be human.

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[232] Mental Capacity Act 2005 s.3(1)(a)-(d). Section 3(1)(a)-(c) codified the test of capacity that is used within the common law and was established within *Re C* [1994] 1WLR 290. These provisions do not apply to those under the age of 16 under the Mental Capacity Act 2005 s.2(5).

[233] Although not specifically mentioned by name cases such as *Whitner v South Carolina* 492 S.E. 2d 777 (S.C. 1997) where a pregnant woman who was prosecuted for placing her in utero child in danger due to the use of illegal drugs during pregnancy; and *Utah v. Rowland*, No. 041901649 (Utah Dist. Ct.-3d Apr. 7, 2004) where Melissa Rowand was charged by the State of Utah with murder of a still born fetus due to refusing a caesarean section which lead to the death of one of her twins. The charge was later dropped to child endangerment (Habiba 2005).

> Therefore, I treat the unconscious patient as a human and therefore I'm saying is the fetus by the same principle a human? If we have any doubt that we should give human dignity to the fetus. IE4

Another interviewee asks:

> If the fetus were to decide as an autonomous individual, would she or he decide to live or not? I think this depends on the outcome. An individual with a partially treated genetic disease may lead an agonizing life whereas a non-treated individual would have succumbed early in life. On the other hand, genetic treatment, which leads to a significant improvement in quality of life would be desirable. The option of in utero testing for therapeutic success should be available in my opinion when prenatal therapy for genetic diseases is offered. IE9

Therefore, both advocate decisions in favour of the fetus, with the latter utilising an indirect fetal benefit option. Despite using different methods the outcome was about trying to identify what the fetus would want or that 'we should listen to the child whispering what it wants' [IE4]. It was recognised by both the clinical and the basic scientist that even if the fetus could choose no one has a way of knowing what it would choose [IE1-6,9-13]. Therefore, the best person to decide would be the mother. A more fruitful development was along the developmental lines, which could support the above two interviewees' views, although the interviewee did not advocate the fetus taking priority over the mother.

> If I'm presenting a case to a colleague I present a picture of the family unit because at the end of the day, and it maybe because of my fetal medicine interest but I think about the fetus, and the continuity into paediatrics and the father is critical to that, so it's a prenatal approach. IE5

Interestingly one interviewee did not directly endorse either of these views but implicitly made their actions dependant on the developmental location of the fetus, thus indicating an intermediary position. However, several interviewees strongly indicated that location did not change their stance [IE2,6,10]. Ultimately, the precautionary principle indicates that the fetus should be treated at certain points overriding the mother's autonomy, if needed. Despite the two individuals not utilising the same language, they both did not push the issue further. Such a stance clearly contradicts the normal autonomy approach to FGT that appears strongly within the sample. Several reasons could explain why the two individuals have a tangential view about fetal rights. These include personal attributes such as religion,

cultural up bringing or one's perception of when 'life begins; but the most pertinent would be the unique careers of each of the individuals, which would suggest the possibility of having stances contrary to norm. Due to confidentiality these issues cannot be explored further. Implicitly, it questions whether an individually orientated ethical framework sufficiently considers and grants weight to the ethical demands of the group. The group in this circumstance is humanity in general, which a fetus biologically is a part of. Framing choices concerning the fetus within the group of humanity means that the interests of the fetus and society cannot be ignored (Widdows 2011). Therefore, fetal interests could be served by human dignity even if the fetus as a patient concept can only influence FGT practitioner at the research conception phase.

8.4 The effect on the maternal fetal divide: maternal autonomy is still paramount

Despite the mother's autonomy appearing as the paramount consideration in FGT, it is evident within the data that all FGT practitioners, independent of experience, recognised that because the fetus is the prime beneficiary of treatment, they are challenging the maternal body through pregnancy and the way that fetal growth is seen within medicine (Casper 1998). The emergence of developmental-biological orientated technologies change the focus from women to the uterine system and the fetus (Samerski 2009). The challenge was not mitigated where the FGT was not directed at the fetus because it was still the prime beneficiary. In challenging bodily integrity, further issues arise, such as fetal rights, fetal duties and the fetus as a patient.

Several key points arise out of the possibility of fetal rights or the fetus being a patient within the work of FGT practitioners. Firstly, the technological revolution that has occurred over the last three or four decades within obstetrics has pushed the fetus to the forefront of clinicians minds (Casper and Morrison 2010). Therefore, one cannot ignore the fetus within FGT because it is the site of intervention and the intended beneficiary. Even if the social context of these decisions does not lead to a position whereby the risks and burdens that are synonymous with pregnancy correlate to pregnant women having a duty towards the fetus (Scott 2002), the fetus

is protected by the actions of FGT practitioners before maternal decisions are needed. Consideration of the possible postnatal effect on the fetus indicates beneficence based obligations towards the fetus (Chervenak and McCullough 2009). By focusing upon obligations, which are necessary within the research protocol of FGT, it is in the postnatal implications of treatment that the fetus as a patient initially appears to situate itself. Striking a balance between maternal risk and fetal benefit is the implementation of fetal interests within research.

Therefore, despite the site of intervention importing issues surrounding the best interest of the next generation the mother's autonomy to decide is still paramount. By placing autonomy as the paramount consideration within the clinic the interview data confirms the documentary analysis. Fetal benefit is still contingent on maternal health, safety and choice. Consequently, issues about the maternal fetal conflict are currently irrelevant in terms of the final decision made, despite FGT further contributing to ethical constructions of the fetus (Casper 1998). Maternal fetal conflict is therefore about maternal physician conflict or maternal third party conflict, because it is these third parties who represent the voice of the fetus. In order to mitigate the mothers autonomy it has been proposed that preventive ethics should be employed, which can include four clinical guides:

1. Informed consent as an ongoing dialogue between the pregnant woman and her physician,
2. Negotiation as a clinical strategy,
3. Respectful persuasion as a clinical strategy, and
4. The proper use of ethics committees (Chervenak and McCullough 1990, 2010).

With the exemption of the two unique interviewees, there was consistently a strong prioritisation of the mother's autonomy over the fetus, which confirms the document analysis. Despite the glimpse of hope for those who advocate fetal rights, these are overridden by the ability of women to control their own choices within pregnancy. However, the 'fetus as a patient' is not a completely useless concept as the fetus is taken into consideration when FGT practitioners are considering risks and what treatments to pursue in the research conception phase. Therefore, certain obligations must be fulfilled to protect the fetus from unnecessary harm, thus bestowing a form of dignity upon the fetus (See Savulescu 2007) and creating a paternalistic bubble

within which pregnant women can exercise their choice (see 6.4.3). Nonetheless, the fetus as a patient concept relies upon the mother confirming that position upon the fetus; therefore, ultimately she can remove that status. The fetus is not the controlling subject within pregnancy, contrary to idea that medical technology has shifted the fetus from the controlled to the controlling subject (Squier 1996). The mother is not the antagonist but the controller of the maternal fetal divide.

Safety considerations included the mother, who takes precedence over the fetus as a patient concept. Therefore, a 100% efficacious fetal treatment would be disregarded if the safety of the mother was too heavily compromised. That predicament raises issues surrounding autonomous decision making and, once again, highlights that autonomous decision making is made within a paternalistic framework; thus, confirming the document analysis. Importantly, the fetus as a patient concept within the clinic confirms the prioritisation of the mother. Therefore, despite the fetus being framed as distinct, separable and separate from the pregnant woman's body in which it resides (Casper 1998, Squier 1996), which can be the sole beneficiary of treatment, clinical application is clearly based upon its dependant moral status (Harris 2000). There was an awareness of the complications that patients with capacity could cause in the future in both a legal and moral sense because of the implications of the full autonomous decisions of mothers where other options were available.

> RC That's a good place to stop there. I was going to ask about if they didn't have capacity to consent but that's a question for a different day
> IE13 It's a good question though because the fetus does not have the capacity to consent or define themselves. We've had cases of kids growing up and trying to sue their parents for not terminating them and allowing them to grow up with these conditions. It's something that we'll have to address at some point.

Given the complexity of issues surrounding treatment without consent and what constitutes the 'best interest',[234] the treatment of incapacitated patients was not explored. Such questions are important because the result of these issues potentially could imperil the production of future generations (Habermas 2003). Nonetheless,

[234] See Mental Capacity Act 2005; Mental Health Act 2007.

the Court of Protection may be asked to intervene in the future, which could have far reaching and profound implications for the treatment of incapacitated patients, as well as the way in which FGT is viewed.

8.5 Conclusion

By representing the interview data in a similar manner to the documentary data, the analysis of the interviews can be seen to move from identifying human dignity within the data to exploring if fetal interests can impose restrictions upon FGT. In doing so, the FGT practitioners confirmed the view that human dignity is not a concept used by FGT practitioners, with concepts such as 'do no harm' being more important. Human dignity is a concept that appears better suited to academic scrutiny of practice rather than an abstract concept which is explicitly used. For example, the data also confirmed that autonomy of the mother is a key principle that guides treatment with informed consent, and time being important in facilitating autonomy. Therefore, autonomy implicitly ensures human dignity is being served through principles such as informed consent. Therefore, the interview data appears to confirm that human dignity does not add to the debate and is not used explicitly as the document analysis implies. However, the implicit assertion of human dignity is through analysis rather than FGT practitioners' explicitly utilising human dignity.

Having identified this implicit assertion then it follows that individual choice is the key. However, in identifying the individual, in the view of the FGT practitioners the fetus is not an individual that can choose, because there is no way of knowing what it would choose. Therefore, the interview data confirms the documentary data through the implicit recognition of human dignity. Despite the fetus not being an individual, the fetus has interests, for example through being represented in the family as a future child or having an interest in having a condition cured. Therefore, intergenerational issues are evident within the working of FGT practitioners, with another ray of light shining through. Nonetheless, as seen within the documentary data, maternal autonomy within the clinic trumps that of intergenerational interests, because fetal interests are still contingent upon maternal health and maternal autonomy

In relation to the research questions the material points to initial conclusions for the first two research questions. Are the intergenerational issues of FGT taken into account? Clearly human dignity through autonomy means that intergenerational issues are taken into account. This in turn means the answer to the second research question as it stands, the views of the FGT practitioners and the documents align. This means that despite issues such as protecting fetal interests, intergenerational issues cannot override the reproductive rights of the mother, her rights trump the rights and interests of everyone else even if treatment could be 100% efficacious. This is one of the challenges that FGT poses to conventional thinking.

The next step is to see whether the interview data further reflects the documentary data or whether scientific progress within the clinic and laboratory is portrayed differently to that within the documentary data. This is important as the initial conclusions to the first two research question could change due to the impact of potential progress. In trying to answer the final research question, chapter 9 investigates the application and manifestation of FGT as a clinical practice. The views of FGT practitioners on scientific progress could point to further areas where FGT may have an impact that was not evident from the documentary data.

9 Interview Data: Scientific Progress

9.1 Introduction

Having seen that human dignity is not an explicitly used concept within FGT and that autonomy is the key concept within the clinic, further issues must be discussed in relation to the progress and future utilisation of FGT. Importantly for the thesis this chapter outlines how autonomy and choice before the clinic can be restricted by a number of factors in the research process such as: treatment options affecting FGT for example abortion; by inherent uncertainty; by funding and the formulation and regulation of resulting treatments. The data within this chapter directly relates to the aims of the thesis which is to ascertain whether there are intergenerational aspects in FGT and whether scientific progress implicitly protects intergenerational interests. The chapter will focus upon the research procedure aspect of the data. The theme of the research procedure focuses upon FGT as a future treatment option for genetic conditions. The themes discussed within the chapter are not exhaustive and other themes were raised within the data such as globalisation, specific technocratic barriers such as engraftment and vectorology, and public engagement. However, these areas are not considered here due to space and the focus of the thesis.

This chapter will focus on the following sub themes of research procedure, factors affecting FGT as a treatment option and mediating uncertainty. Section 9.2 will outline how FGT is presented as a future treatment option. In presenting FGT as a treatment option the factors that influence the progress of FGT from an experimental model will be revealed in section 9.3. These factors include the influence of funding, the inherent uncertainty within the FGT and other available treatment options. The theme of other treatments provides a clear example of the convergence of autonomy of the patient, choice within medical decisions and the research procedure. Because of the identified convergence of the principles that are key within the thesis an in-depth discussion will occur (9.3.4) to exemplify how autonomy, choice, intergenerational issues and medical research can cause ethical and legal dilemmas. Following the discussion of 'other treatment options' section 9.4 will focus upon ways in which FGT practitioners can overcome or mediate these barriers. These factors include conducting safety tests through risk assessments,

providing a convincing argument and producing ethical work through collaboration. The chapter will then conclude by summarizing the detailed analysis and the implications that the interview data has revealed.

9.2 Research procedure: framing the practice of fetal gene therapy as another treatment option

From the outset of the theme of research procedure it is evident that the research process is to design a treatment option for severe genetic conditions. Importantly, this frames how FGT will be delivered within the clinic and, ultimately, the impact upon the previous theme of human dignity through autonomy. Thus this sub section provides the foundation upon which the factors within the clinic are based. That base is the delivery of FGT as another treatment option.

> RC […] so you see it [fetal gene therapy] as another treatment option?
> IE3 Yeah, it's another treatment option, but the problem is it's a gene. But the gene is like when we give vaccinations of viral genes into little children and little babies to prevent smallpox's and polio militias. That has been immensely successful. So I see it as an extension of that.

Therefore, FGT is another treatment option for serious genetic conditions within pregnancy. It is compared to other treatments that occur within pregnancy and neonatal development and that helps establish FGT as a credible option. The comparison to other tested prenatal treatments which have overcome their own difficulties is where FGT as a treatment option should be aimed.

> It's a bit like fetal blood sampling and saying that your fetus is anaemic and we're going to give it a small blood transfusion by injecting blood into the placenta. It's a perfectly acceptable treatment, why would the mother say 'actually no I'm going to have an abortion now and I'm going to abort this pregnancy?' It just seems strange because there is a perfectly viable option to treat that child. That's the kind of end point I'd like to see it coming to. If you get diagnosed with this horrible disease, you can terminate, but there is also the option to treat the child, a free option to do that. No pressure or anything. But I'd like it to be at a stage where you get to point of fetal blood sampling so why wouldn't you do it? It's a routine procedure that is available all over the world. That would be the ideal situation to be in one day, all over the world. IE12

By comparing FGT to other current medical interventions helps provide ethical guidance as well as forming a basis for the acceptance of FGT. In other words: if X

(a current medical practice) is acceptable and Y (an experimental medicine) significantly resembles X then Y should also be acceptable. Those current practices have (at least to some extent) overcome the major scientific and ethical hurdles that would additionally stand in the way of the progress of FGT. Therefore, the interviewees expressed the desire to make FGT a normal prenatal treatment option. However, FGT is not yet a routine treatment and so the experimental and pioneering elements were stressed.

> Ok so the major obstacles will be firstly we have to establish that fetal gene therapy is very much in experimental mode. So there hasn't been any group that has taken it into the clinic. IE13

Because FGT is an experimental treatment it still needs to overcome various practical and scientific barriers that will be discussed below. However, the goal is to make it a credible treatment option. By identifying FGT as another treatment option within pregnancy for serious genetic condition there is an issue about how to propose the treatment. The resemblance to other treatments (highlighted in the examples above) means that the process of offering therapy is not seen as a barrier to the progress of FGT.

> [W]e're very used to talking to women in diagnosing fetal abnormalities and introducing the idea that they can have a termination if that is their chosen option. So we would provide it as one of a range of management option. We would never prioritise them, that is up to the parents. So yeah in that context we would add gene therapy as another option. But we wouldn't use termination of pregnancy as a lever to say you can have a termination of pregnancy or our gene therapy. IE6

The above extract demonstrates how FGT would be approached in the clinic and once again how comparison to other current practices is an important part of making FGT feasible and credible. The introduction of FGT to patients will increase choice.[235] Previously, those in receipt of their own genetic information before pregnancy occurred had the following preventive options: (i) have no children, (ii) take the risk and hope that their child will be unaffected, (iii) adopt a child, (iv) the use of assisted reproductive technologies such as prenatal diagnosis with selective abortion, or sperm donation, or the use of pre-implantation diagnosis after in vitro

[235] Issues regarding 'choice' will be discussed in relation to abortion below to highlight the tension within practice.

fertilisation of intracytoplasmic sperm injection (Fletcher and Richter 1996, Pembrey 1995). Ultimately, there is the choice of having a child with the condition and opting for palliative treatment if no corrective treatment is available. Where a genetic or congenital abnormality is identified during pregnancy the treatment options are: do nothing and have a child with a severe genetic condition or choose to terminate the pregnancy (Chervenak and McCullough 2009, 2010, Coutelle 2008). However, the interviewees presented FGT as another treatment option regardless of prior genetic knowledge (David and Peebles 2008). Women will freely be able to choose between pregnancy, termination and therapy.

It is proposed that FGT would be offered as another treatment option from which the patient has to choose.[236] There would be no extra weighting towards any of the options, and the interviewees stressed being open, honest and frank in conversations with the patients. In doing so, FGT would not be pushed as a cure, but as an experimental treatment option for mothers to consider in the management of their genetic or congenitally affected fetus and just like any other treatment option (David and Peebles 2008).[237] Therefore, despite the claims of FGT treatment increasing fetal patienthood (Casper 1998) the option is framed within a reproductive framework with other options. Despite an awareness of the influence of the other factors within a pluralist society that would affect the uptake of FGT (see below); there was an overall confidence that when FGT is efficacious, safe and has obtained ethical approval that it would establish itself initially as an experimental treatment option that would be used. The experimental aspect of the treatment was constantly referred to in order to emphasize the uncertain elements involved and confirmed the literature of Chervenak and McCullough (2010) [IE1-13].

Once FGT is approved there appear two main themes that could potentially hinder FGT progressing. These are factors affecting the utilisation of FGT as a treatment option (9.3) and mediating the uncertainty of a clinical trial in FGT (9.4). These two themes will be dealt with separately in the following sections.

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[236] See chapter 2.

[237] Thus, following EMA and GTAC guidelines upon the difference between therapy and experimental treatment.

9.3 Factors affecting the utilisation of fetal gene therapy as a treatment option

Presenting FGT as another treatment option raises questions such as: what may hinder FGT becoming a treatment option? The factors that appeared as barriers to the transition of FGT from an experimental treatment to an acceptable treatment option include: it being scientifically possible, regulation, funding, uncertainty, and other treatment options. Ultimately, FGT has to be scientifically possible but the next sections focus on these other factors and will highlight intergenerational aspects as well as the handling of scientific development of FGT in the clinic. However, there are many barriers to FGT because it is a developing science.

> I think it's a difficult situation as there are two separate ideas. So there is what is actually happening and how science is progressing, and what is physically possible and what is safe and what is being published. And then there is the public perception of what that is and that may not necessarily be the same thing. IE11

The above extract indicates just a few of the factors that are seen as barriers to FGT. The interviewees expressed many other factors that would appear as barriers to the translation of therapy to the clinic as well as the acceptance of FGT as a treatment option. These mitigating factors can be divided into preclinical, intra clinical and trans-experimental barriers. Preclinical barriers to the progress of the FGT were expressed in terms of vector efficacy, toxicology and patient safety, highlighting the importance of safety studies before scientific work translates into the clinic.

The majority of the documents analysed were connected to the regulation of FGT. Given the vast array of regulations an important factor to consider was whether regulation was a hurdle to the progress of FGT. As will be seen in the next section it appeared that despite the importance of regulation it was not a major hurdle to the progress of FGT.

9.3.1 Regulation is important but not a major concern

FGT is a highly regulated area but the current regulatory model, despite playing an important function, was not seen as a major barrier to the overall progress of FGT. In the view of the FGT practitioners within the UK, regulation is another hurdle that

is currently well focused and adopts the right approach even when the intergenerational aspects are taken into consideration. One interviewee remarked.

> I think that we'll just get over them as another scientific hurdle. The more experiments and changing variance in different ways to be better and insertions, they are just problems to solve really. Yes, they're immediate hurdles, not bigger picture hurdles. They're just the next thing on the ladder but they're not going to stop you from making the medicine better. IE11

Therefore, regulation is just one of the hurdles that FGT must overcome. Other scientific hurdles may cause bigger obstructions to the progress of FGT but that is not to undermine the role of regulation within the research process as it has an important function within the research process. In fact, the interviewees commented about how well they are regulated as 'they are there to keep us safe' [IE11] and within the UK the regulators are seen in a positive light.

> [R]egulation will play a very important role in reaching general consensus in the population because it will be a sensitive issue. But I think that good science is good science, is good science you know. So if it's good science eventually it will win the argument like stem cells and other things. If it's not good science, if it's not strict enough it shouldn't go ahead and it's fairly simple. I think that regulators are there not only to be negative but to be positive and at least in Britain I think that's the role that GTAC is playing. In other countries and on the continent I'm not always convinced by about that. But I think in Britain that's the way things are going. IE1

Therefore although regulation is still an important factor it is not currently a major hurdle to scientific progress. Within the sample there is an expected division, because of a hierarchical structure, between the PhD students and senior interviewees who are dealing directly with regulation. The PhD students were fully aware of, and observe the regulations but it is the research group leaders who deal with regulators and regulation in detail.

> RC You've mentioned about safety but actual regulation you don't necessarily see as a problem as long as you do your safety studies, animal models correctly, follow the guidelines, so you don't really see that as a hurdle?
> IE7 Well no, as long as we stick to the regulations I think it should be fine. Yeah things should be fine, from my own perspective I've not handled the regulations as much as XXXX or what therapeutically what to do, I don't have to work on that, or answer questions on that. It's basically the boss's job.

However, despite the undercurrent of regulation being an important part of the

research process, it is not seen as a hindrance because the scientific approach to FGT and regulatory guidance upon the area are currently aligned. An example of this can be seen when the interviewees talk about the most beneficial point of intervention and, which diseases to target.

> You're trying to get in there before organ damage has occurred and when you might have easier access to the tissue. For example, cystic fibrous before you've formed a layer of mucus over the epithelial cells, which you want transvect. So you'd be going in earlier because you can; and because you want to provide people with an option to termination of pregnancy; and you're going to get a better result doing it at that stage than later on. IE6

Therefore, the point of damage makes the focus of treatment upon the next generation an important factor and confirms the GTAC guidelines upon what diseases an in utero approach should be used (Gene Therapy Advisory Committee 1998).[238] Therefore, regulation confirms the science behind a fetal approach with many of the interviewees confirming that this is the right approach [IE1-6,9-13]. In fact, having regulation that confirms this approach is beneficial for the next generation by preventing damage.

> So taking the example of cystic fibrous much of the damage to the lungs happens prenatal. Once the baby is born most of the damage has already occurred and there is very little that can be done to reverse that damage. Whereas if you administer a therapy prenatally then you can stop most of that damage from happening. [...]. It has been shown that a fetus is more tolerant than an adult to gene therapy because their immune system has not completely developed. So a vector can have a greater benefit, a beneficial effect a greater therapeutic effect on a fetus that on an adult. So before this immune competence occurs it is important to administer the vector at that time to achieve maximum therapeutic efficacy. IE7

Therefore, the point of intervention is considered in relation to the teratogenic[239] timescale of the fetus as a human being. Control over the point of intervention is predetermined by the biological nature of the disease and when damage occurs. It is important to stop the irreversible damage that is created in utero, thus why an in utero approach coupled with teratogenic concerns is needed. However, for any fetal

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[238] Gene therapy Advisory Committee 1998 s.27(c) states that the disorder or disease treated would need to be life threatening, or associated with severe disability, and for which no suitable treatment is available after birth, in order to justify intervention in utero.

[239] Relating to, or causing developmental malformations (National Institute of Health 2011).

treatment, the FGT practitioner's treatment options are limited by birth. Therefore, despite the shared understanding of pregnancy and birth being a critical developmental stage for a separate human to be established, it is not these boundaries that concern FGT practitioner. Therefore, the established boundaries for biomedical treatment are challenged (Williams, Wainwright et al. 2008). The practical implication is that the interviewees did not limit their work to prenatal work. Their practice goes beyond the imposed time frame which pregnancy enforces upon both mother and fetus (Adam 1995). The practice is connected to the linear development of a child from conception through to childhood. That developmental connection is highlighted by the teratogenic concerns that FGT practitioner have. If they were solely concerned within the boundary of pregnancy then future teratogenic concerns would not be of paramount importance to FGT, which regulation currently reinforces through its guidelines upon fetal intervention. However, within the interview sample there was an underlying recognition that a serious adverse or perceived unethical incident could result in regulators shutting FGT down.

> I think it's regulation as you need to pass phase one, two, three, four and I think that gene therapy is really it's a big issue. Back to 1999 where one case ended up with leukaemia. So in the States they banned this stuff. So I think gene therapy needs a very nice regulation and you need to care about safety of course. IE8

Another interviewee focused upon why FGT has this problem. It appears to stem from the general fear surrounding gene therapy. With FGT being a sub speciality of gene therapy, that fear transcends into FGT as well.

> I think the problem is that gene therapy is highly scrutinized. Certainly for us that work in the gene therapy field and not personally even though we're quite close to the clinic, it seems if there is a single adverse event people are running around screaming. Yet thousands of people die each year from paracetamol. Penicillin would never have been passed by the FDA. So you got drugs that you can buy off the shelf or prescribe, which are pretty dangerous and people will accept those risks. And yet gene therapy a single bad thing and people are horrified and I think that it's just because it's a gene. IE3

Interestingly, the sample group did not see regulators or regulation as hindering their progress which appears contrary to the general view of clinical research regulation (Department of Health 2010, Paul, Anna et al. 2008). Generally, the interviewees praised the work of regulators as well as the current rules within which they work especially given the good reasons and the current experimental status of treatment.

Therefore, once the regulatory boxes were ticked clinical trial approval would be difficult but not impossible. Such comments were based on those who had had previous dealings with regulators in general, thus principally an area of comment for the post PhD members of the interview group. The current PhD students were aware of the process but expressed their own caveats to their opinions such as a lack of regulatory experience. Due to no clinical trial having been proposed to GTAC the only guidance that the senior practitioners used were conversations that had begun and experience with Ethics Committees and the phase 0 clinical trial proposal in the USA (Office of Recombinant DNA Activities 1999). Importantly, the biggest caveat raised by those dealt with structural abnormalities that blurred the boundary between therapy for the mother and therapy for fetal benefit. The blurred boundary meant that it would not be easy to ascertain the stance of GTAC about their treatment proposal, hence the reason why early conversations before a clinical trial application was submitted have been started. However, regulators were not seen as a particularly difficult obstacle to FGT progress.

9.3.2 Funding as a hindrance to fetal gene therapy progress

The FGT practitioners appeared to suggest that even if FGT was scientifically possible and fulfilled ethical criteria a huge obstacle to overcome is how to acquire funding. The economic environment is not directly amenable to funding FGT because of the inherent perception of it as being 'risky'. Therefore, the lack of venture capital could lead to FGT progressing slower than expected, which was seen as one of the major obstacles for FGT

> I think the main obstacle will be getting the money to do it because XXXX doesn't have the money to do it, I don't have that much money, we have to raise it from investors who would want to produce this product. Capitalism does not like taking risks. And that will be very difficult. The psychological barrier of saying a treatment for pregnancy - wow! Treatment for small children – wow! Let's invest in Brill cream or invest in bananas. So finding people who want to invest in this. And we might have to get the money from grant giving bodies like the XXXX who have already funded us to do the XXXX experiments and so to take it into man might need the health service funding the research. IE4

The lack of private investment and reliance on state funding makes the funding of fetal research subject to the political debate of what research bodies ought to be

funding. The documentary data is silent on this point, but ties into broader research funding issues. Research is subject to the political changes, especially within a recession whereby certain research areas go unfunded.

> XXXX and I had an idea with a social scientist that we wanted to explore patients/healthcare workers views on fetal gene therapy and other issues like informed consent process. We couldn't find any way to get it funded. We looked at various bodies and they wanted to fund people doing ethical research, but not an ethical project. So it's a bit of a problem really. The Wellcome Trust used to fund all sorts of ethical research but don't any more. IE2

Although all of the interviewees were in receipt of some form of funding they highlighted that it has fallen onto governments and institutions to fund such endeavours.[240] The combination of the other possible choices before FGT and the historical problems that have occurred in gene therapy and experimental medicine in pregnancy (Thalidomide and Epilim) creates a vacuum of funding for FGT outside of research councils and institutions. Within the interview data the effects of such huge, one-off catastrophes were recognised as having wide ranging impacts beyond funding and upon the progress of FGT in general. Such an issue becomes a problem within FGT because the cost of the amount of follow-up data required by a post clinical trial may financially outweigh the initial clinical trial. A related concern was the length of necessary follow-up [IE1-3,5,8,10-13].

> [T]here are a lot issues surrounding delayed or long term adverse effects. So we put a vector into a fetus and is that vector going to cause a mutation at any point in time into the host genome? Is the vector going to make its way into the germ cells of the fetal recipient and then in 20 or 30 years time when the surviving time the child wants to start their own family, is this vector, which in most cases based on a virus going to be transmitted to the next generation? So you're talking about a really long follow-up. A long follow-up in the monkey and an even longer one in human patient. So that will add to the cost of translation. IE13

Connected with the necessary length of follow-up several interviewees [IE1,3,10,12] highlighted the timescale of the FGT practitioner.

> [...] in fetal gene therapy particularly you have a narrow time limit to do things. I see another time scale, that's the time scale of the

[240] For example, Ark therapeutics has been able to fund such endeavours into fetal growth restriction with aid from an EU Framework Programme 7 Grant of almost €6 million (Genetic Engineering & Biotechnology News 2012).

> researcher, the observer like you and the patient. We feel that we've made terrific progress in a short time but if you have the disease it's not quick enough. Yes we'd like to do things quicker but you have to do things properly and you shouldn't rush yourself into things that aren't ready. IE1

Therefore, intergenerational issues involve the FGT practitioner as well as the intended recipient of treatment. The documentary analysis did not highlight such issues, but merely pointed to 'long term follow-up.'[241] The sample indicates that the length of the follow-up should equate to the length of time that the fetal generation survives [IE1-3,5,8,10-13]. The length of necessary follow-up identified by the sample poses several questions to consider relevant to investment, insurance, patient fatigue or loss and viral epidemiology. The follow-up may even include the corrected fetus's own offspring, as well as maternal follow-up, in order to ensure safe somatic therapy has occurred (Abi-Nader, Rodeck et al. 2009). Therefore, there is a direct conflict between market efficiency and social efficiency because of the short time frame within which private investors operate, as opposed to the long time frame that is needed for the practice to be conducted safely (Welsh 2006). Therefore, the cumulative cost of a FGT clinical trial in the introductory phase will significantly outweigh the cost of palliative postnatal therapy. The decision to fund further endeavours may rest with countries which have a crippling genetic problem (such as within the thalassemia belt)[242] and the social economic climate may indicate pursuing a genetic, rather than a protein, therapy regime prenatally if it is more economically viable.

It is clear that intergenerational issues surrounding patient follow-up include the FGT practitioner, which ultimately affects funding. Such intergenerational aspects are not referenced to dignity; they are contingent and lack the timeless element that human dignity has (Dupré 2009). Therefore, the combination of these separate

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[241] Long term follow-up under Regulation (EC) 1394/2007 Art 14 and Directive 2001/83/EC Annex 1which is expanded upon through the European Medicines Agency (2009) document 60436/2007 Guideline on Follow-up of Patients Administered with Gene Therapy Medicinal Products which states: The clinical follow-up period is dependent on considerations such as the characteristics of gene therapy medicinal products, the anticipated time for the occurrence of delayed adverse reactions, the clinical indication and expected life expectancy of the treated patients.

[242] The thalassemia belt extends from the Mediterranean East through the Middle East and India to South East Asia and South through Africa (Rodak et al 2007).

issues relating to follow-up illustrate that time has multiple timeframes (Adam 1995, Adam and Groves 2006, 2007, McKenzie and Davies 2002). In recognising the multiple time lines that are operating within the clinic and overall practice of FGT, future generations have to be important in the decision making of all actors involved (Adam and Groves 2007). It is through the knowledge of what action can be achieved in the future that, as protagonists of that future, it follows that responsibility rests with us towards our own future and the future of others. The creation of social and legal rules regarding the incorporation of future generations appears to fulfil such a responsibility. The issues relating to the different time lines must create a responsibility for research funders, patients and FGT practitioners themselves, which must be reinforced. However, within a society that is pro autonomy how can these duties be enforced? Through legislation? A contract for treatment?

Clearly a fetus cannot be a party to a contract and without knowing what a fetus thinks one cannot establish whether the contract is entered into willingly by either fetus or mother (due to social and goal orientated pressures), thus breaching fundamental contract principles (See Chitty and Beale 2008).[243] The consequences of breach of a contract for those deemed eligible to be a party to it could have huge social, legal and ethical consequences. Such consequences would need a full investigation as would any proposed regulation. Furthermore, long term follow-up would need to include the possibility of autopsy of the mother, future child and possibly third generation persons (Office of Recombinant DNA Activities 1999), which could create questions relating to the current regulation of autopsy. Under the Coroners and Justice Act 2009 would that mean that all deaths of those in receipt of FGT (both mother and fetus) should be treated as an 'unknown death'[244] for safety reasons? Such a change could be seen as controversial, but the salient point is that long term follow-up for FGT and the different time frames in operation could cause significant legal and social problems, which funders would want to avoid. These long term problems create further uncertainties within research, which the interview sample highlighted as a major concern within the progress of FGT.

[243] Also see the Unfair Contract Terms Act 1977 and unreasonable contract terms.
[244] Corners and Justice Act 2009 s.2(b).

9.3.3 The uncertainty of treatment

In the view of FGT practitioners the inherent uncertainty of FGT could lead to FGT not being utilised. Uncertainty can be characterised in four ways: risk (quantifiable risk), uncertainty (quantitative significance is unknown), ignorance (lack of knowledge) and indeterminacy (recognising the open ended and conditional nature of knowledge) (Wynne 1992). The FGT practitioners appear to engage and address all four of these under the term uncertainty in conjunction with 9.4. The uncertainty was not only related to the immediate risk of treatment but also to long term follow-up and the potentially bigger concerns related to society. These will be dealt with in that order. Uncertainty relates to potential restriction any upon maternal choice, but also highlights the potential of FGT to impact beyond the clinic, which is highlighted by the third research questions. Firstly, there are general concerns about the uncertainty of treatment.

> Depending on the virus it may not have any long term effect but the point is that we don't know so we can't say that there definitely not going to be any effect or there's no major concern. We can't say that as we don't have that information at the moment. So this is one of the blackholes in clinical trials and we have to tell the patient that we don't know but we have some confidence that the future offspring are going to be problem free. IE13

Possibly the most influential factor in the utilisation of FGT and a possible barrier to such treatments reaching clinical trials or being chosen by patients is the inherent uncertainty about the therapy within humans. Some of the uncertainties included: the unknown long term effect of introducing viral vectors into the genome even if the half life of the vector is short; whether the animal data would translate into the human model; and if the treatment would be 100% efficacious. Regardless of the amount of data accumulated within animal models, clinical trials of any investigations in human subjects are intended to:

> [D]iscover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational

> medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.[245]

Therefore, discovery of the unknown implicitly implies uncertainty about the procedure that will occur. In the extract below one can see how the site of intervention changes the dynamics of uncertainty.

> RC So scientific uncertainty seems to be the main thread and what you can control. But how is that different from any other clinical trial? There is always uncertainty in clinical trials.
> IE Yes there is but with many interventions there has already been a lot of preparation and background work to show that it is efficacious and safe for most drug trials. The obvious parallel there would be thalidomide and that was in the days when drugs were not tested in humans and rarely in animals never mind pregnant animals. So we learnt a lesson from that. So I think that on the other hand with a number of drugs that appear on the market, they are used widely, their drawbacks are not so dramatic and they come apparent some years later. So there are similar parallels there as well but with gene therapy, especially in utero, there is a range of uncertainties at the moment still. Surgical procedures are in some respect simpler, for example the surgical procedures tried out for the fetus, but then the risk to the mother are potentially greater as well as the fetus. The other thing about the fetus, in a similar extent but not quite the same as in the child, is that you have such a long period ahead for follow-up and development where you don't quite know what might happen. So there is a bigger question mark really. IE10

It is clear that uncertainty and risks within FGT are larger than the inherent individual risks involved with other clinical trials. The risks associated with FGT transcend current generations and extend to possible future ones. The focus is upon the individual (see chapter 6), which can serve as a hindrance to problems relating to collectives such as humanity in general (Prior, Glasner et al. 2004). However, there is an awareness of larger social implications.

> I think if that impacts on the whole of society or on just those four with the disease, that's still a positive thing. I think you do have to think about what impact that would have on the greater society […]. But I think that whatever you do could have bigger implications but then the likely hood of some horror thing happening is so tiny given all the regulations and all the small steps that need to happen before anything even gets near a human, never mind a big clinical trial is extremely low. IE11

[245] Directive 2001/20/EC Article 2 (a).

The documents connect risk to the 'environment' and the individual but not to the larger social risk posed to society and the human species in general from the effect of, for example, a generation of babies with birth defects. It provides further evidence that most medical applications consider individual risk rather that collective risk (Welsh and Evans 1999). Nevertheless, those collective and societal concerns are incorporated into FGT through teratogenic concerns for the individual as well concerns relating to vectorology. For example, the interviewees were aware of these risks, which included the effect of a transgene upon fetal and neonatal development. These developmental concerns, known as teratogenic concerns, are highly prevalent within the decision making of clinicians relating to pregnancy (Lyerly, Mitchell et al. 2007). The concerns included the effect upon the future parents if those uncertainties manifested themselves, as well as the increased incidence rate of future disabled children, who would otherwise not have been born. Therefore, the interviewees' concerns transcend into the next generation because of the concerns relating to the future child. By implicitly ascertaining whether to offer a pregnant woman treatment, the FGT practitioners make ethical judgements about what is an acceptable outcome for the future quality of life of the fetus. Therefore, intergenerational criteria are relevant within FGT because of the risk to the future child, as well as the effect those decisions have upon society at large.

Unlike the documentary data, which declares a discipline that can answer any question of risk or uncertainty through further scientific models; the interviewees explicitly state there are questions that science cannot answer until clinical trials are conducted [IE 1-13]. However, new forms of uncertainty create new forms of uncertain risk (Nowotny, Scott et al. 2001), which creates a tension between what GTAC professes as ethical research, because according to 27(b) research is ethical when the risks are known (Gene Therapy Advisory Committee 1998). Underlying the uncertainty of FGT was the interviewees' apprehension concerning previous drug trials, such as the thalidomide incident, and the adverse reactions that affected gene therapy in general, such as the Jesse Gelsinger and Jolee Mohr deaths (Deakin, Alexander et al. 2009). The apprehension is related to the effect of these adverse events and the result upon their work. As a consequence the work to mediate the uncertainty of research and the informed consent procedure becomes even more

important. However, having framed FGT as a treatment option it is the alternative treatment options that appear to create doubt over whether FGT would be utilised.

9.3.4 Other treatment options: In particular abortion

In particular the option of abortion was highly prevalent within the data. This is important because abortion is distinctly a right of the current generation over the next generation. If the regulation of abortion was to be changed then the rights and interests of the next generation could be seen to restrict present maternal autonomy, and thus provide a clue for answering the research questions. For this reason the discussion surrounding abortion will be longer than in the previous sections in this chapter. However, it is clear that in the view of FGT practitioners they would not restrict the right of abortion, even to pro abortion patients, despite abortion playing a major role in how FGT will progress.

> All the way through fetal medicine there is this interesting undercurrent really. Is the treatment that you're providing to the fetus compatible with what the neonatologist would do if that baby was delivered? And that is sort of important in a way because if you were going to do something that in a way no neonatologist would do or would dream of doing after birth, then you should ask yourself: what is it that is so different about a fetus in utero, which makes that allowable? So the most gross example of that is termination of pregnancy. IE6

It is evident within the views of the FGT practitioners that abortion is a recurrent procedure that has implications for FGT. Abortion is prevalent within the theoretical conception of FGT when treatment options are proposed, and post therapy because the option is legally available due to Abortion Act 1967. Most prominent within all the interviewees' narratives was the effect that abortion has upon FGT as a treatment option:

> Of course at the moment if you can diagnose the disease prenatally then abortion rules in this country means women have fairly readily available access to termination of pregnancy as a management option. So if you're going to introduce a gene therapy that may or may not cure a fetus that would be very unattractive to somebody whom would have certainly would have considered termination. IE6

The above extract shows how abortion looms within the minds of FGT practitioners in England and Wales. The extract below also highlights that, despite FGT being a treatment with global application, 'abortion' looms over FGT even in the theoretical

stage within countries where abortion and PND are available.

> Yeah. I gave a talk on this brain stuff and some guy in the audience said 'what's the point of this?' So I was like hmm and he carried on 'a mother who has had prenatal diagnosis and diagnosed with this particular disease would just terminate. There is no argument. She wouldn't risk this when she could terminate having a child.' So I said 'yeah that's a fair point and she may well choose to terminate if she wants to, I'm not going to argue that point. She has a right to terminate and she may well choose to terminate. But there are certain situations where the mother may not choose to terminate whether that be social, or ethical, or religious reasons or geographical reasons because it's illegal to do so in that country. So suddenly our proposal becomes very relevant. IE12

Therefore, the availability of abortion could severely hinder the progress of FGT unless patients choose not to terminate. Unlike other areas of decision making within pregnancy, which appear to compare the risk of intervening against the exclusion of not intervening (Berer 2005), FGT is compared to other treatment options in terms of the efficacy of the treatment. Abortion can have a 100% efficacy in achieving its purpose.[246] Yet, due to the uncertainty of FGT, the normalisation of abortion within developed countries (Berer 2005), the efficacy of abortion, and the certainty of doing nothing at all, FGT appears to be the third and final option. Nevertheless, it is not uncommon for parents to choose not to abort in these circumstances (Coutelle 2008).

Research suggests that although moral values are important the choice to seek termination of pregnancy is a pragmatic one that reflects the impact of pregnancy and childbearing on personal and household circumstances (Lie, Robson et al. 2008). Comparing the abortion rate under the Abortion Act 1967 s.1(1)(d) to other certified abortions may provide light upon this area. Where an abortion is performed because of risk of the child being handicapped, 2290 abortions were carried out in 2010 (Department of Health 2011).[247] However, in 2008 there were 4254 children born who had reported congenital abnormalities (Office for National Statistics 2009). The

[246] Depending on when the abortion took place and which drug(s) is used. For example the success rate for first trimester medical abortion with mifepristone ranges from 93 – 99% (RCOG 2011). In some cases the abortion must be attempted again, thus reaching the 100% efficacy.

[247] Under the reporting structure abortions under the Abortion Act 1967, abortions conducted under s.1(1)(d) are reported under reason E.

continuing birth of those with congenital abnormalities clearly confirms this pragmatism (Office for National Statistics 2009). Therefore, FGT could be used within the abortion debate as a tool to justify an anti-abortion campaign for conditions that potentially could be cured by treatment. Technology is always changing and reframing the abortion debate as well as the public's acceptance of abortion laws (Callahan 1986). As illustrated above, framing FGT as a treatment option must surely call into question the use of abortions by pro-life advocates just as the introduction of IVF promoted debate surrounding therapeutic abortion (Michael and Buckle 1990). Nonetheless, the statistics upon the use of abortion may indicate that there are still those who choose not to abort when they legally could do.

With the ability to perform elective abortions late into gestation[248] there was a sense of exclusion of those who had a preference for abortion as a treatment option. The exclusion was both practitioner and patient imposed exclusion. Practitioner imposed exclusion is exclusion from the trial because the practitioner has removed a patient from the trial because of their possible affinity to abortion. Patient imposed exclusion is where patients remove themselves from the option of being included in the trial because they have chosen abortion as their therapeutic treatment or have utilised Assisted Reproductive Technologies (ART) to exclude the genetic problem. Practitioner imposed exclusion is also where by a candidate for the treatment is excluded because they do not attain the standard set by the practitioner.

Patient imposed exclusion appeared to raise ethical problems surrounding the diversity of the intended recipients of the treatment, which concerned the interviewees. Given that the risk of non chromosomal abnormalities increases with socio economic deprivation (Vrijheid, Dolk et al. 2000), families from higher socioeconomic status are more likely to utilise ARTs (Carrell 2010: 721). Therefore, issues surrounding the initial sample population exist before the option of abortion is applied. In addition, those with atheistic backgrounds or backgrounds where their religion does not prohibit them from utilising abortion would also reduce the diversity of the sample group.

[248] Abortion Act 1967 s.1(1)(a).

Practitioner imposed exclusion is not uncommon within clinical trials regularly utilising certain candidates (Tunis, Stryer et al. 2003). It has been proposed for fetal surgery that in order to avoid ethically unacceptable study design there should be no exclusion of participants because of their preference for elective abortion, and should include adversely affected infants and elective abortions as outcomes (Chervenak and McCullough 2009). To do so would include 'take a chance' patients, which in turn raises further ethical questions about offering FGT to patients with this attitude. The literature and interview data suggest that candidates should be offered the choice because not to do so would violate the mother's autonomy in deciding if a pre-viable fetus is a patient of not (Chervenak and McCullough 2009, Coutelle and Rodeck 2002).

However, serious ethical questions arise from those 'take a chance' patients. It should be noted that the 'take a chance' patients who would accept and care for an affected child regardless of success or failure of the treatment, are not the most pressing ethical consideration (Coutelle, Themis et al. 2005). It is those who have a preference for abortion that cause ethical uncertainty. In taking a chance and choosing then to terminate a fetus if the desired outcome has not been reached, what does that say about FGT as a mode of fetal research? The fetal patienthood is confirmed by the mother and thus FGT cannot negate a mother's option to terminate (Chervenak and McCullough 2009, Coutelle and Rodeck 2002, Fletcher and Richter 1996). As a result the role of abortion as an option that can lead to unethical research must be considered, because it is clear that having an autonomy led system could lead to perceived 'unethical' research. For most women when amniocentesis was introduced, having the option of abortion was a key consideration before utilising amniocentesis (Rothman 1994). To remove abortion as an option could be detrimental to FGT and could reduce patient numbers to a minimal amount. It would be a stark example of the removal of choice from patients and an increase in the paternalistic bubble that was seen within the documentary analysis.

However, what would stop maverick practitioners from trying to recruit those who are pro abortion and utilising that stance for further medical knowledge? Could

autonomy within this specific case legitimately be restricted to stop the unethical manipulation of a fetus? These questions highlight the balancing act that needs to be addressed between ethics, scientific progress and the rights of others. If the balance is in favour of autonomy then 'unethical' research could be carried out. It could be unethical in terms of fetal rights or societal views about the function of medical research. Dr French Anderson's preclinical proposal for gene therapy is a clear example whereby it was suggested that those who would abort could receive treatment and still continue to abort (Office of Recombinant DNA Activities 1999). As Dr Michael Wilks, chairman of the ethics committee of the British Medical Association in 1998 expressed: 'I find it very difficult to accept that it is ethical to perform this kind of research on a woman who has made up her mind to have a termination, particularly as it is not of any benefit to the patient' (BBC News 1998). Issues over fully cured then aborted fetuses could be outside the legal limit as section 1(1)(d)[249] would no longer apply, therefore would then a mother be forced to have a child they would originally have aborted? Given that the HFEA has continually stressed the importance of research being limited to 14 days of embryonic development or before the primitive streak appears,[250] such issues need to be addressed. However, if the balance goes too far towards 'ethical' research it could lead to the issues highlighted in the previous paragraph. All the above questions are important because the important themes of the thesis (ethics, rights, law and scientific progress) are all competing to be dominant and which one of these concepts is deemed paramount will ultimately shape the practice and legislation of FGT.

Within the context of those principal concerns the question of choice within the clinic is raised. If autonomy is the primary principle to be adhered to then mothers should be able freely to choose regardless of social or medical repercussions. Within the thesis there is the underlying assumption that choice within the clinic is freely exercised but it is evident within genetic services that choice is restricted by service provisions and possible professional measures of success (Chadwick 1993, Clarke

[249] Abortion Act 1967 s.1(1)(d).
[250] Whichever is first under the Human Fertilisation and Embryology Act 1990 s.3(3)(b) as amended by the Human Fertilisation and Embryology Act 2008.

1990). These services and measures of success could lead to subtle coercion to make it appear as if choice is available whereas in fact it is not. Current cost cutting measures such as reducing 'unnecessary tests' within the NHS indicates that certain patients who previously had a choice would no longer be offered certain tests or procedures (Telegraph 2010). Therefore, choice is heavily politicised. There is also an issue surrounding the exercising of choice. Choice within the clinic is dependent on the doctor patient relationship because, the doctor is there to give the patient all the information needed in order to make an informed decision, and the doctor should then implement that decision once the patient has made it (Williams 1988). However, as interviewee four indicates:

> In my experience as a doctor a lot of it depends on the relationship between the patient and doctor. The majority of my patients say 'doctor you decide' and I practice paternalistic medicine. I think that's what most of my patients want when they're seriously ill. They don't want to have to decide whether they should have an operation or tablets or this or that. They say doctor decide. Now that's not politically correct. IE4

Bryan et al (2006) indicated that choice within drug treatment of coronary patients has frequently been overridden by clinicians and Britten et al (2003) found that only a minority of all prescriptions were "wanted, necessary and appropriate". An article in the Lancet goes further to suggest that patient choice is a poisoned chalice and patients themselves do not want choice (Calne, Calne et al. 2008). Therefore, an awareness of the exercising of choice by patients must be monitored. If choice vis--vie autonomy are key values then patients must feel they have exercised their own choice and not that of the medical profession. The documents clearly indicate that paternalism should no longer exist in medical law;[251] it must be the patient's decision, which has not been unduly influenced;[252] and removing choice, which would deprive an individual of a choice between two methods, is a breach of duty by a physician.[253] However, the 'why wouldn't you?' argument leads to an opt out rather than an opt in discussion, which makes choice a negative not a positive action. The 'why wouldn't you?' argument fails to appreciate the resulting harm of a negative result because the likelihood of a negative result is small. It also fails to

[251] *Chester v Afshar* [2004] UKHL 41.
[252] *Re T (Adult: Refusal of Treatment)* [1993] Fam 95.
[253] *Birch v University College London Hospital NHS Foundation Trust* [2008] EWHC 2237.

consider those who would proactively choose to have disabled children. The manifestation of case law indicates that the principles of choice and autonomy are not always adhered to within medical settings.[254] Therefore, choice and autonomy must be seen to be exercised in every circumstance without prejudice. The result is that the 'why wouldn't you?' position cannot be adopted within the clinic.

Despite the issues surrounding the above barriers to the progress of FGT the interview data provided areas in which these barriers could be mediated. These included undertaking safety studies through risk assessments, producing a convincing or solid argument and by producing ethical research through collaboration. Each of these will be discussed below.

9.4 Mediating uncertainty and barriers to progress

The three ways of mediating uncertainty are risk assessments, a convincing argument and producing ethical research. Each of these factors plays an important role in the progress of FGT but they are not decisive on their own. For example a convincing FGT practitioner can be undermined by unsafe yet ethical research. The three examples are useful tools for FGT practitioners and show that intergenerational aspects are taken into consideration, yet, once again, they do not determine the outcome because through mediating these barriers it is maternal choice and autonomy that is paramount. However, in producing this convincing argument it is for fetal benefit and therefore fetal interests are being upheld.

9.4.1 Safety first through risk assessments

Within the sample the main aim is to provide a treatment that is efficacious. However, that aim of an efficacious treatment is not a *carte blanche* tool to conduct any type of FGT. As indicated within the documents (chapter 7), research safety is a paramount concern linking the two concepts of risk-benefit ratio, and the safety of

[254] *Re MB (Caesarean Section)* [1997] 2 FLR 426; *Birch v University College London Hospital NHS Foundation Trust* [2008] EWHC 2237. For example, personal experience has revealed that there is little choice over preoperative sickle cell testing for those from Afro Caribbean backgrounds even where both parents have been tested and found not to be carriers, because of practical surgical considerations.

treatment, which can reduce uncertainty to an acceptable level. Therefore, creating a convincing argument should help to mediate the uncertainty of practice for proposed patients, thus allowing FGT to progress. Within the interview data safety and risk assessment emerged as key concepts, thus confirming the documentary analysis. However, unlike regulation, they emphasize that the most important issue is safety, which has a knock on effect on whether FGT would be utilised:

> I think the most important factor that is, that we are constantly asked about whenever we present our data and is one of the things we clearly want to know is: are viral vectors safe to administer in a pregnant woman. So safety is the most important issue. And again if even if the vector can benefit the fetus, if gene therapy improves fetal growth people are still concerned that for the sake of the fetus are you going to inject are large dose of viruses into the mother can you prioritise the benefit of the fetus over the mother. What if the vector does some benefit for the fetus but in turn harms the mother. Can you actually do that? So these are some of the things that we are constantly being asked about and XXXX are investing a lot into, doing a lot of toxicology studies. IE7

In order to build a convincing argument the animal models that are conducted must provide data that strongly suggests that the treatment is safe. Safety is a widely defined concept within the interview sample and is connected, for example, with the concept of harm and risk assessment. One interviewee highlighted the accompanying definitional issue of safety within FGT. The interviewees differentiate between molecular and practical safety studies and how that differentiation affects the judgment of what is 'safe'.

> If you do all the biochemistry and you do all the clinical tests that they do in hospitals then these mothers were deemed completely normal, completely fine. If you do PCR on the blood, so if you do really, really ultra sensitive microbiological tests on the blood, then yeah you do occasionally see signs of the virus in the mother. But it's one of these things, clinically it's fine. It's a normal mother, there's nothing wrong with her and she' absolutely fine. But if you start digging deeper and deeper and deeper, when you end up at the molecular scale you're going to find something. Is that safe or isn't that safe? Is that a clear cut study or not? Would that support fetal gene therapy or does it reject it? Again you got to weigh it up. IE12

Therefore, the remit of safety is not only one of scientific certainty, but also of risk perception. In conducting safety and risk assessments there are concerns for both mother and fetus, but also teratogenic concerns that arise out of the uncertainty of genetic interventions, thus engaging with the intergenerational aspect of their work.

By utilising animal models that closely resemble the human model the uncertainty of the treatment can be reduced, but never entirely eliminated. Therefore, one might not be able to achieve 100% risk free treatment, but will achieve a risk to benefit ratio that would make FGT acceptable. By utilising animal models to define as close as possible risk-benefit ratio not only for the individual patient, but also on a broader level of public health, as with gene therapy in general, FGT is permissible (Fletcher and Richter 1996).

9.4.2 Producing a 'convincing argument'

Once the risk-benefit ratio has been scientifically achieved, then consideration of the use of a convincing argument appeared throughout the sample range. The use of a convincing argument appeared to help FGT practitioners to get permission for a FGT trial as well as engaging with the problems raised by progressing technologies such as uncertainty, risk, ignorance and indeterminacy. In the production of a convincing argument there is an implicit acceptance that merely citing scientific fact is not enough (Parliamentary Office of Science and Technology 2002). However, it could potentially call into question how certain the uncertainties are, as highlighted in 9.3.3. Despite this, the credibility of FGT practitioners would (in their view) hopefully be enough to ensure that patients choose FGT. As one practitioner stated:

> I think it's going to be our ability to convince both the patient and the clinicians that this option of intervention and possible therapy has a high probability of success in order to legitimise getting the funding to do this, getting the patients to do this, putting the patients through this procedure without actually being able to guarantee 100% efficacy for successful survival of the affected fetus. […] It's going to be a gamble in the initial phase stages of it. So somehow we will have to have such a convincing argument and such good data from the none human primate before we go into the clinic because there is so much more at stake than with adult and to some extent child experimentation. IE13

The convincing argument is the same as establishing a solid argument since solid arguments are also about legitimising the therapy.

> At the moment it's all about making the argument and providing proof of concept. And if we can do that and say we've done X,Y and Z and this is perfectly applicable to the clinic then it'll make our lives easier to push it forward and getting money for your work. So it's all about building a solid argument that people will accept, believe whatever you want to call it, […]. IE12

The convincing argument is infused with safety and risk-benefit ratios, which will decide if FGT will be accepted by regulatory authorities.

> So for genetic conditions where we see factor 9 deficiency where it's all or nothing, but with growth restriction or perhaps preterm labour, if someone previously delivered at 24 weeks and you prevented them from going into labour, then fantastic. But if the delivery is predicted at 30 weeks, do you give them the therapy or not? It's going to be a balance of risk of what you know from how good it is to the risk of giving the therapy. IE2

Another interviewee remarks:

> […] it's all about that risk-benefit ratio, which will alter across time depending on what data we generate and how many patients it's been tried on. So that's constantly going to be in flux and could as easily go back the other way and completely cease to be as development has become wide spread. Only time will tell. IE5

Therefore, constructing a convincing argument will depend on the facts of each case and is based upon the safety and risk-benefit ratios. The convincing or solid argument is utilised not just for convincing regulators to permit clinical trials, but ultimately for patients. The 'convincing argument' is about having strong scientific data that suggests that within a human model the treatment is efficacious and safe. However, mere fact is not enough because underlying the conveyance of that information is honesty and being a credible source of information. Honesty about the difference between human and animal models; honesty about the uncertainties of treatment, despite the measures to mediate them appearing as conclusive; honesty about the massive "gamble", as one interviewee put it, about taking the treatment, were all areas of consideration. This honesty makes their advice credible. Credibility is central to the convincing argument, which is no different from other discplines and is dependent on trust as well as credibility (Wynne 2002), especially in areas where risk communication is needed (Renn and Levine 1991).

One has to be clear that the sample refers to being up front and honest with patients, which differs from coercion. For example, guidance from the USA indicates a clinician should recommend the treatment above all others if it is efficacious (American Academy of Pediatrics Committee on Bioethics 1999). The honesty of the FGT practitioner enhances the autonomy of the patient and facilitates choice as well as reinforcing the credibility of the FGT practitioners. Therefore, implicitly

within the interview data the informed consent of the patient was a paramount consideration. It is a patient's right whether or not to accept that uncertainty exists, and informed consent is the proposed method for resolution of the existing uncertainties (Djulbegovic 2001, Djulbegovic and Clarke 2001).

Perhaps uncertainty should be viewed as a friend rather than an enemy of science (Djulbegovic 2001, Djulbegovic and Clarke 2001), because when it is recognised and acknowledged more effective resolutions can be devised (Djulbegovic 2004). Uncertainty cannot be eliminated from medical decisions (Martinez 2012, McCullough 2012). Therefore, one has to ask:

> Against the background of this growing unawareness and non-knowledge in the wake of the modernization of knowledge, the question of deciding in a context of uncertainty arises in a radical way. If we cannot know the effects of industrial research, action and production—as is already generally the case in the fields of genetic engineering and human genetics—if neither the optimism of the protagonists nor the pessimism of their critics is based on certain knowledge, then is there a green or red light for techno-industrial development and mass utilization (Beck 2000: 217)?

This is where the FGT practitioners can address the issue of uncertainty. The documents appear to ignore this issue by presenting linear value neutral balance between risk and benefit, which ignores the impact of risk if it occurs and how the severity of a 'risk' is perceived by the patient and or public (Slovic 1987). Risk within the data and documents is reduced to statistical models focused within the clinic trial and laboratory setting (Beck 1992b, Prior, Glasner et al. 2004). However, the convincing argument goes one step further and is about responsibly managing epistemic uncertainty within the clinic (Martinez 2012, McCullough 2012).

In order to produce a convincing argument the 'risk' conveyed to patients will have to be understood and should include the perceived risks within society. All these factors help manage uncertainty within FGT due to FGT practitioners having comprehensively thought through all the issues of uncertainty relevant to FGT (McCullough 2012).[255] However, not evident within the document analysis is how

[255] Although not discussed within this chapter several interviewees recognised the importance of public opinion and acceptance [IE1,3,5,10,11,13] through communication with the public [IE2,3,11].

the uncompromising models for testing toxicology forces novel experimental medicine to conform to pre-existing models. Therefore, the FGT practitioners are developing models to satisfy the current criteria for gene therapy toxicity studies, rather than developing toxicity models that best suit the FGT in order to resolve issues of uncertainty and safety. Developing these models has slowed down progress, but not halted it. The interviewees were aware that public acceptance and risk perception were important sub topics to mediating uncertainty, therefore, without in addition addressing how the patients would respond to risk, their strong argument would fail (Slovic 1987). The acceptance of the role of abortion is a direct result of anticipation how patients may respond to the uncertainties of the treatment. However, that is different from the public's perception, which includes the perception of FGT by non FGT practitioners. In understanding the possible responses that patients potentially have to the risks of FGT, FGT practitioners are able to create ethically acceptable methods through collaboration.

9.4.3 Producing ethical research through collaboration

Beyond the ethical guidance from governing documents for clinical practice and scientific progress already identified, or the document analysis, ethical guidance is ingrained into research through collaboration and comparison of research. Collaboration works in several ways. There is collaboration between the basic scientists and the clinically based scientists; collaboration between FGT practitioners in general; and collaboration between junior and senior FGT practitioners in general. The first type of collaboration appears as the most significant form of collaboration within the sample.

> Yeah, we're totally plugged in with the clinicians as my boss is XXXX is a clinician. The guys down XXXX are all clinicians, but we tend to take a more basic approach. I'm not saying they don't do basic science, but we just do basic science. And we can be guided by the scepticism and enthusiasm, so for the XXXX stuff XXXX kept on saying that you'd never get an obstetrician putting a needle into a fetal XXXX, but a neurosurgeon will do this into an adult or child, but not an obstetrician because you're poking a needle randomly. So now we're using vectors that can target the XXXX from an intravenous injection, which again obstetricians do put needles into the circulation and that's an existing technology. So yeah we are guided a lot by what they think and say. IE3

The conversations that occur are important to produce work that has a higher probability of getting approval by external ethical bodies such as GTAC.

> IE2 So XXXX gene therapy, we did some ultrasound guided gene therapy into XXXX at the equivalent of 12 weeks pregnancy and it was jolly difficult. We injected it but it was very difficult. We didn't have any losses but I can't hand on heart say to mother that I am going to stick a needle under ultrasound guidance into your babies XXXX and it will be fine because I very much doubt that it will be fine.
> RC Doubt you'd get GTAC approval for it.
> IE2 Exactly, so what's the point even going down that way.

If communication of possible ethical dilemmas did not occur to basic scientists then the credibility of research could be negatively impacted. This is a two way process between clinician and scientist.

> RC So having that bridge between your blue sky thinkers and practitioners that see mothers day in day out with severe genetic conditions is important?
> IE2 Sometimes I say to them "we can do so and so" and they're like "o we didn't know that you could do that in a human" and I'm like "Yeah!" or sometimes we have to say to them "why don't we try it this way because we can go into circulation at 12 weeks" and they're thinking 'can we do that? 'And I'm like "Yes you might have a miscarriage but hey, you warn them of that about the risk of miscarriage, we have to do that every day of the week when we do an amino" it's a terrible thing to happen but they know what the risk is.

Therefore, the reciprocal process is useful for both clinicians and basic scientists. The pooling of clinical and basic science produces research which avoids perceived ethical and practical barriers within the clinic. There is recognition within the sample of the different factors within the treatment process and the consequence upon what is ethically acceptable practice. These factors include: what is scientifically possible, what would be accepted by clinicians as a possible treatment option; what would be accepted by patients as a possible treatment option; and what would be accepted by ethics committees as an ethically acceptable practice. Given that research is becoming more translational, from the laboratory to the clinic (Soderquest and Lord 2010), the communication of ethical dilemmas before translation occurs is important. Because the fetus will hopefully become a child that collaboration occurs with neonatologists and scientists as mentioned above [IE3,6,11,12] and between disciplines to resolve scientific hurdles and guide practice [IE2,4,6].

In identifying communication of perceived ethical dilemmas as an issue, autonomy is framed within choices already made by FGT practitioners. The example used in the quote above [IE2] is referred to by many of the interviewees as an example of good collaboration between scientists and clinicians. It also explicitly demonstrates the implicit bubble in which autonomy is framed within the documents. The risk to the mother is held to be the paramount consideration, but in a truly autonomous system those risks should be weighed up by the pregnant woman. However, because there are a vast number of stakeholders in clinical research, each with their own different perceptions of risk, there is a deep question of "whose risk is it anyway?" FGT practitioners, regulators, and the public legitimately have deep concerns about risk in clinical research, yet, these concerns should not excessively restrict research or eclipse the interests of patients (Deakin, Alexander et al. 2009). As mentioned within the documentary analysis, autonomy appears within a paternalistic bubble because of risk concerns (See 6.4.3, 7.2.1 and 7.3). Patients are increasingly trying to claim ownership of risk and to have a voice in decisions about the risk levels they are exposed to, thus bursting the paternalistic bubble (Epstein 1996). Within the present circumstances the decision is not to research highly invasive fetal treatments whereby fetal interests do override the future autonomous choice of a pregnant woman. It could even be said that the fetus has a right not to be manipulated because it would potentially become a full holder of human dignity. Because of the future rights that the fetus would hold, agents have to act in a way that respects that future dignity (Knopoff 1991). Therefore, it is within the ethical collaboration of scientists that the fetus as a patient concept and fetal rights emerge as significant restrictions upon the autonomy of mothers and FGT practitioners.

9.5 Conclusion

In conclusion, the interview data in relation to the research procedure frames FGT as another treatment option which is aiming to make the transition from an experimental treatment option to a normalised treatment option. The FGT practitioners compare the experimental practice to other current normalised practices, thus giving them a target to achieve that would present FGT as a less radical practice. However, by framing FGT as a treatment option several hurdles

arise besides the specific scientific hurdles, such as vectorology and engraftment rates, that could hinder the progress of FGT. These factors include regulation, funding, the uncertainty of practice and other treatment options, in particular abortion.

Regulation is not a major hindrance to the progress of FGT, because currently regulation and therapists are on a common path. However, that homeostasis can be torn apart by one 'unethical' incident such as was the case for gene therapy. Funding could emerge as another hurdle to the progress of FGT because historically in utero research is not an area privately funded due to liability for an unsuccessful outcome. The length of necessary follow-up coupled with the need for research to be continued beyond the time of the initial head FGT practitioner also cast doubts over where the necessary funding could be obtained. The uncertainty of the treatment is a major concern to the sample because of the consequent effects of patients choosing abortion over FGT, where some risks cannot be known until the first clinical trials have been conducted. Other treatment options pose significant questions about how to balance autonomy, ethics and scientific progress while also maintaining a practice that is socially acceptable. It also raises questions about the underlying assumption of choice with regards to genetics, which cannot be ignored and needs monitoring.

These hurdles can be mitigated by the safety studies that are currently being conducted, because from these safety studies the therapists can construct a convincing argument as to why the research should be allowed and why patients should choose to have the treatment. There is an inherent understanding that certain practices would be tolerated by patients if they received ethical approval. Here, communication and collaboration between the basic scientist and clinician is key to creating ethically acceptable work. A convincing argument could be construed for practices that are just on the edge of social or ethical acceptability, thus strengthening the argument for therapy.

However, concerns regarding the interplay between autonomy, scientific progress and the rights of others are apparent within the data. These factors appear important in connection to the research questions. The example of abortion indicates that when

autonomy, ethics and scientific progress collide there is no easy solution to fully reconcile all three. The example of ethically acceptable research being created through collaboration is another area whereby the paternalistic bubble is created before patient choice, as was evident within the documentary analysis. Therefore, autonomy is being restricted, which indicates that intergenerational aspects are restricting autonomy. However these examples lead to questions about whether the resolution of this conflict is legitimate. The application of the PGC is now important to find answers to these types of questions. It is clear that human dignity as an abstract concept is not going to resolve these issues. Therefore, in order to provide resolution to the potential issues chapter 10 will identify and select five of the most relevant issues from the data and will then ethically analyse the issues in order to help fulfil the target of the thesis.

Resolving Issues with the Principle of Generic Consistency

10 Identifying Key Issues and Relationship Within the Data

10.1 Introduction

Having collected and analysed the data there are several issues that stand out in the data that need resolving. Within the interview data it was evident that a practical hurdle to the progress of FGT was the option of other treatment options that definitively worked.[256] Those options were either choosing to abort or choosing to do nothing. It was clear within the data that there is a balancing act between the autonomy of the mother, ethical research, legal research and ethical regulation. The balancing act was relevant to many issues including whose interest can override those of another within FGT, the problem of current regulatory restrictions, and the problem of uncertainty within FGT. In order to resolve these issues the Principle of Generic Consistency (PGC) was identified in chapter 5 as the most appropriate ethical principle to do so. It should be noted that although there are many issues that arise from the data this chapter will focus on the five selected issues outlined below. Before the PGC is used to identify, elaborate and attempt to resolve these issues, some definitional and procedural issues regarding rights will be attended to.

Section 10.2 will outline the five main issues that arose out of the data sources and which all relate to the research questions. Section 10.3 examines the status of agency of the key individuals in FGT. In sections 10.4 and 10.5 the chapter will return to the PGC by outlining the interaction between the agents and potential agents in order to connect the relationships to the issues highlighted in section 10.2. Section 10.6seeks to resolve the five issues since it is seen to be evident that there is a tension between autonomy and the rights of others as FGT progresses to the clinic. Section 10.7 concludes the chapter.

The issues fell into the five themes: human dignity, maternal choice, maternal autonomy, constraints upon clinical/research progress and uncertainty within the clinic. All these highlight issues related to the three research questions and help to

[256] See 9.3.4.

narrow the application of the PGC in the thesis. In order to apply the PGC to the outlined issues each 'agent' within the practice of FGT must be identified. Those 'agents' will be the mother, FGT practitioner, and the fetus. Although it may appear purely agent focused, agents take into account their duties to others and, therefore, wider issues are taken into account, such as whether scientific progress should be continued (see 10.6). Given that the roles of the mother and FGT practitioner differ within FGT, the mother will deal with issues surrounding the remit of rights; whereas the FGT practitioner analysis will focus upon the remit of duties within FGT. By identifying those possible agents discussion can take place surrounding the relationship between the mother and FGT practitioner; the mother and fetus; and finally the FGT practitioner and fetus. By discussing the relationship between parties under the PGC resolution to the issues identified at the beginning of the chapter can be found. The PGC is also useful because it can identify the procedure that can resolve conflict, which might result in a set of specific or general rules, or in the need for adjudication by a third party in certain circumstances (where a case by case basis is needed outside of the rules) (Beyleveld and Brownsword 2006).

10.2 Outlining issues

The five issues that this chapter will focus on result from the findings in chapters 6 to 9 and are as follows:

1. Human dignity is not a useful concept within the practice of fetal gene therapy despite appearing to be so within regulation.
2. Is the paternalistic bubble that maternal choice is situated within, ethically correct according to the PGC?
3. Can a mother's autonomy be overridden by fetal interests given that the point of intervention is the only viable point of correction?
4. Are the current regulatory restrictions upon FGT practitioners justified?
5. Does the inherent uncertainty within fetal gene therapy meet the criteria for informed consent or render it ineffectual given that the nature of that uncertainty will affect future generations and their future autonomy?

Each of these issues needs elaboration in order to provide guidance upon the substantive point within each issue, and to understand how they relate to the aim of the thesis. It will be apparent that the issues have overlapping themes. Therefore, in

order to reduce repetition each theme will first be dealt with substantively and then referred back to where applicable.

10.2.1 Issue1: Human dignity

Here the underlying assumption that human dignity is a useful and prevalent concept within FGT and bioethics in general is questioned. Section 6.3 presents human dignity as an explicit and implicit guide. However, section 8.2 questions the usefulness of human dignity, concluding that human dignity was not prevalent in shaping the ethical practice of FGT practitioners. Other concepts emerged within the interviews, such as the usefulness of collaboration between the differing disciplines to create more 'ethical' practice. The identification of human dignity being the foundational tool of analysis within the thesis could lead to the conclusion that the utilisation of the PGC as an analytical tool is not applicable as it has been contended that human dignity is not a useful concept. Two points rebuff that argument. Firstly, the PGC is dialectically necessary;[257] therefore, it does not rely upon abstract concepts for validation. Secondly, as shown within chapter 5 even if the explicit concept of human dignity is rejected, then given the contingent human right argument of the PGC,[258] the PGC can still be utilised as the ethical theory of analysis. In fact, the term human dignity does not appear in Gewirth's early work. However, the consequence of the PGC still being applicable is that the implicit nature of human dignity as identified within both data sets is relevant. To assess the usefulness of the implicit nature of human dignity within the practice of FGT issues two to five must be assessed.

10.2.2 Issue 2: Maternal autonomy

Issue two relates to the tension between the autonomy of the mother and the rights and interests of the fetus. Sections 6.4, 8.3 and 8.4 indicate maternal autonomy is paramount, however what is critical here is whether the fetus has any moral status.

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[257] Statements are dialectic when they are made or accepted by an agent and then examined in order to ascertain what they logically should do. It becomes dialectically necessary when the statements it presents reflect judgements all agents necessarily make on the basis of what is necessarily involved in their actions (Gewirth 1978: 44). Also see 5.5.

[258] See 5.6.

If it has then the rays of light identified in sections 6.6 and 8.3.3 become relevant. It is important to state that 'overriding' refers to an active intervention to override a mother's expressed wish. An 'override' includes what a mother should morally do under the PGC to restrain their own autonomy in favour of her duties towards her fetus. It should be noted that fetal status is also important within issue three. If the fetus has moral status then situations may arise whereby restrictions to other agents may be justified. Issue three also draws upon the dilemma of comparing the refusal of treatment postnatally to that in utero.[259] Nevertheless, it is clear from the interview and documentary data that the mother's autonomy is paramount and cannot be overridden. Only fetal interests, not fetal rights, are taken into account in the research phases through safety and risk assessments. However, is this enough? It is clear that the intergenerational aspect of FGT is highlighted because the answer to such an issue has to consider the possible effect on the next and future generations. Central to answering this question is the weight given to those generations. Therefore, the weight given to possible and future agents under the PGC is important because it will help ascertain which goods of each agent can override one another.

10.2.3 Issue 3: Maternal choice

As seen above sections 6.4, 8.3 and 8.4 indicate that the individual, i.e. the mother within FGT has paramount choice within the clinic. Identifying maternal choice makes one question whether maternal choice is absolute or not because sections 6.6 and 8.3.3 indicate possible erosion of this principle. More importantly, sections 7.3 and 9.4 clearly show that, just as in regulating scientific progress, the result is a reduction in choice. However, if autonomy is absolute then agents should be allowed to choose any treatment they deem appropriate. If that is the case then regulation should reflect that position and not impose any paternalism. Importantly, the issue is not about an individual's ability to choose but about the restriction of choice before they even set foot into the clinic. Therefore, issue three deals with regulation of FGT practitioners and what limits can be imposed upon them, as well

[259] If the parents of a child refused to consent to treatment then a doctor could apply for a court declaration to decide if treatment is in the child's best interest. See Mental Capacity Act 2005 s1(5), 15 and Children Act 1989 s1(1).

as the consequent effects further down the research trail such as long term follow-up. Therefore, issue three is linked to issue four because if the regulatory restrictions are justified, the consequent effect is that choice within the clinic will be restricted. Several questions arise about the specific point of choice within the clinic and human dignity. Would any restriction of autonomy violate human dignity? If choice was unrestricted, would a refusal of treatment violate human dignity if it did not respect species integrity? Therefore, these types of question must be considered.

10.2.4 Issue 4: Constraints of clinical practice and scientific progress

Despite regulation not being viewed as a major concern in 9.3.1, it is clear from the data that some regulatory restrictions, such as germ line therapies and the high safety thresholds, constrain clinical practice and progress. Therefore, issue four is linked to issue three. The relationship between agents within the issue is important because if duties are owed between agents then, regardless of an ethical system that promotes pure autonomy, autonomy will be restricted by the duties held between agents. The consequence is that these duties can be enshrined within regulation thus leading to a justified paternalistic bubble. With regards to germ line prohibitions within FGT section 8.2.1 highlights that utilising human dignity as the foundation for a prohibition appears contradictory. Surely eradicating conditions that make the simplest form of agency nearly impossible upholds human dignity? Through the PGC it will be shown that the current prohibition is valid but the logic behind it needs to be corrected. Regulation should focus upon the safety, risk and the state of current scientific knowledge as reasons for prohibiting germ line therapies within FGT (Beyleveld and Brownsword 2001, Deakin, Alexander et al. 2009, Editorial 1999, Pattinson 2002). The consequent effect for future generations is that by their interests not having agency, debilitating conditions would continue to plague future generations. By focusing upon safety and current scientific knowledge it would also uphold the next generation's interest in not being caused further harm to their agency abilities.

10.2.5 Issue 5: Uncertainty and clinical progress

Finally, the interplay of informed consent and uncertainty appears as relevant to clinical progress. Despite the scientific certainty within sections 7.3, 9.3.3 and 9.4 indicate how the inherent uncertainty of scientific progress can impact upon future clinical trials by making FGT practitioners produce convincing arguments as well as ethical research through collaboration. Importantly, the issue is not just about whether uncertainty renders informed consent impossible, but it also questions if the inherent uncertainty of FGT and the possible negative effect upon a future agent justifies prohibiting therapy completely. To further complicate issues the rules governing the targeting of specific diseases indicates that therapy would be the only realistic chance to cure conditions with high morbidity and or mortality (Gene Therapy Advisory Committee 1998). Therefore, the risk of an uncertain outcome has to be balanced against such regulation. The issue also has to take into account how the inherent uncertainty has to be balanced against the future agent's rights because 'uncertainty' may impose restrictions upon that future agent's liberty, which may contravene the PGC.

Within all these issues there is the underlying theme about how the individual is situated within the wider context of society and the human species. For example, the paternalistic bubble could be formed by scientific endeavour through collaboration and perceived ethical approval or it could be created by society, for example the ban on social reproductive sex selection (Harris 2005a, b). The interplay of other treatment options such as abortion in sections 9.3.3 and 9.3.4 highlight that these issues should be viewed within the wider social context and includes questions of moral inclusion.

In order to resolve these issues the PGC will be used because, as outlined in chapter 5, the PGC is deemed within the thesis as the most robust theory associated with human dignity. Some of the issues above can be resolved by identifying the status of the fetus, because if the fetus has no moral status issues regarding choice will rest firmly with the mother and thus will not violate human dignity. As a consequence if the fetus has no status questions over ethical practice become about public

acceptance rather than ethical practice. It will also confirm that regulation within the area is ethically correct in relation to the PGC and therefore human dignity. However, before the PGC is used, procedural and definitional issues must be addressed. These issues include the definition and remit of rights and duties, the difference between competing and conflicting rights, and clarification of future and potential agents.

10.3 Issue over future and potential agents

Within this chapter the terms future and potential agent are often referred to. These terms must be clarified as they have differing meanings and protection under the PGC. Future agents should not be confused with potential agents. A future agent is a being that will in the future possess the intrinsic moral status of an agent rather than being a potential possessor. Therefore, a future agent can be a being in the next or any future generation. Yet a potential agent can only refer to a being whose agency status is unknown. Pluhar (1995) advocates the use of the differentiation between future and potential agents. The differentiation offers protection to those potential agents as future agents because potential agents have no moral intrinsic value. To afford protection to those outside of these criteria (to essentially a future agent that has no moral intrinsic value under the PGC) stretches the credibility of duties under the PGC. However, where an agent acts in such a way that the intention is to bring into being an agent, future agency becomes important (Beyleveld, Quarrell et al. 1998). For example, where a mother chooses not to abort a fetus with the intention that she wishes the pregnancy to come to term and produce a child, the future health of that child becomes a relevant consideration. Therefore, such future agency arguments are important where abortion is not an option due to the focus within the thesis upon intergenerational issues. It should also be noted that any potential or future agent that possesses any form of behaviour synonymous with agency will be afforded protection through the ASA and precautionary principle. Therefore, a fetus at best is a potential agent if future agency is not considered.

It is worthwhile noting that within this chapter, and throughout the thesis, the agency relevant issues are related to treatment of debilitating characteristics rather than those which seek to genetically enhance an agent's capacity. Therefore, intervention is to

rectify the agent to within 'normal functioning parameters' in the scientific sense of the word. Also, the argument deployed under the PGC is valid for both somatic and germ line interventions (Beyleveld and Brownsword 2001: 155). The effect is that if it is permissible to have somatic interventions that would uphold the dignity of a fetus then the same is true of a germ line intervention.

In order to identify resolutions to the issues, the PGC will be used to identify the status of the mother, FGT practitioner and fetus. Because of the clinical situation in which the mother is found the analysis will be conducted relatively to her rights and the FGT practitioners will be analysed in terms of their duties to other agents. However, both analyses are relevant to both types of agent.

By identifying the ethical position of the potential agent issues arise surrounding the tensions between autonomy and which way those conflicts could be resolved under the PGC. As stated within chapter 5, the resolution of the same conflict could result in two different answers under the PGC, both of which are permissible under the PGC. Therefore, an issue can arise where agents cannot agree about which permissible route to take under the PGC (Beyleveld and Brownsword 2006). Ultimately, the PGC must call time upon disagreements and where there are many plausible outcomes the agents involved must settle their difference either by consent or because the PGC requires a determination (Beyleveld and Brownsword 2006).

Before the status of each being involved is assessed it is important to address the role of third parties such as fathers, society and the state. These parties may have legitimate status within certain decisions of FGT. Where appropriate their role and possible rights and interests will be assessed and highlighted. It should be noted that Gewirth contends the PGC is a community of rights because society must enforce each other's rights, but also because agents have to recognise and accept obligations to society such as social contribution (Gewirth 1996).[260] Therefore, society is, in effect, being taken into consideration in the analysis and exercising of individual

[260] Because all persons are to some extent social products in that they receive nurturing from the family and wider society (such as schools and clubs) it is a necessary condition of their being successful agents. (Gewirth 1996: 82-84).

rights. So what are these rights and interests of a mother, FGT practitioner or fetus? Each will be analysed individually before moving on to the relationships between these parties.

10.4 Status of beings

10.4.1 Mother

The PGC was outlined in 5.5 but in short the PGC can be summed up as: I have a right to have the generic features and other possible agents have a right to have the generic features ≡ All agents have a right to have the generic features ≡ Principle of Generic Consistency. (Beyleveld and Brownsword 2001, Gewirth 1978).[261]

Therefore, an individual, in this case a mother, with full capacity has full moral status under the PGC. Therefore, she is entitled to the basic goods, which includes life itself, capacities involved to make choices and the mental equilibrium sufficient to translate one's preference into active pursuit of one's purpose (Beyleveld and Brownsword 2001). They are also entitled to the non subtractive goods and additional goods that all agents under the PGC are entitled.

There is no controversy about the status of a pregnant woman as an agent under the PGC. She has the right to choose what medical treatment she can refuse or consent to. That position is confirmed and reinforced within the documentary analysis and within the interview sample.[262] However, case law in relation to autonomy clearly indicates that there is a limit to what a person can consent to.[263] Also, there is a qualitative difference between the right to consent and the right to refuse. The case law centres upon a positive right rather than the negative right of non interference. Therefore, human dignity emerges as a merely constraining, apparently self afflicting conduct. The case law clearly indicates that there is an objective value attached to

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[261] For expansion of the PGC see section 5.5.
[262] See 6.4 and 8.3.
[263] *R v Brown* [1994] 2 WLR 556; *Council d'Etat* (October 27,1995) req. nos. 136-727 (*Commune de Morsand-sur-Orge*) and 143-578 (*Ville d'Aix-en-Provence*) which was confirmed by in the United Nation Human Rights Commission case *Wackenheim v France* CCPR/75/D/854/1999; and *Peep Show BVerGE* (1981) 274**.**

human dignity.[264] However, under the PGC an agent has the ability to waiver their own generic rights, unless doing so leads to, or involves, the violation of a duty to another agent. A prime example is suicide, whereby under the PGC an agent can end their own life because, in a way similar to the abstract concept of human dignity, the rights under the PGC are categorical instrumental ones, not intrinsic ones (Beyleveld and Brownsword 2001). However, Gewirth maintains that there are certain duties to oneself. If Gewirth is correct then the paternalistic bubble created by regulation and evident within the documentary and interview data will be justified because regulators would be justified in creating legislation that sought to prevent actions that violated those objective standards.

Gewirth raises three specific points in relation to duties to oneself. They consist of distinguishing between an agent's present and longer range (future) perspective; differentiating between different aspects of the psyche and maintaining an equilibrium; and thirdly treating various aspects of one's agency as agents that have rights, thus evoking the duties that one would hold against another agent (another form of equilibrium) (Gewirth 1978: 336).

Beyleveld and Brownsword (2001: 106-108) offer a concise and focused analysis of the three propositions, which focus upon three simple responses. Firstly, the PGC is not a duty under the PGC, but a rational requirement; it is dialectically necessary, therefore deriving duties from others does not derive from duties to oneself; and finally, the balancing of different parts of agency are only components of agency not separate singular pieces of agency. Ultimately, the PGC is based upon a will conception of rights. Therefore, one can waive their own rights, hence eliminating or rejecting any duty owed to oneself. Therefore, regardless of the arguments utilised by Gewirth, if committing suicide is acceptable (Gewirth 1978) then regardless of the hierarchy or equilibrium that Gewirth proposes, the right to waiver rights to oneself will ultimately prevail. The consequence of such an ethical theory means that a mother can waiver her rights in relationship to herself, which could lead to her own death if she wishes.

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[264] Ibid.

On first inspection regulation should allow any self afflicting treatment chosen by the individual regardless of the risk. The consequence would be that FGT practitioners could invest in treatments that had a high risk to benefit ratio and leave that decision up to the patient. A stark example of this is chemotherapy patients who have little or no chance of surviving treatment. Therefore, futile treatment at any cost could be developed, because the choice of risk lies with the agent.

However, within pregnancy there are two aspects to medical treatment that result in treatment not being a purely self afflicting piece of conduct. Firstly, within any medical treatment a physician or team of scientists, nurses, radiologists and so on would be needed; and secondly, within pregnancy there is the embryo or fetus to consider. Because the status of the embryo is in question, utilising precautionary theory identifies that treatment within pregnancy involves another possible agent. With all things being equal that possible agent would develop into a child which would possess the abilities and cognitive functions which that impairment dictates. Therefore, the status of other beings such as the FGT practitioner and fetus also need identifying as they may identify a conflict of rights or the imposition of duties, which can constrain the rights of an agent.

10.4.2 FGT practitioners

FGT practitioners are agents who have the same rights and duties as any agent under the PGC. Therefore, the focus within this section will be upon their duties towards other agents. These duties will be relevant for the mother as well because these duties apply to all agents. It could be argued that they also have a duty (the strength of which is dependent on who that third party is) to third parties such as society in general and the environment because of the possible consequences of their work.

Within FGT there is the need for additional help from a whole team including scientists. The same rights and duties apply to those team members. Therefore, they are also under duty to prevent possible direct or indirect harm to rights holders. It is important to note that such duties mean that FGT practitioners are also under a duty

to provide accurate information throughout the research process and must not falsify information.

In order to comply with the PGC, a FGT practitioner should not place an agent under risk of generic harm, which includes killing another agent or performing unnecessary procedures. Under the PGC it is also impermissible to put possible agents at risk of generic harm where this is not likely to prevent greater generic harm to a possible agent (Pattinson 2002: 133). Such statements impose duties between agents which result in certain restrictions being imposed because of the duties imposed upon an agent to another agent. For example, the uses of risk-benefit ratios within new treatments which would establish the levels of possible harm. Another is the creation of clinical equipoise, which means a doctor cannot waiver the duty to provide the best treatment or act in their patient's best interest (Freedman 1987).[265] Therefore, risk minimisation is a key principle (Council of International Organisations on Medical Science 2002, World Health Organisation 2002, World Medical Association 1947). However, risk minimisation requires the reduction of risk to another agent but not the maximisation of benefits (Sachs 2011). Risk minimisation is best characterised by risk-benefit calculations within the data (Health and Safety Executive 2007).[266]

Within the interview sample it is evident that a self imposed style of regulation would be in place even if an 'at any cost' mantra to research was prevalent, because of the reaction of both society and the media to gene therapy. The Jesse Gelsinger and Jolee Mohr are stark examples of the public and media reaction. The maverick paternalist would be greeted with the same reaction, which is possibly best seen within the Alder Hey inquiry whereby acts that were illegal and immoral were not mediated by the beneficial effect that occurred (House of Commons 2001).

Rights are not absolute and duties are no different. Duties may be imposed through legislation or a moral framework. Nonetheless, where those duties conflict with the

[265] A discussion upon clinical equipoise can be seen within (Freedman 1987). However, within the thesis, it is referred to under the banner of best interest.
[266] The Medicines for Human Use (Clinical Trials) Regulations 2004.

agents own rights then a limit can be placed upon the duties imposed by a rights holder. For example, a rights holder has a right to an abortion, but only in so far as the clinician in question is not a conscientious objector.[267] The conflict of rights here amounts to the imposition of a duty to refer to another clinician who does not object (General Medical Council 2011).

It is worthwhile noting that under the PGC an agent is under a duty not to treat another agent merely as a means (Beyleveld and Brownsword 2001, Gewirth 1978). Such instances include treating another agent as if they cannot express their own will or refuse consent. Therefore, a FGT practitioner must accept the refusal to treatment of another regardless of how they arrived at that conclusion.[268] They are also under a duty not to utilise patients purely as research tools, which would instrumentalise the patient and be contrary to the PGC.

However, there is a limit to the amount of paternalism or restriction of choice that can be exercised. For example, if something is merely difficult then regulation should not restrict FGT practitioners from doing such practices without justification to do so. Restrictions can be imposed where rights between agents are competing or are in conflict. Within pregnancy identifying the status of the fetus is paramount in considering whether there is any conflict or competitive rights at stake. If the fetus does have protection as an agent then further restrictions or duties can be imposed upon an agent because some agents need protecting due to their inability to protect themselves.

10.4.3 Fetus

Under the PGC the fetus is considered as a potential or future agent. Both future and potential agents can have their own interests taken into account and in some circumstances have its interests protected. It is here where the status of the fetus is assessed. However, it should not be considered that the fetus is a patient, but rather as a being where its agency status is unknown.

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[267] Abortion Act 1967 s.4(1).
[268] The only caveat is for those who lack capacity to consent, which is not within the remit of this thesis.

The document analysis clearly indicates that the fetus has no legal status.[269] Although apparently obvious, under the PGC a potential agent does not have any duties imposed upon it; however, what protection a potential agent receives is problematic (Beyleveld, Quarrell et al. 1998). In order to ascertain whether or not one is confronted with a potential agent the two evidential rules are used as identified in 5.8 (See Beyleveld and Pattinson 1998: 27). To aid our evaluation of a being's agency status there are four categories of empirical evidence (Beyleveld and Pattinson 1998) which can be used under precautionary theory when there is conflict between the fetus and mother, or the fetus and third party. Therefore, if there is evidence of a possible agent showing patterned organismic behaviour (displayed by living organisms); purposive behaviour (as being motivated by feeling and desire); intelligent behaviour (as being susceptible to learning by experience); or rational behaviour (value-guided, and characteristics of an agent) (Beyleveld and Pattinson 1998) an agent must accept the possibility that the being may be an agent itself. In terms of rights and duties these vary as potential agency increases during pregnancy. Yet, a potential agent has an interest in receiving treatment, which would increase the agent's ability to carry out functions if the risk to increasing the harm already sustained was outweighed by the benefit that the fetus would receive (Beyleveld and Brownsword 2006, Pattinson 2002).

As it has been stated, an agent only acquires human dignity through agency. However, those who can display proportionate features of agency will be afforded that same proportion of protection under the PGC (Beyleveld and Brownsword 2001). A practical example is abortion. The example of abortion is useful within the context of FGT because within the data abortion was highlighted as an area of ethical concern. Whether abortion is contrary to the PGC is dependent on whether terminating a fetus involves less of a violation of the PGC than is involved in causing generic harm to the fetus and/or mother (Beyleveld and Brownsword 2006). Therefore, destroying an embryo or fetus is not a violation of human dignity *per se*

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[269] *Re F (In Utero)* [1988] 2 W.L.R. 1288; *Paton v United Kingdom* [1980] 3 EHRR 408; *Vo v France* (2005) Application No 53924/00; *Attorney-General's Reference (No. 3 of 1994)* [1998] A.C 245*; Re MB (Caesarean Section)* [1997] 2 FLR 426.

(Beyleveld and Brownsword 2001). Where it can be said there is a sound rights based argument then abortion will not be contrary to the PGC.

The rights based argument must take into consideration that an embryo or fetus will never have a greater moral status than the mother and an embryo has a lower moral status than a fetus. Therefore, where a pregnancy places the mother's life in immediate danger an abortion will not be contrary to human dignity. However, this restriction must be made on a sound rights based argument. This is comparable to the justification that parental autonomy can be restricted in a child's best interest.[270] Whether the current 'abortion on demand' limit of 24 weeks is justifiable is questionable under the PGC. Before week 12, the embryo is simply a collection of cells that show no purposiveness. Yet, post twelve weeks of gestation a fetus can start to exhibit purposiveness. Once sensory nerves have reached the skin, which occurs at about 10 weeks, mechanical stimulation of the body can produce reflex movements (Royal College of Obstetricians and Gynaecologists 2010). Also, at about 18 weeks a fetus will withdraw from a needle and launch a stress response following needle puncture (Gitau, Fish et al. 2004). However, it has been argued that a fetus cannot feel pain until week 24 of gestation because the cortex is not intact, which is perceived as fundamental in the perception of pain (Royal College of Obstetricians and Gynaecologists 2010). Pain is merely just one piece of evaluative data for the purpose of agency but post 24 weeks agency relevant features appear to be more prominent. However, the biological development of a fetus suggests that a fetus has agency relevant features before 24 weeks. From week 13 rapid body development occurs while the fetus takes on more human features and beyond 16 weeks starts to move (Tortora and Grabowski 2001).

Therefore, between 12 and 24 weeks the fetus should be attributed some protection under the PGC with precautionary theory because the biological development of the fetus indicates that some protection should be imposed. Therefore, if FGT occurs before 12 weeks then issues over ethical research and the balancing of rights and duties between mother and fetus are irrelevant. After 24 weeks where there is a

[270] Children Act 1989 s1(1).

conflict or competition of rights then the threshold for a mother's right to triumph over the fetus' right to life will be significantly higher. Between weeks 12 and 24 precaution must be taken.

The abortion analysis can be translated into the FGT debate. As has been seen in chapter 2, ideally FGT should occur before the immunological response of the fetus has developed, which has been recognised as early as the 13th week of gestation (Coutelle, Themis et al. 2005). Currently interventions have been targeted post week 7 when the primordial germ cells have been compartmentalised due to the possibility of inadvertent germ line transmission (Coutelle and Rodeck 2002, David and Peebles 2008) with week 14 being the point of intervention in the in utero stem cell transplantation for X linked SCID trials (Westgren, Ringdén et al. 2002). The point of intervention will be condition dependant, but one cannot ignore the possibility of embryo gene therapy because the fetal stage occurs after the 56th day of gestation (Tortora and Grabowski 2001). If that is so, then there should also be an analysis of the ethics of in utero therapy in general rather than just specifically FGT.

There are practical implications that would suggest that FGT would occur within the fetal development period because, unless pre implantation genetic diagnosis is conducted or the parents genetic history is known, then the relevant information would be acquired at 10 weeks from the first ultrasound scan, or 12 weeks from a CVS, or 14 weeks from amniocentesis or 20 weeks from the second ultrasound scan (Royal College of Obstetricians and Gynaecologists 2005). Therefore the majority of FGT will fall within a grey area whereby substantive analysis is needed to ensure ethical research and ethical regulation occurs, as the X linked SCID trials indicated by being conducted at 14 weeks of gestation (Westgren, Ringdén et al. 2002).

Having mentioned future agents, it is worthwhile identifying what protection, rights and duties future agents have. Future agency is engaged when an agent acts in such a way that a potential agent will manifest itself as an agent in the future. Under the PGC agents owe duties to future agents *as agents* equal to those that they owe to present agents (Beyleveld and Brownsword 2001, Pattinson 2002). Future agents only acquire protection if they are treated in a way that allows them to develop

(Pluhar 1995). However, a future agent has protection as a potential agent because of the characteristics that it possesses at the current time. The importance of future agency is simple and is demonstrated in a situation where a mother acts in such a way that she is willing to give birth to a child and can take into account the interests of that future agent visa vie the child. In other words, the long term prospect of that potential agent can be considered as well as the potential agent's current interests. Therefore, if FGT occurred before the 12th week of gestation only a future agent would have any interest worth taking into consideration as it is clear from the abortion debate that pre week 12 a mother's rights will always trump the embryo's interests.

Under the PGC agents are required to take into account the generic rights that a potential agent will possess in the future. As a result, problems emerge in relation to fetuses that have genetic conditions meaning that they will never fully posses all the basic goods required for agency. It is clear that in the majority of cases the reason that FGT will be needed is because those future agents will not possess the generic features needed to function. Therefore, depending on when FGT occurs one could legitimately argue that the fetus has nothing to lose, thus reengaging earlier risk-benefit arguments. However, if it is known that the fetus will never gain GFA then what duty do other agents have towards it? Quite simply an agent with no generic features is dead and, therefore, not relevant. A condition such as Gaucher's disease, which severely compromises the ability of an agent to use their GFA does not indicate that they have no protection under the PGC because of precautionary theory. Therefore, those potential agents still have limited protection under the PGC.

Having identified the status of the three main beings within fetal gene therapy, the relationship between those agents must be examined in order to help identify the solutions to the issues outlined at the beginning of the chapter.

10.5 Relationship between beings

10.5.1 Mother and FGT practitioner

Both mother and FGT practitioner are agents with full generic features under the PGC. Therefore, the relationship between the two rests upon rights and correlating

duties. There is little in the way of controversy to say that when a mother presents herself to a FGT practitioner she has a right, at least to some extent, to medical treatment (Jackson 2009). FGT practitioners within that relationship have a duty to treat a patient subject to their clinical judgement, the consent of the patient and the possibility of being a conscientious objector.

In order to provide consent mothers need all the available information so that they can come to an informed decision. Therefore, consent procedures provide a set of correlating duties for the FGT practitioner to fulfil. Under the non subtractive duties of the PGC, FGT practitioners have a duty to provide accurate information in order to facilitate consent. The documents and interview data strongly support that stance (See 6.4.2 and 8.3). However, the inherent uncertainty within FGT makes the notion of one hundred per cent accurate information unattainable. The caveat of 'something might occur that we are not sure of' within gene therapy cannot truly be said to be a low risk until human studies are done. Therefore, the distinction between research and therapy is central. Research refers to 'an activity designed to test a hypothesis and contribute to generalizable knowledge' and that 'the practice of accepted therapy' are 'interventions that are designed solely to enhance the well-being of an individual patient and that have a reasonable expectation of success' (Office for Protection of Risks 1979). Therefore, a FGT practitioner is under a duty to explain the difference between therapy and research, but also to explain the experimental nature of research. They are under a duty to explain all the possible treatment options and what each treatment option involves, as well as the relative risks and chances of success (Pattinson 2002).

Following the informed consent process a mother has the right to accept or decline treatment and the FGT practitioner has a duty to accept the decision. Regulation consistently reflects that position (General Medical Council 2009b).[271] Yet, as stated in Section 5.5 whether choice is being truly exercised is another issue. Undue influence or coercion is not acceptable as under the voluntariness of the PGC choice

[271] Offences Against the Person Act 1861; *Chatterton v Gerson* [1981] QB 432; *Re C (Adult: Refusal of medical treatment)* [1994] 1 WLR 290; *Re T (Adult: Refusal of Treatment)* [1993] Fam 95.

is exercised as an unforced choice. Consent due to coercion is no different from forced choice as there are compulsory undesirable outcomes which the agent must choose, with a realistic threat of another worse choice if the option is not consented to (Gewirth 1978: 252). Within the context of FGT such coercion would include manipulating information or applying pressure to take a course of action that was not freely entered into.

Important for this relationship is the balance between the duty of the FGT practitioner to reduce the risk of treatment and the mother's autonomy to choose what risks she is willing to take. It has been suggested that where a treatment option is unethical because the risk is too high, that is paternalism in action (Pattullo 1982). Paternalism was evident within the documentary analysis whereby autonomous choice was only actionable within a paternalistic bubble.[272] Therefore, if a mother presents herself willing to consent to any procedure and there is a team of FGT practitioners willing to do the procedure, where is the ethical dilemma?

Although this is an apparent pragmatic and logical question, the answer is there is no dilemma. FGT practitioners within this relationship still have the duty not to put the patient under unnecessary risks, which is trumped by a mother's right to choose. For example, when a treatment course is dangerous for a mother she can choose to take that course regardless of the risk to her own life. However, a FGT practitioner is still under a duty not to damage agency relevant features of another agent. The most of extreme of which would be to kill another agent. Therefore, any 'treatment' that is actively seeking a result that would lead to the death of the mother would not be justified under the PGC. Therefore, the duties upon FGT practitioners imposes a restriction upon the type of treatments, which justifies the paternalism within research and clinical ethics (Jansen and Wall 2009)

Here 'actively' refers to any treatment whereby the main accepted result is death and includes any result that is achieved recklessly or negligently. Therefore, the issue of double effect is a relevant consideration. The legality of double effect is not up for

[272] See 6.4.3.

debate within this thesis, but it is clear within the FGT scenario that it may be irresistible not to infer criminal liability due to a strong causal link which is distinct from the palliative care situation whereby death is inevitable (Jackson 2006). Therefore, double effect is not an important consideration here. One has to remember that the status of the fetus will be important within FGT, because the possible implications could affect the relationship between the mother and the FGT practitioner. Therefore, the relationship between mother and fetus should be explored.

10.5.2 Mother and fetus

The relationship between the mother and fetus is one that in the majority of circumstances does not need to be explored because pregnant women will most often do what is best for their fetus (Rothman 1994). In those circumstances a discussion surrounding competing and conflicting rights is not relevant. However, due to the symbiotic relationship, many treatments have different implications for each being, which can mean that each being's interests do not align (Dickens and Cook 2003).

Because the relationship between the mother and fetus is constantly changing the amount of weight given to the potential agent grows as the fetus grows. Yet, given the practical considerations explained above, the focus is on the relationship beyond the 12th week of gestation. That is not to say that the position is the same for FGT that could occur earlier than week 12 of gestations, but because of time and space the analysis will be focused upon the status of the fetus from 12 weeks onwards. The only compromise to this position is when a mother confirms the status of future agency upon the embryo. However, that consideration is dealt with by the general consideration of future agents.

As stated earlier, agents owe duties to future agents *as agents* equal to those that they owe to present agents (Beyleveld and Brownsword 2001, Pattinson 2002). Nevertheless, where a mother is expressly stating that she will continue the pregnancy then one may take into account the future as well as current interests of the fetus. However, the position is dependent on there being no countervailing or overriding rights of others that would be violated by employing a particular

technology (Beyleveld and Brownsword 2001:155). Therefore, it has been argued that these duties include the duty of easy rescue (Savulescu 2007), the duty to seek medical attention for her sick child (Knopoff 1991). Here, unlike other special relationships that are forged between parents and children, the mother is in a unique position to help the fetus (Knopoff 1991). Clearly a competing and overriding right is that of the mother's autonomy to that of the fetus' right to potentially having full agency relevant rights. FGT involves having to obtain the consent of the mother because of the violation of her bodily integrity that has to occur in order to operate upon the fetus. Therefore, any fetal rights must be balanced against the mother's autonomy and the invasion of her bodily integrity. Conversely a mother's autonomy is enough to allow access to the fetus in order to operate.

Here, it is the difference between a potential agent and a future agent that is pivotal to what interests can be considered. A future agent with a debilitating condition would have an interest in gaining agency relevant characteristics. Under the PGC an agent owes future agents equal rights and interests as those granted to present agents. Therefore, if there was no countervailing and overriding rights it would be a violation of a future agent's generic rights not to have FGT employed (Beyleveld and Brownsword 2001: 154-155). However, there is no obligation upon the pregnant woman to confer the status of future agency on a fetus just because, at that point in time, there is fetal therapy which potentially could be used to cure or prevent her fetus' condition (Chervenak, McCullough et al. 1994). Her overriding rights are her own autonomy and right to bodily integrity. However, where a mother acts in such a way as to refuse the option of abortion it could be contended that where the future health of that potential child is taken into consideration within the remit of conditions that can only be treated in utero, then the question turns to a balance between the autonomy of the mother and the condition in question to be treated.

Although 'enhancement' is not distinctly within the remit of the thesis it is worth briefly considering whether in this relationship there is a moral obligation to create children with the best chance of life (Beyleveld and Brownsword 2001, Buchanan, Brock et al. 2000, Pattinson 2002, Savulescu and Kahane 2009). As described earlier in the thesis the discussion of FGT is focused upon therapy rather than

enhancement. But if there is a persuasive argument for enhancements then corrective therapies would automatically be included. Yet, under the PGC it is clear that enhancements are not needed for an agent to be able to exercise their GFA. Therefore, an agent has no generic right to an enhancement (Beyleveld and Brownsword 2001).

Although outside the jurisdictional remit of this thesis it is worthwhile noting that some American states, such as South Carolina and Utah, prioritise duties within pregnancy over a mother's autonomy.[273] Therefore, establishing duties within FGT may have a more persuasive effect in certain jurisdictions. However, a duty is not the same as a compulsory duty. Under the PGC one may have duties to another and can act against those duties if they wish, but they will be acting in an immoral way. The severity of punishment that ensues depends upon the duty at stake. The punishment will depend upon the relationship between the parties. Therefore, another relationship to examine is that of the fetus and FGT practitioner as the FGT practitioner may have duties towards the fetus.

10.5.3 FGT practitioner and fetus

Unlike the relationship between a mother and FGT practitioner, which is the relationship between two separate autonomous beings with full agency; the relationship between fetus and FGT practitioner is complicated by the location and increasing agency status of the fetus. There is, however, a direct relationship between FGT practitioner and fetus in two situations. Firstly, where the mother has consented to a procedure that allows access to the fetus; and secondly, from their general duty within the PGC to take into account the rights and interests of potential and future agents.

It is apparent from the first situation that the relationship between FGT practitioner and fetus is heavily dependent on the mother as a gate keeper. In fact, it has been argued that it is here where conflict within the maternal fetal divide is created.

[273] See *Whitner v. South Carolina*, 328 S.C. 1, 492 S.E.2d 777 (S.C. 1997); *Utah v. Rowland*, No. 041901649 (Utah Dist. Ct.-3d Apr. 7, 2004).

Therefore, the discussion should be centred upon maternal physician conflict (Van Bogaert and Dhai 2008). Nonetheless, where the mother has consented, the rights and duties will never be more than that owed to the mother because the mother is an agent compared to the 'potential agency' status of the fetus.

Under the PGC regulation should not restrict therapy that seeks to help those possible agents that would be non-viable or would have a low moral status that would significantly impair their ability to exercise functions under the PGC. Therefore, the safety and risk elements that need to be satisfied would be condition dependent. For example, conditions such as Edwards syndrome[274] or type two Gaucher's disease[275] would have a significantly lower risk threshold than a condition such as haemophilia, which can be treated postnatally.

However, the approach above appears to have an 'at any cost' for those debilitating conditions such as Edwards syndrome whereby the risk threshold that needed to be crossed would essentially be that of imminent death to the fetus as agency function is severely limited because of the condition. Without regulation, stopping the 'at any cost' mantra for a fetus could be utilised if the damage to the mother is limited. In other words, where the risk to the mother is low, where is the harm in a high risk strategy for diseases which severely debilitate the functioning of agency?

Excluding the relationship and correlating duties to the mother, it appears that under the PGC as long as further harm to a fetus does not occur as a result of the treatment then it should be pursued. That includes conducting research where it is known not to produce a benefit. These conditions must apply to both potential and future agents

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[274] A congenital condition that is characterized especially by mental retardation and by craniofacial, cardiac, gastrointestinal, and genitourinary abnormalities, is caused by trisomy of the human chromosome numbered 18, and is typically fatal especially within the first year of life. Also known as Trisomy 18 (National Institute of Health 2011).

[275] A rare hereditary disorder of lipid metabolism that is caused by an enzyme deficiency of glucocerebrosidase, that is characterized by enormous enlargement of the spleen, pigmentation of the skin, and bone lesions, and that is marked by the presence of large amounts of glucocerebroside in the cells of the mononuclear phagocyte system (National Institute of Health 2011). In type 2 Gaucher disease (acute infantile neuropathic Gaucher disease), liver and spleen enlargement are apparent by three months of age. Individuals usually die before two years of age (National Institute of Neurological Disorders and Stroke 2011).

because it is morally impermissible under the PGC to inflict further harm to the GFA.

By applying the PGC to the different relationships evident in the five issues identified at the start of the chapter it is clear that these relationships need to be applied. The relationship between mother and FGT practitioner appears contingent upon a mutual relationship between the two, with a duty upon the FGT practitioner to act within the confines of those duties. However, once the relationship between mother and fetus as well as fetus and FGT practitioner are introduced the picture is not as straight forward. Other duty based obligations are then in play, which may impact upon the application of the PGC upon the issues. The FGT practitioner has an obligation towards the fetus (gestational dependant) as well as the mother having a duty to help her fetus develop into a child, once she has decided not to abort. Therefore, the balancing of these obligations and rights must be applied within the issues.

10.6 Resolving issues

For the sake of completeness all the issues outlined in section 10.2 will be dealt with in the order that they are outlined. There is significant overlap between the issues and hence the resolutions. Therefore, where the resolutions overlap the reader will be referred to the initial discussion of that theme. Where relevant, the interests of third parties such as the state and father will be addressed. However, it must be considered that the resolutions to these issues are yet to be situated within a social context. Therefore, they are ideal philosophical resolutions that are yet to be mediated by society, even though under the PGC the following resolutions are what 'ought' to happen. Once the issues have been addressed the chapter will conclude.

10.6.1 Issue 1: Human dignity is not a useful concept within the practice of fetal gene therapy despite appearing to be so within regulation

The first issue relating to the usefulness of human dignity is answered without reference to specific agents but in reference to the PGC. As has already been stated, the usefulness of the term 'human dignity' as an explicitly used concept is answered

by the FGT practitioner's views.[276] However, the PGC also shows that the intrinsic nature of human dignity as identified by the documentary analysis is problematic.

To have a will conception of rights means that human dignity cannot be intrinsic in the same sense that the documentary analysis identifies. Human dignity is dependent on the formulation of the PGC and the resulting rights and duties. Therefore, for human dignity to be done acts must be in accordance with the PGC. It is the implicit nature of human dignity that becomes important as suggested by the interview data and the further documentary analysis. Therefore, to ascertain if human dignity is a useful concept, the answers to the issues below become important as they outline whether or not FGT is implicitly contrary to human dignity.

Despite being able to prove that human dignity as an underlying concept is important through the PGC, it is strongly emerging as an intrinsic concept that adds nothing significant to the discussion (Gewirth 1983, Macklin 2003, Melo-Martin 2011, Salvi 2001). It is an uncompromising concept when it is raised in order to question the legitimacy of any other position (Somsen 2005). Therefore, human dignity is an important analytical tool when associated with an ethical theory (in this case the PGC) as an implicit concept. However, human dignity as an explicit stand-alone concept is not a useful or necessary practical tool for regulation or practice of FGT.

Despite stating that human dignity as an explicit tool is not useful, it does appear as a concept that will continue be used for the foreseeable future. The use of human dignity allows regulators to avoid the appearance that they are seeking to regulate morality and it has the political advantage of avoiding taking a particular religious perspective (Caulfield 2003). In addition, the frequency and level of the documents in which human dignity is explicitly cited means that the explicit use 'human dignity' is here to stay.

[276] See 8.2.

10.6.2 Issue 2: Can a mother's autonomy be overridden by fetal interests given that the point of intervention is the only viable point of correction?

From the data it was seen that a mother's autonomy within FGT is paramount.[277] However, this causes tension for regulators where autonomy is placed above everything else. Issue two indicates that a carte blanche remit of autonomy is not possible within a theory or system that advocates rights and duties. Therefore, autonomy is justifiably restricted in certain situations. It is already evident that the paternalistic bubble can be increased to include fetal interests and this can affect maternal choice. However issue three, below, looks to take that restriction further. It seeks to restrict autonomy after the paternalist bubble has been created. It is here that the relationship between mother and fetus is crucial. It is clear that the ultimate decision of life or death of a fetus under the PGC is justified until week 12 whereby the status of the fetus is unclear. Therefore, it is the relationship after week 12 that must be examined, which will be applicable to future agents where abortion is not an option for a mother.

It must be contended that where a mother is not willing to have an abortion, she is under a duty to consider the future agent's interest. Considering that the rules dictating when FGT treatments can be developed mean that there are no postnatal treatments, then it is in that future agent's interest to undergo therapy (See Gene Therapy Advisory Committee 1998). Therefore, a mother is under a duty to future agents to have therapy and it would be a violation of the PGC, and therefore human dignity, if a mother did not elect to choose therapy. Within the context of England and Wales there is no duty within the regulations to compel a person with capacity to receive treatment. To do so would be battery.[278]

However, as indicated within the interview data, these decisions, particularly in relation to FGT and a mother's right to abortion, cannot only be viewed within the confines of the maternal fetal divide. The effect upon society's view of such actions

[277] See chapters 6-9.
[278] Offences Against the Person Act 1861 s.42.

must be considered as the effect upon 'ethical' research could lead to a mother's choice being restricted.

Within the PGC 'ethical research' is research that abides by the PGC. It is clear that where a being or agent is instrumentalised then the research will not be ethical. Under the PGC the purpose behind any genetic intervention must be analysed because if the purpose of a genetic intervention seeks to instrumentalise the future agent then it will violate the PGC. To instrumentalise an agent means that in order that the rights holder X is not treated as an end (a generic rights bearer) X must be capable of being a rights holder which, under the PGC, are only agents (Beyleveld and Brownsword 2001: 161).

Clearly where a mother presents herself as being pro abortion then the instrumentalisation of the potential agent has to be considered. However, there is a fundamental difference between being pro abortion and actively forwarding yourself for research because you have already taken the decision to abort. As indicated in 9.3.4 how do you regulate such an ethically and socially controversial area where the option to abort is a fundamental choice?

Several solutions are viable under the PGC. Treatment could be restricted to those who would not consider an abortion. However, the practical outcome of such an option would be to drive patients towards abortion and potentially stifle the progress of FGT. The potential effect upon the subject cohort could also raise significant ethical issues. Another controversial option is not to offer treatment to those who present themselves as wanting an abortion regardless of outcome. Ascertaining the potential patients' views before the therapy is offered would be legitimate clinical trial criteria in the early stages of research. Nonetheless, it is those who would abort regardless of the outcome that should be excluded, not those who might abort. Therefore, the potential agent is not instrumentalised through being used as just an end for research and ultimately a mother's choice will not be restricted because they will still receive their abortion, although earlier than they would have wanted. Once treatment has become efficient and distributed, then the restriction could be lifted as

research is no longer being conducted and the instrumentalisation of the fetus is not relevant.

Another restrictive approach would be to remove the option of abortion if treatment is successful. If the results of the intervention occurred post 24 weeks then essentially an abortion would be illegal and contrary to the PGC, except in the case of an emergency.[279] One cannot view these suggestions in isolation as the removal of abortion as an option could heavily impact upon the uptake of FGT because abortion is an important option for mothers (Rothman 1994). However, a successful treatment would engage the normal abortion laws. If FGT was successful in ameliorating diseases and treating congenital malformations then this option is the most sensible and would conform to the PGC. Conversely, where the treatment only partly ameliorates a condition, depending on the seriousness of the condition the option of abortion may still be available where that condition is incompatible with the GFA. Therefore, choice is once again restricted but legitimately under the PGC, and would not need a substantial regulatory change.

Therefore, fetal interests can override a mother's autonomy in certain circumstances when abortion is being considered, but what about the fetal interest in receiving treatment where abortion is not an option? As discussed earlier in relation to a mother and a fetus, a mother will be under a duty towards a future agent to have FGT and will act contrary to the PGC by not having therapy. Where FGT becomes true therapy and future agency is confirmed, the State may have a legitimate interest if the State adopts a public health model that seeks to avoid harm to specific groups (Buchanan, Brock et al. 2000). However, the State must still adhere to the PGC. Therefore, unless other countervailing duties arise the State would be legitimate in enforcing that duty even where the damage would occur by omission (by not acting to correct the defect) (Beyleveld and Brownsword 2001). The duties would be much like those currently in operation under the Children Act 1989 because future agents are afforded the same status as present agents. However, pregnancy does have a special relationship whereby the overriding rights of the mother would trump such

[279] See the Abortion Act 1967 s1(1)(b) and (c).

regulation. Therefore, where the risk to the mother's health, both physical and psychological, was a greater risk than the risk to the fetus under the PGC it would be immoral to enforce a duty upon the mother. Therefore, practically such a rule would be unenforceable because an expectant mother could legitimately argue that forcing therapy upon her fetus, which she does not want, would lead to her own psychological damage and resentment towards that child.

10.6.3 Issue 3: Is the paternalistic bubble that maternal choice is situated within, ethically correct according to the PGC?

Having outlined the relationships between beings under the PGC, it is clear that an element of paternalism from the regulators to society, and thus the individual, will be justified within the regulation of FGT. As was seen in chapter 7, the paternalistic bubble relates to regulators imposing conditions upon FGT practitioners, which ultimately shapes the available choices within the clinic. The duties imposed upon FGT practitioners towards other agents, such as the duty not to place another agent under the risk of generic harm, results in certain behaviours and activities having to be banned. In banning certain behaviours then the regulation of risk is legitimised. The net effect is that choice within the clinic will be restricted because certain practices are not permissible regardless of consent. Therefore, the paternalism seen within the data, such as the assessment of safety and risk of GMOs (Health and Safety Executive 2007),[280] is justifiable under the PGC.[281]

However, the above only provides guidance and does not identify what level of risk is acceptable or what outcomes other than death and impairment to the basic goods are acceptable. It also fails to define the remit of 'unnecessary risk', because for some mothers anything that will save the life of the fetus and not kill themselves is a necessary risk to take. Therefore, the same tipping point regarding what level of risk is acceptable is applicable. Nevertheless, would a treatment be acceptable where the result is the need of blood transfusions for the rest of the mother's life whereas the fetus is fully treated? Under the PGC as long as a treatment does not place an agent

[280] Genetically Modified Organisms (Contained Use) Regulations 2000.
[281] This point relates to uncertainty and will be discussed further in issue 4.

under risk of generic harm then the choice of taking on that risk will lie with the mother. Therefore, regulation looking at safety could be more liberal in terms of the risks that the mother can consent to. The bottom line is that where there is a significant risk of death and damage to the GFA, such as brain function, it will not be ethical under the PGC. It should be stated that here the PGC is not being interpreted as implying risk-benefit calculations are wrong *per se*, but that they should be reconsidered.

The remit of risks and benefits cannot be medically confined but must include social and environmental elements. It is here that the PGC is considered a constraint by virtue of what society wants itself to be (Beyleveld and Brownsword 2001: 11). One also has to consider that the environment could be relevant under the basic goods of the PGC because where a GMO gets into the ecosystem it could affect an agent's ability to obtain sustenance. The regulations on genetically modified organisms do include environmental risk assessments and are legitimate pieces of regulation (Health and Safety Executive 2007).[282] Through such pieces of regulation society's interests as rights holders are taken into account, which must impose a certain level of paternalism. However, beyond these limits it should be the patient that decides what risks they are willing to take (Djulbegovic 2001, Djulbegovic and Clarke 2001).

However, does that level of patient and societal protection, as well as the need for results, justify a strict long term follow-up because of safety concerns? Clearly entering into a contract with provisions for follow-up is part of clinical research. The length of follow-up within FGT would be unparalleled due to intergenerational issues. Follow-up would be needed on the mother, the fetus and possibly the fetus' offspring (Coutelle, Themis et al. 2005). Clearly freedom of contract can only apply to the mother in this instance and the fetus up until the point of Gillick competence.[283] Beyond that point the child would have to decide whether to

[282] Directive 2001/18/EC; Directive 2006/86/EC; the Medicines for Human Use (Clinical Trials) Regulations 2004.
[283] Where a child is deemed competent to consent to treatment without the need of parental consent. *Gillick v West Norfolk and Westbech Area Health Authority* [1986] 1 AC 112.

continue with follow-up. It would then be up to that future teenager to decide if they would want to carry on the follow-up. However, are future agents under a duty to other agents to provide follow-up data so that safety measures can be constructed properly? Such a duty appears weak at best, but any serious complications no doubt could, and should, be brought to the attention of FGT practitioners. Therefore, a duty to inform FGT practitioners of any serious health conditions such as any malignancy could be imposed. That duty would be applicable to both mother and fetus. Therefore, long term follow-up of the current and next generation is possible.

There is a note of caution about how free and voluntarily the contract entered into under FGT would be. As noted in 5.5, voluntariness is assumed within the thesis. However, it is not beyond plausible thinking that such follow-up terms would be ignored for the potential of a healthy/healthier child. Also, the regulation of germ line alterations goes beyond the individual and into the realm of the regulation of technologies with a potential impact upon the whole of humanity and future generations to come. Therefore, the issue of germ line alterations will be dealt with in issue four.

10.6.4 Issue 4: Are the current regulatory restrictions upon FGT practitioners justified?

It is clear from the resolution of the previous three issues that imposing conditions, such as safety protocols, to acquire informed consent, are legitimate restrictions of a FGT practitioner's freedom under the PGC. One example within the regulation of FGT is the prohibition of germ line therapies.[284] It has been seen that there is a difference between the practice of FGT and the picture that regulation paints with regards to human dignity. As shown within the interview data this difference is seen none more so than in the prohibition of germ line technologies, which are prohibited because they violate human dignity.

[284] Directive 2001/20/EC Art 9(6), Directive 2009/120/EC Art 4(2)(a), Council of Europe Convention on Human Rights and Biomedicine 1997; The Medicines for Human Use (Clinical Trials) Regulations 2004.

The risk of deleterious mutation that may occur in the future is inherent within sexual reproduction as well (Salvi 2001: 533). In addition, the prohibition because of safety concerns is time limited because of the fast pace and unpredictability of science (Bernier and Bregoire 2004). As already stated, the risk of generic harm is the standard used to assess what would be a permissible risk. Therefore, even with the uncertainty of FGT where viability issues arise,[285] the future being has so much to gain by even partial amelioration. However, the same rules imposed upon somatic interventions apply; therefore, if the germ line intervention is not likely to prevent greater generic harm to a possible agent it is morally impermissible (Pattinson 2002).

The best example of instrumentalisation raised in issue two is the use of FGT to determine what a fetus will become and value. The violation of the PGC and therefore dignity comes from the intention of not granting equal rights to the child of the future (Beyleveld, Quarrell et al. 1998). Nonetheless, such points are moot within a therapy that seeks to restore the GFA to within a 'normal range'. FGT is not about selecting traits, but is about restoring functionality of genes (Buckley, Rahim et al. 2011, Coutelle 2008, Coutelle, Themis et al. 2005, David and Peebles 2008).

However, FGT can still engage objections from disabilities groups due to issues surrounding the right to inclusion, and the loss of support. These arguments, however, are not necessarily prevalent when the PGC is applied. For example, according to the loss of support argument, if genetic interventions are routinely used to reduce the likelihood that future children will be affected by disability, the community of people living with disability will shrink (Buchanan, Brock et al. 2000). Yet, there are serious evidential flaws with the loss of support argument (See Buchanan, Brock et al. 2000, Malek 2008) and the argument fails to consider the interest in not having a disability. More importantly, the fears of producing a genetic underclass under the PGC are countered by the duty to assist those who do not have full generic functions, whether this be through taxation or other measures (Beyleveld and Brownsword 2006).

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[285] Many fetal deaths have genetic abnormalities that are not detected by conventional cytogenetic analysis. Malformations, deformations, syndromes, or dysplasias have been reported in up to 35% of fetal losses undergoing perinatal autopsy (Silver 2007).

Within regulation it is clear that any clinical trial that is known to result in germ line modifications is unacceptable and therefore un-licensable.[286] It is clear under GTAC guidelines that where the outcome of research is not known it is unethical research (Gene Therapy Advisory Committee 1998). However, given the uncertainties within FGT there will be in the words of Donald Rumsfeld '[…] [T]here are unknown unknowns' (U.S. Department of Defence 2002).[287] These unknowns are radicalized risks within industrial technical–scientific projects, which produce unintended risks, which are incalculable and beyond the control of modern day science (Beck 1992a, 1999). However, given the extent of animal models that will be undertaken that unknown risk will be reduced to its known minimum. Therefore, as long as that information is communicated to those involved and the purpose is to avoid inadvertent manipulation of the germ line, then that mode of research is acceptable under the PGC thus confirming the current stance (Clothier 1993).[288] Also, under the PGC, where somatic interventions are acceptable then so also will be the germ line equivalent because the relative harms are comparable. Therefore, in principle, avoiding known inadvertent germ line interventions would be permissible, because of the current state of germ line research, rather than imposing a complete ban on germ line alterations *per se*. It must be recognised that reconciling such underlying ambiguity is an ongoing problem for modern societies and risk assessments have arisen as the method with which to confront and minimize them (Beck 2009).

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[286] Council of Europe Convention on Human Rights and Biomedicine 1997; The Medicines for Human Use (Clinical Trials) Regulations 2004 s.19(4).

[287] The quote in full reads: 'Reports that say that something hasn't happened are always interesting to me, because as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns - the ones we don't know we don't know' (U.S Department of Defence 2002).

[288] Directive 2001/20/EC Art 9(6), Directive 2009/120/EC Art 4(2)(a); The Medicines for Human Use (Clinical Trials) Regulations 2004.

10.6.5 Issue 5: Does the inherent uncertainty within fetal gene therapy meet the criteria for informed consent or render it ineffectual given that the nature of that uncertainty will affect future generations and their future autonomy?

Firstly, it should be identified that issues surrounding informed consent are not restricted to FGT. Informed consent within genomics and medicine in general is an area of hot debate. For example, there are issues surrounding informed consent and bio banking when a child's information is used (See Holm 2005). However, the issue here is about whether the uncertainty of therapy renders the informed consent process ineffectual and therefore FGT should not be continued. The underlying assumption of fetal consent to the medical intervention must be acknowledged but the answer to that question will never be known. The attempted wrongful life actions symbolize that one can never be sure about this. Nevertheless, under the PGC one can assume that an intervention that would restore GFA would be a positive thing. Therefore, presumed consent such as in the case of emergency medicine would resolve such an issue (Allhoff 2005).

Under the PGC uncertainty is not necessarily a problematic issue with regards to informed consent. FGT practitioners must acquire accurate information and ascertain as best they can within the limits of their knowledge. That does not mean that a FGT practitioner can go blindly into a project. They must still work to reduce the risks involved, which would involve utilising the risk-benefit calculation as seen in issue three. Therefore, as long as uncertainty is reduced to the level that current scientific knowledge can be expected to achieve and the information about uncertainty is communicated then the PGC will not be violated. Examples of such steps can be seen within the guidance upon informed consent (General Medical Council 2009a).

However, is this a carte blanche green light for technology to proceed (Beck 2000)? That is a possible outcome, but other options are available such as: wait until our knowledge and understanding of genetics in vitro increases and then reassess the risks; or stop research into anything where the consequence of uncertainty could possibly result in unknown harm; or accept the limitations of risk assessments with

staggered progress and constant reassessment through phased clinical trials. Currently, the last of these options is in place, which fulfils the PGC in the immediate instance, but consideration must go into the issue of uncertainty and long term damage.

Given the nature of the uncertainty the level of follow-up is critical. Therefore, can uncertainty within FGT demand patients to adhere to the follow-up procedure? Follow-up has to be adequate, but in making long term follow-up adequate it can significantly increase cost, which can lead to failure of a project.[289] As stated within 10.6.3, uncertainty of treatment cannot provide a strong enough duty to compel future agents against their wishes to continue with future follow-up. However, long term follow-up procedures are a legitimate clause to impose within a contract as long as they are not deemed too restrictive upon an individual. Therefore, a balance between the adequacy of follow-up and restrictive conditions is needed. For example, follow-up testing that involved testing a mother's blood every week at 1pm on a Monday, clearly is an excessive inroad into liberty, yet yearly tests would not be. The balance has to be struck between the frequency of testing, the risk of future health problems and the risk associated with the vector and the GMO used (European Medicines Agency 2009).[290] Legitimate clauses that include the permission to conduct post-mortems upon the mother and future child up until the point of Gillick competence could occur as part of the Coroners and Justice Act 2009. Such informed consent would have to have a provision for emergency recall and life time testing of patients. It would need an amendment to the Corners and Justice Act 2009 to include future autopsy of the mother, future child and possibly third generation persons (Office of Recombinant DNA Activities 1999).

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[289] See 9.3.2.

[290] For example: the potential for and extent of chromosomal integration of a vector/ gene; capacity of a vector/ gene for latency/ reactivation; capacity of a vector for inadvertent replication after complementation by viruses causing escape from latency and reactivation and eventually leading to mobilisation; persistence of expression of the gene/vector/gene product; replication incompetence or competence of a vector; potential for recombination or re-assortment; altered expression of (a) host gene(s); biodistribution to target / non-target organ(s) / tissue(s) /cell(s); known interactions with concomitant treatments or known interactions associated with previous exposure to potent agents (chemotherapy, radiotherapy etc.) (European Medicines Agency 2009: 5). All of which will vary depending on the vector used.

10.7 Conclusion

In conclusion, the issues raised above had an undercurrent of the tension that autonomy can have within a system which needs to take into account the rights of others. These other rights holders include FGT practitioners and future agents such as a fetus. That tension manifests itself within the data as the paternalistic bubble that is evident within the regulation of FGT, which in turn restricts maternal choice in order to protect future generations. The majority of the regulations cited are consistent with the interpretation of the PGC as they all reach the same conclusion despite following different modes of interpretation. Third parties such as society are taken into consideration because of the correlating rights and duties that are enforced within the PGC.

By utilising the PGC it is evident that the state of regulation on the whole is legitimate and within the interpretative confines of the PGC. However, it is confirmed that the term human dignity does not add anything significant to the debate and, thus, the views of FGT practitioners are consistent with the PGC, which points towards the implicit nature of human dignity. Yet, because of the implicit nature of human dignity through concepts such as autonomy or the GFA, the term human dignity is not needed within the debate of FGT. Therefore, the removal of 'human dignity' from regulative provisions would clarify why certain techniques are prohibited.

The PGC has also helped to provide some resolutions to some of the ethical dilemmas identified within the issues. There are acceptable ways forward, which balance the rights and duties evident within the FGT scenario. The PGC is consistent with the data findings that it is only in very exceptional circumstances that maternal autonomy does not trump fetal interests/rights. It is only when future agency is compelled upon the fetus that a duty arises for a mother to have surgery. It could be considered legitimate for the State to impose a duty upon a mother to have therapy subject to the extent of her bodily invasion. However, the mother's psychological health must be taken into consideration and where damage to that

psychological health would be long term the mother's autonomy would have to prevail.

Further consistency between the interview data and the PGC is seen as both identifying significant knowledge deficits as the reason why there are research restrictions upon germ line therapies and why unspecified long term follow-ups are needed. These restrictions result in the safety protocols and the paternalistic approach within FGT regulation. Such criteria result in FGT practitioners being placed under a duty not to damage their patients GFA. However, uncertainty does not render that duty impossible, merely that informed consent and a consequent long term follow-up must be communicated and agreed upon by the patient. Conditional reportage of serious illness appears as a legitimate way to continue long term follow-up. Nevertheless, there is a need to consider the recourse that FGT practitioners would have if the correlating contract and/or duties are not adhered to. It is the balancing of these rights and duties which ultimately need justifying as FGT progresses and as any kind of recourse is pursued. By balancing such rights and duties future generations are taken into account and their prospective interests are taken into consideration. Therefore, any attempt to cure a condition 'at any cost/risk' is not a prospect for FGT when interpreted through the PGC.

11 Conclusion

11.1 Introduction

Having established the field through the contemporary history of FGT, then introducing the maternal fetal divide, it became apparent that intergenerational interests was a central issue to be addressed. Through establishing the foundation of human dignity within the regulation of FGT, the PGC was established to be an appropriate tool for analysis. After months of collecting data from documentary sources as well as interviewing some of the world's leading FGT practitioners, the data was analysed thematically. The thematic approach highlighted areas such as the lack of explicit use of human dignity by FGT practitioners. The practice of human dignity is manifested through other concepts such as autonomy at both a regulatory and a practice level. The competing interests of generations were clearly evident because FGT is framed as another treatment option for future patients. From the analysis and inductive comparison between the documentary and interview sources, five key issues were identified in 10.2, with the PGC used to try and provide adequate resolution to these issues, thus leading to the recommendations below.

Firstly, section 11.2 the overall impression of the data will be discussed. It will codify the comparisons and contrasts within the sources. The overall impression will include reflections upon the importance of this multidisciplinary thesis as well as identifying the significance in using such a methodology within an area where ethics, law, social science and science are all involved. Section 11.3 will then refer back to the original research questions and seek to answer them by drawing upon the data findings. Following on from those answers, section 11.4 will propose some recommendations, because within an area such as FGT resolving potential issues before they happen will help increase its acceptance. Section 11.5 presents some suggestions for further research and section 11.6 concludes the thesis.

11.2 Overall impression

Overall the documentary and interview data compared and contrasted each other. There were many similarities within the data sources, especially when referring to the implicit use of human dignity. Autonomy and informed consent emerged as an

implicit recognition of human dignity. Furthermore both sources strongly assert that the mother's autonomy is paramount within the clinic.[291] Future generational interests appear within the reasoning of the documentary and interview data and appear as rays of light for the protection of future generations' interests.[292]

One significant difference between the interview and documentary data is the use of the term 'human dignity'. It is clear that the picture the documents profess about human dignity is not actually found in the work of FGT practitioners who are situated in the UK. The interviewees struggled to define and pinpoint exactly what human dignity entails.[293] That does not mean that human dignity as an analytical tool is not useful, but in terms of practical application it does not add to either the debate or practice.

Another similarity between the data sources is the emphasis upon safety. The remit of safety goes beyond the mother and includes maintaining safety towards the fetus and future generations.[294] Here the impact of intergenerational interests is most evident because if intergenerational interests are taken into account then choice further down the research trail is reduced. It is at this point where maternal interests are also taken into account in addition to maternal choice. In other words, risk-benefit calculations take precedence over treatment choice, thus imposing a paternalistic bubble. As a consequence, the research areas for FGT practitioners are restricted, thus resulting in reduced choice within the clinic. Autonomy within the clinic is never one hundred per cent autonomy, but it is autonomy to choose a set of predetermined choices within a paternalistic bubble. This would appear problematic when using the PGC to interpret the data, but precautionary steps must be taken which makes the restriction upon choice valid. For example, where the status of a fetus is in question and the impact upon them would outweigh the benefit, practitioners/mothers must take steps to protect those potential agents. Therefore, restriction upon research and ultimately choice, where the risk to the fetus outweighs

[291] See 6.4 and 8.3.
[292] See 6.6 and 8.3.2.
[293] See 8.2.
[294] See 7.3 and 9.4.1.

the benefit, are legitimate. However, where research is high risk to the mother and not the fetus, autonomy should prevail.

Both sources acknowledge the uncertainty within FGT.[295] Yet what legislation does not appear to stress is the communication of that uncertainty, with uncertainty being extinguished through further scientific studies, such as toxicology.[296] It is the production of a convincing argument that will calm fears regarding uncertainty.[297] This is not evident within regulation, because FGT practitioners have to deal with the implication of uncertainty through the consent process. The communication of that uncertainty to patients does not invalidate the consent process when utilising the PGC as an analytic tool as seen within 10.6.5.

It is evident from the scientific progress chapters that the work of the FGT practitioners looks beyond the regulatory confinements. These issues include the interplay of abortion within the clinic, funding, and the explicit acknowledgement of the effect of uncertainty of treatment. The FGT practitioners appear to confirm the author's assessment that germ line technologies should be banned, but not indefinitely. Within the interview data concerns regarding the interplay between autonomy, scientific progress and the rights of others are apparent. The example of abortion indicates that when autonomy, ethics and scientific progress collide there is no easy solution to fully reconcile all three. The PGC identifies that any possible resolution of these issues is not straight forward since the stage, type and condition in question will alter whether fetal interests override maternal wishes.

11.2.1 Some reflections

If humanity is to become the master of technology instead of its subject, then research in areas such as FGT must be more comprehensive and go beyond a six page report (Gene Therapy Advisory Committee 1998) and must be continually revisited as regulation and science develop. This thesis is part of that process and

[295] See 7.5 and 9.3.3.
[296] See 7.3.1 and 9.4.1.
[297] See 9.4.2.

has identified problems, such as abortion, long term follow-up, uncertainty and human dignity, as areas in which FGT is potentially ahead of regulation.

Using such a methodology encourages those outside of science to write and explore the unknown. As stated in 2.6.2, areas of emergent technology must adopt a prospective approach to reduce these uncertainties. The exploration of FGT, despite not being completely unknown, has been a task which no doubt will help FGT practitioners, regulators and academics control as much uncertainty that inevitably surrounds new practices before clinical trials. Given the ethical considerations surrounding FGT an inductive ethical model must be used to help guide practice. This is highly relevant, if not fundamental to establishing future practice that will control technology, yet still allow it to progress. Therefore, despite lacking data fields such as patient ethnographies, in order to tackle these inherent difficulties a multidisciplinary approach within emerging technology fields with an ethical analytical tool produced rich data. In addition this methodological approach is used by the National Institute of Health (1999) to investigate such emerging areas.

Within emerging complex areas, such as FGT, multidisciplinary work combined with a mixed methodological approach is the best method to truly explore a multidisciplinary practice. As stated in 9.4.3, the different areas can help improve and progress an area forward. With the addition of an outsider's perspective such a methodology becomes significantly important to the practice as a whole. This is especially so when there has been little written about this method and therefore it can be used as a foundation or model for further specific work. It can also provide FGT practitioners and regulators with an impression of the vision that they are portraying to others.

The chapter will now return to the original research questions and discover what answers have been provided by this multidisciplinary and mixed methodological approach.

11.3 Research questions

11.3.1 Are the intergenerational issues of fetal gene therapy taken into account by both direct and indirect stakeholders?

Clearly, from the data intergenerational issues are taken into consideration. From a regulatory stance, at face value, regulation applicable within the clinic appears to be focused upon the human dignity manifested as autonomy.[298] Fetal interests are discussed but they are ultimately not relevant. However, within the regulation of FGT fetal interests are protected. For example, the rules governing the diseases for which FGT can be developed and the regulation governing safety do take into account future generations as well as the current ones. Nonetheless, considering the progress of FGT towards resolving congenital abnormalities, as well as further possible progress that has occurred, GTAC should revisit the area. The recommendations below, which are not evident within their report, should now also be taken into account (Gene Therapy Advisory Committee 1998).

From a practitioner stance the care over the fetus as well as the mother directly takes into account both their interests. In terms of third parties such as fathers, it was clear from both sources that their input was ultimately relevant. It should be noted that within the interview data 'parental decisions' was referred to, but ultimately it was then deferred back to maternal autonomy. Therefore, indirect stakeholders are relevant, but not taken directly into consideration. Importantly, both data sources confirmed that birth was the point where those parties would have separate rights.[299]

11.3.2 Can intergenerational issues override the reproductive rights of the mother?

The answer is dependent upon the area in which the rights and interests of the mother and fetus are being considered. When regulators are considering the areas within which FGT practitioners can operate, the interests of generations become a purposeful and relevant consideration that can ultimately restrict maternal choice within the clinic. For example, any treatment that would place the life of the fetus at

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[298] See 6.4 and 8.3.
[299] See 6.5.1 and 8.3.1.

risk with little chance of success would be prohibited from clinical practice. Therefore, choice is restricted by the paternalistic bubble, despite the potential gain. Another example is where treatment would impact upon future pregnancies despite the possible impact upon the fetus that currently needs treatment. Here it is future offspring that are impacting upon maternal access to certain treatments within pregnancy. It is also worth noting that it is at this point that maternal choice can be restricted due to patient safety. Therefore, implicitly the fetus as a patient concept is taken into account, thus implementing the maternal fetal divide identified in chapter 4.

These restrictions appear to emanate from human dignity. Yet, on closer inspection safety concerns and public policy considerations are better placed to provide an explanation.[300] It also appeared in the interview data that what therapy options patients would choose was a factor taken into consideration. Therefore public perception of FGT, and science in general, would appear important, as well as the communication of those feelings/opinions to FGT practitioners. However within the clinic, it is a different story. As stated in 6.4 and 8.4, it is clear that maternal autonomy is paramount. The mother may choose to prioritise intergenerational rights and interests; but, ultimately that is her choice and they cannot override her. The data confirms the position where the fetus is seen as a patient, which is contingent upon maternal consent to operate.

Within 10.6.2 it is clear that fetal interests can override a mother's autonomy in a limited set of situations when abortion is being conducted. Also where abortion is not an option a mother will be under a duty towards a future agent to have FGT and will act contrary to the PGC by not having therapy. As mentioned within 10.6.3, certain areas within the paternalistic bubble are not valid. The consequence of this is that the PGC would allow a wider remit for research than is currently available. However, in potential prospective research areas such as germ line technologies, regulation is correct, even if the reason behind it is not. Nevertheless, under the PGC

[300] See 7.4 and 7.5.

in certain, limited circumstances intergenerational issues can override maternal rights.

11.3.3 Have intergenerational issues impacted upon the areas that fetal gene therapy has, and will have an effect upon?

The clearest area where intergenerational issues are demonstrated is within the divide between germ line and somatic interventions. The interview data and documentary analysis also highlights that the regulation and practice of FGT is governed by a divide between mother and fetus. Areas such as consent and long term follow-up are examples where the impact of such technology is seen firsthand. GTAC guidelines combined with the interviewees' proposal of FGT as another treatment option[301] indicate that for conditions to be amenable by FGT they must have an intergenerational aspect. Clearly, abortion is an area within the interview data where FGT raises significant questions regarding not only intergenerational interest, but also how FGT is viewed as a practice.[302] However, as seen within 10.6.3, when using the PGC as an analytical tool certain paternalistic regulatory restrictions are not valid.

However, within the regulation of FGT key areas of consideration regarding intergenerational aspects are missing. The documents frame the intergenerational aspect of their work in terms of inheritance or germ line issues. Consequently, a difference between biological intergenerational issues (germ line) and intergenerational issues *per se* (future reproductive choice, the environment etc) emerges. This will impact upon issues regarding confidentiality, future reproductive choices, consent, contracts and long term follow-up procedures (i.e. post mortems) as seen within 9.3.3. FGT practitioners cannot be expected to deal with areas such as contract and confidentiality. However, they should have an input regarding those issues as they are at the coal face of progress.

[301] See 9.2.
[302] See 9.3.4.

Having considered the data and identified areas in which ethics can provide guidance or avenues of resolution in relation to the research question, it is now appropriate to suggest recommendations that appear valid from the data. Although a wealth of recommendations could be proposed, the five most prominent have been identified and are discussed below.

11.4 Recommendations

It is clear from the data and the ethical analysis that changes in line with the PGC should be introduced. These recommendations include:

1. The removal of 'human dignity' from regulation, including its indirect application;
2. Make the prohibition upon germ line technologies conditional, therefore allowing FGT practitioners to conduct germ line research within animals once knowledge deficits have been satisfied;
3. Further investigate how abortion, informed consent, long term follow-up and confidentiality can be maintained and regulated ethically.
4. Reconsider how far bodily integrity can be respected where abortion is no longer an option and treatment is only available within pregnancy;
5. Review of research funding in relation to long term studies of fetal gene therapy.

Each of these will now be elaborated in turn in order to provide the justification for each recommendation. Following from those recommendations, where further research has been proposed, those proposals are in addition to the recommendations.

11.4.1 The removal of 'human dignity' from regulation including its indirect application.

It is clear from the data findings and resolution under the PGC, that removing 'human dignity' is a strong recommendation for FGT regulation within the UK.[303] Commentary by academics such as Macklin (2003), Melo-Martin (2011) and Salvi (2001) is clearly supported by the data findings. Despite the use of the term 'human dignity' it only appears implicitly within the regulation of FGT within the UK, the recent intellectual property case of *Brüstle v Greenpeace*[304] clearly indicates that where human dignity appears in the preamble of a directive, it will be taken into

[303] See 8.2 and 10.6.1.
[304] Case C-34/10 *Oliver Brüstle v Greenpeace E.V.* [2011] OJ C 362, 10.12.2011, p. 5–6.

account within ECJ interpretation of directives. Therefore, it is important that regulators within England and Wales actively create regulations to fulfil their obligations under EU law, rather than just deferring their responsibilities by referencing the directive directly. By removing 'human dignity' the debate will not be stifled and it will remove the ambiguity of the term in any regulation.

11.4.2 Make the prohibition upon germ line technologies conditional, therefore allowing FGT practitioners to conduct germ line within humans once knowledge deficits have been satisfied

In connection with the removal of human dignity from regulation, the regulation of certain techniques/technologies such as germ line interventions must be reconsidered. Such a recommendation must start with the caveat that currently the ban on germ line technologies is reasonable. However, by removing human dignity from regulation, it should be reaffirmed that safety and knowledge deficits need to be satisfied within animal models after successful somatic FGT. Although contingent upon the future status of somatic interventions, imposing a long term *de facto* ban upon germ line technologies currently appears valid. Such a step may be seen as substantially hindering the progress of germ line therapies. The underlying tone of fear and safety accompanied by the interviewees' recognition of the impact of negative stories connected to pregnancy and gene therapy implies precautionary small steps must be taken in this area.

11.4.3 Reconsider how far bodily integrity can be respected where abortion is no longer an option and treatment is only available within pregnancy

Before proceeding with this recommendation it is important to draw attention to three important assumptions. It would appear valid to assume that the population involved in such a decision would be minimal, because in the majority of cases patients would do what is 'best' for their fetus. Secondly, such recommendation is condition dependent. Therefore, it would be relevant to consider severe genetic or congenital defects (which are the criteria for FGT research). Finally, this recommendation is contingent upon FGT becoming a working viable treatment and

the level of intervention needed. For example, open utero surgery compared to transplacental injection. Therefore, this recommendation is not applicable while FGT is at the stage of clinical trials or before the treatment is perfected.

Nonetheless, it is clear from the data that the rules currently governing autonomy, abortion and the point of intervention collide. The answer to such a collision includes cost benefit analysis, but also how society views someone who actively refuses to provide their genetic offspring with treatment. Postnatally the question of best interest arises,[305] which must be considered when interpreting that data with the PGC if the point of intervention is post 12 weeks of gestation. This consideration will have more weight the longer gestation occurs. Yet, post 20 weeks of gestation, it is clear abortion is problematic under the PGC unless the fetus fulfils the criteria of exceptions under the Abortion Act 1967.[306] It is here that best interest considerations, such as the fetus as a patient, should occur.

If one considers that the children can survive premature birth of at least 22 weeks of gestation (See New Scientist and Reuters 2007) where best interests of that child can occur, then the issue of bodily integrity must be questioned under the PGC for interventions at this point. However, scientifically intervention would need to occur at least post seven weeks when the gonads have been separated, but also when the organ that would need intervention has differentiated itself. The point of intervention is therefore more than likely to occur post 12 weeks. It would be here that the fetus as a patient concept proposed by Chervenak and McCullough would be applicable to assess the best course of action. It would fulfil the PGC requirement to take into account those agents as if they were in existence, due to the nature of the treatment proposed.

Couples are not allowed to actively implant embryos with known genetic defects,[307] then why allow a pregnancy to continue without treatment where abortion is not an

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[305] Mental Capacity Act 2005 s.4.
[306] As argued previously by the author in (Childs 2007).
[307] Human Fertilisation and Embryology Act 1990 Sch 3, s.13(9) as amended by the Human Fertilisation and Embryology Act 2008.

option? Albeit the debate concerns in utero considerations not ex utero, which are the realm of the mother.[308] Yet, under the PGC such a decision is not ethically valid. It could be contended that such a decision is qualitatively different where the question to be considered is not about life itself, but the future quality of life. In other words, such a situation gives rise to a violation of bodily integrity for the best interest of the future child akin to if that child was already born. The question of abortion would not be removed as given the criteria for FGT; the option of abortion would always be applicable. Nevertheless, it is clear that the decision to do nothing or abort is significantly changed by the introduction of a treatment option, which would help improve the quality of life of the future child.

Although this thesis is concerned with patients who have capacity, one cannot ignore the fact that if the mother was considered to lack capacity, treatment of the fetus would clearly be in the mother's best interests.[309] Best interests include interests beyond medical interests, but are the considered benefit to the person.[310] Clearly having a healthy/less severely handicapped child is more in the parent's interest than having a child that would be born with more severe conditions.

Connected to such a question is how to deal with those who receive FGT and are only partially ameliorated. Clinical judgement will have to be consistent in determining what quality of life that future child would have. However, under the PGC, it would appear valid where that information is not known by the mother to continue to allow the option of abortion in those circumstances. As a result, it would reduce the uncertainty of treatment. Where the treatment is perceived to have worked, abortion would not be an issue since then the abortion rules relevant to 'normal' fetuses apply.

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[308] See 4.4.1.
[309] For best interests see Mental Capacity Act 2005 s.4.
[310] For example, it can be considered in the interest of a person to be a bone marrow donor to an ill sibling, because of the emotional, psychological and social benefit to the mother/sibling (*Re Y* (*Mental Patient: Bone Marrow Donation)* [1996] 2 FLR 787).

11.4.4 Further investigate how abortion, informed consent, long term follow-up and confidentiality can be maintained and regulated ethically.

Although in general the current regulation does a sufficient job in coping with the majority of issues there are some areas which must be addressed. The debate must also be widened to include what a mother can and cannot consent to. The effect of this debate can shape what research can be conducted. The conclusion may be that the current restrictions are valid in order to protect those who are vulnerable. However, that position would have to be contrasted with the position where a mother's decision to refuse treatment is presumed to be valid and voluntary, even in the most extreme of circumstances that could lead to their own death.[311] Therefore, the question has to be: How and why are these circumstances any different for FGT? Clearly, the difference lies between the right to consent and the right to refuse. The law is clear upon consent to treatment being distinguishable from consent to grievously bodily harm (GBH).[312] Yet, given that FGT would be considered treatment regardless of who the patient is, it is the distinction of treatment from GBH, which indicates that line of reasoning, is invalid.[313] These distinctions are irrelevant for those agents with capacity, because the issue is about the prevention of harm to another being. It would also be irrelevant, because one can consent to activities which merely carry the risk of injury or harm, never mind omitting to prevent harm.[314] Therefore, given the conditions present for FGT the interplay between abortion and FGT must be investigated further, as well as the ethical consequences that may have an impact on the perception of FGT as a practice.[315]

Contractually, long term follow-up is problematic in several ways, including making an unborn child party to a contract to merely maintain adequate contact with patients after treatment. However, it would be appropriate to include an amendment to the Coroners and Justice Act 2009, as well as to the Human Tissue Act 2004 in order to

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[311] *Re C (Adult: Refusal of Medical Treatment)* [1994] 1 WLR 290; *Re MB (Caesarean Section)* [1997] 2 FLR 426.
[312] *R v Brown* (1993) 2 WLR 556; *Boyea* [1992] Crim LR 380.
[313] *R v Brown* (1993) 2 WLR 556.
[314] *Dica* [2004] EWCA Crim 1103.
[315] See 9.3.4.

facilitate post mortems upon those who have undergone FGT.[316] Nonetheless, identifying who such patients are raises questions about centralised medical records. There are numerous options that could be investigated to resolve this issue. One such way could be through a central database that could be accessed (akin to a Google search) by the medical practitioner who pronounced the death if the family is unaware of the death. Another method may include giving these patients a different medical record to standard patients, one which flags up an issue regarding their medical status. Connected to this are confidentiality and the right not to know issues. Therefore, confidentiality issues must also be investigated, due to the complexity of the issues initially raised and identified in relation to gene therapy by the Polkinghorne committee (1989).

11.4.5 Review of research funding in relation to long term studies of fetal gene therapy

From a practical stance, it is clear that the work being conducted by FGT practitioners is subject to funding. However, given the unique safety concerns and the recommendations made above, funding is difficult to obtain. As IE4 poignantly expressed:

> Capitalism does not like taking risks. And that will be very difficult. The psychological barrier of saying a treatment for pregnancy - wow! Treatment for small children – wow! Let's invest in Brill cream or invest in bananas!

In order to resolve issues surrounding long term follow-up outside of animal studies, funding must have a contingency for appropriate long term studies to be conducted. Given the impact of technologies such as FGT, government funding should be in place for FGT practitioners in order to cover these long term follow-up studies. Such contingency may include an obligation upon the FGT practitioner or institution to conduct the future research depending on the status of the initial FGT practitioner. In conjunction with a review, practical implications, such as compelling future

[316] For connected issues regarding post mortem examinations with and without express permission of a coroner see Human Tissue Act Code of Practice 3 and the Human Tissue Act 2004 s.11.

generations over the age of majority[317] to be submitted to clinics for testing, would need to be resolved.

11.5 Further Research

From the data it is logical to conclude that not all possible data analyses were conducted. Given the embryonic nature of FGT there will be many avenues to explore for further research. Further interviewing could be conducted to ascertain what future plans regulators such as relevant members of Parliamentary committees, GTAC and EMA have regarding FGT. In addition, patient groups, which would seek to benefit (or be disadvantaged, depending on your stance on the impact of genetic treatments) should be contacted regarding the progress of FGT. Further research into the areas indicated within recommendation three is a priority as it is apparent that FGT will be entering the clinic in the very near future.

In conjunction with the further interviewing, as within other areas of biotechnology, a survey of the public's attitude towards some of the dilemmas highlighted within the thesis should occur. However, a note of caution must be given since a public survey should not be taken as the major reason to prohibit a practice, such as social sex selection (Harris 2005a, 2005b). To avoid any such allegations the survey should form part of a comprehensive investigation.

As mentioned within the thesis, it has been assumed that the mother in question has capacity. The divide is somewhat artificial, because when FGT becomes a publicly accessible procedure, issues regarding incapacitated patients will be just as relevant. The artificial divide can be seen within the thesis where it has indicated that there may be questions regarding the capacity of patients to decide. Therefore, further research should be done to ascertain when it would be in the best interest of those patients who are incapacitated. Furthermore, this would help provide practical guidance to FGT practitioners. It would also serve as an area in which research could investigate how to improve FGT to all those involved.

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[317] Currently 18 years old under the Family Law Reform Act 1969 s.1.

11.6 Conclusion

FGT is constantly developing as a possible treatment option. However, its development raises questions that this thesis has tried to highlight and provide recommendations to resolve these issues under the guidance of the PGC. Human dignity emerged within the literature as an underlying concept with the current regulation that underpins FGT, together with the maternal fetal divide as identified in chapter 4. By utilising semi structured interviews and documentary analysis the thesis has investigated the emerging technology of FGT. The thesis does not try to provide every answer to every problem indicated within the data, but it has addressed what it considers the most important aspects of FGT. It highlighted the underlying concept of human dignity within regulation and how 'human dignity' is not explicitly used within practice, and it foregrounded the interplay between abortion and FGT. Utilising the PGC it has helped resolve some of the substantive issues within the thesis. However, given that the areas for recommendation range from the removal of human dignity from regulation to a review of funding for FGT practitioners, it is clear that the thesis has only touched the tip of the iceberg. However, with a number of areas to investigate further, work by those other than FGT practitioners is also not over. As the number of professionals, treatable conditions and availability of treatment increases FGT should, in the words of Dr Harrison a pioneer of fetal surgery:

> Proceed with Caution....and Enthusiasm (Jancelewicz and Harrison 2009: 235).

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Appendix A – Participant Information and Consent Form

Fetal Surgery: Engaging the debate between the balancing of ethical theory, scientific progress and the rights of others
Participant Information and Consent Sheet (Interviews):

I would like to invite you to participate in my PhD project on engaging the debate between the balancing of ethical theory, scientific progress and the rights of others in reference to in utero genetic interventions. The following will give you a short overview of what this means for you and the information you decide to give me. Before you decide if you would like to participate in the research, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully. Do not hesitate to talk about the study with other people.

Who am I?
My name is Richardo Childs and I am Economic and Social Research Council funded 1+3 PhD student at Cardiff University, currently doing my PhD. I am supervised by Dr Ian Welsh from the School of Social Sciences; and Prof Ruth Chadwick of Cardiff Law School. If you would be interested in taking part or have any questions concerning the research, feel free to contact me at [redacted] email: childsrs@cardiff.ac.uk. You can also contact my supervisor Dr Ian Welsh at +44 (0)29 208 75403 ext. 75403 or email welshi@cf.ac.uk. I would be happy to answer any questions and look forward to meeting you.

Why am I doing this research?
Fetal surgery may have started purely as a form of surgical intervention to correct birth defects, but the advent of the genomic revolution has created a situation, where by genetics is now a relevant part of fetal surgery through genetic testing and possible in utero applications. The fetus has been viewed as a site where gene therapy and stem cell transplantation can overcome current obstacles within research. However, in using the fetus as a possible site for intervention, ethical issues are raised, such as the intergenerational aspect of genetic interventions, but are intergenerational issues are evident within the research of those who are pushing the practice of fetal surgery forward?

Who can take part?
I am approaching people who have expertise with *in utero* gene therapy, either as current researchers within laboratories or not, plus those who have previously research within the field of in utero gene surgery.

What would be involved?
If you choose to participate, I would like to discuss your views on the role of public confidence within your own research. The interview would last up to 1 hour. I would like to cover the following topics:

1. The nature of the research that you are involved in and your role within that research.
2. How decisions are prioritised within your research. For example, balancing personal and professional decision to those of funders.
3. The approach taken within your present and/or future practice of in utero gene therapy.
4. The place of human dignity in research decision making in your field/work

5. Whether intergenerational aspects are important within your work
6. When explaining issues such as consent to patients what factors are and will be important? Will the impact of potential intergenerational issues be explained to patients?

For those whom are currently MSc students the above questions will be made in reference to not just their personnel view but how and whether issues of inter-generational equity are addressed by their 'seniors'. An mp3 record of the interview will be taken, so that I have a record of what was said.

What will I do with the information?

I will transcribe the interview data so that I have a written record to analyse. If you are interested, I will provide you with either an audio or written copy of the interview. The transcript will not be used for any other purpose other than being be read and used by me and my supervisors for the purpose of the research. The information from these discussions will be the basis of my thesis, which will be assessed in order for me to gain my PhD. The transcripts might also be used to write and publish articles in academic journals. You are welcome to see the final thesis and/ or a copy of the articles before they are published.

Will everything you say to me be kept private?

You can say as little or as much as you wish. The audio recording of the interview and subsequent transcript will be kept on a data encrypted hard drive for 5 years, due to Data Protection law. Both sets of data can be requested by you within that period. Within the transcript the names of yourself as well as those people who you mention will be anonymised so you will not be identifiable.

In addition at the end of the thesis, the anonymised transcripts of the interviews may be submitted to the 'Qualidata' archive, at the University of Essex, which will store them and make them available to future researchers as part of my PhD funding. There is a separate declaration of consent for the uploading, storage and future use of your information process; and you are free to opt in or opt out of this data usage but still be able to participate in the study.

What if you change your mind about taking part?

Participation is voluntary and you are free to withdraw from the study at any point you wish, without giving a reason.

Consent Form: Fetal Surgery: Engaging the debate between the balancing of ethical theory, scientific progress and the rights of others

Name of Researcher: Richardo Childs

Please initial

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason.
3. I consent to have the interview recorded and the use of anonymous quotations in the final thesis.
4. I agree to take part in the study.

_____	_____	_____
Name of participant	Date	Signature

I confirm that I DO/ DO NOT (please delete as appropriate) give consent for the anonymised transcripts of the interviews to be submitted to the 'Qualidata' archive, at the University of Essex, where the data will be stored and made available to future researchers.

_____	_____	_____
Name of participant	Date	Signature

_____	_____	_____
Name of person taking consent	Date	Signature

2 copies : 1 for participant (original will be scanned and emailed to you) and 1 for research file.

Appendix B - Interview Question Schedule

Introduction

1. To start the interviews it would be good if you could give a quick biography about yourself and how you become involved/interested in this in utero gene therapy?

2. Could you outline the area of your clinical expertise, the nature of the research that you are involved in and your role within that research?

3. What do you see as the main factors impacting upon the prioritisation and progress of the in utero gene therapy agenda currently? Are there tensions between any of these factors?

4. In identifying the factors relevant to the research process, what issues are most important when working on an in utero gene project? Are the results the most important thing? Whose interests are paramount?

5. What will be the biggest hurdles for the progress of in utero gene therapy to clinical application? Will in utero gene therapy ever move from somatic to germ line alterations? If not, why?

6. I am now going to ask about hypothetical issues that if the work that you current in utero translate into clinical practice, beyond clinical trials, what do you envisage as the factors that would operate within the clinic? Whose interests need to be taken into account?

7. Continuing the prospective theme, what is relevant in the literature of genetic interventions are the intergenerational issues that are raised by in utero gene therapy; therefore, when explaining research issues such as consent to patients what factors will be important? What information is paramount? Will the impact of potential intergenerational issues be explained to patients?

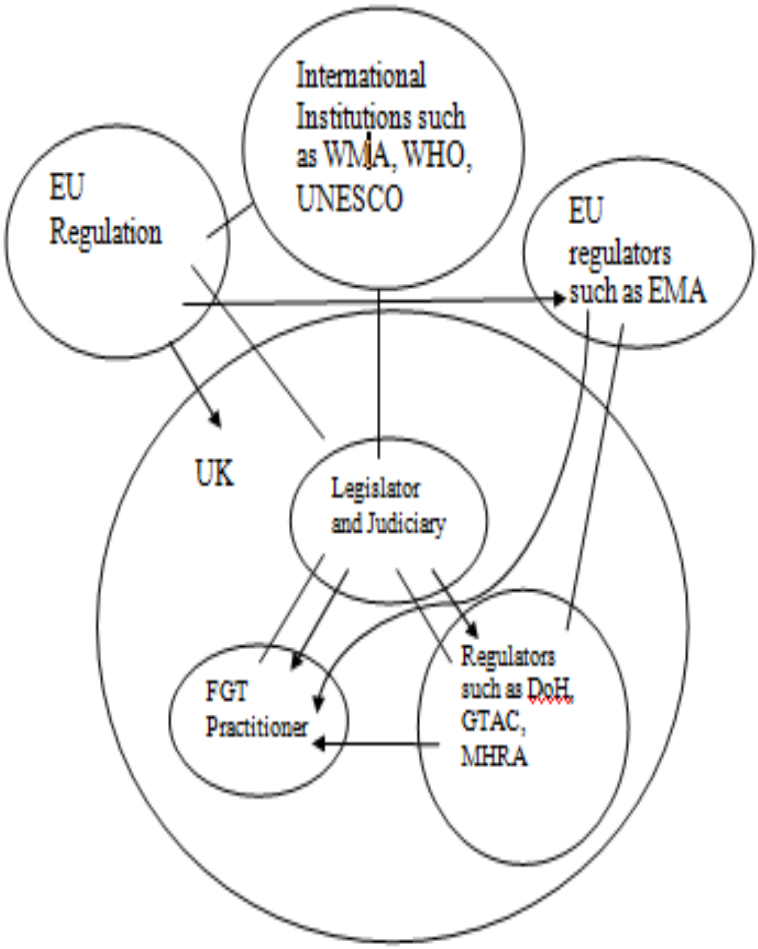
8. What is also raised from the literature is the concept of human dignity. Although, it ahs bee argued it is vague what the role, if any, are played by guiding principles such as the place of human dignity in shaping the research process. Are you aware of these sorts of factors operating in your field of work?

   If these factors are not present what principles guide your work?

9. And finally is there anything we have not covered that you think is important to the areas we have discussed

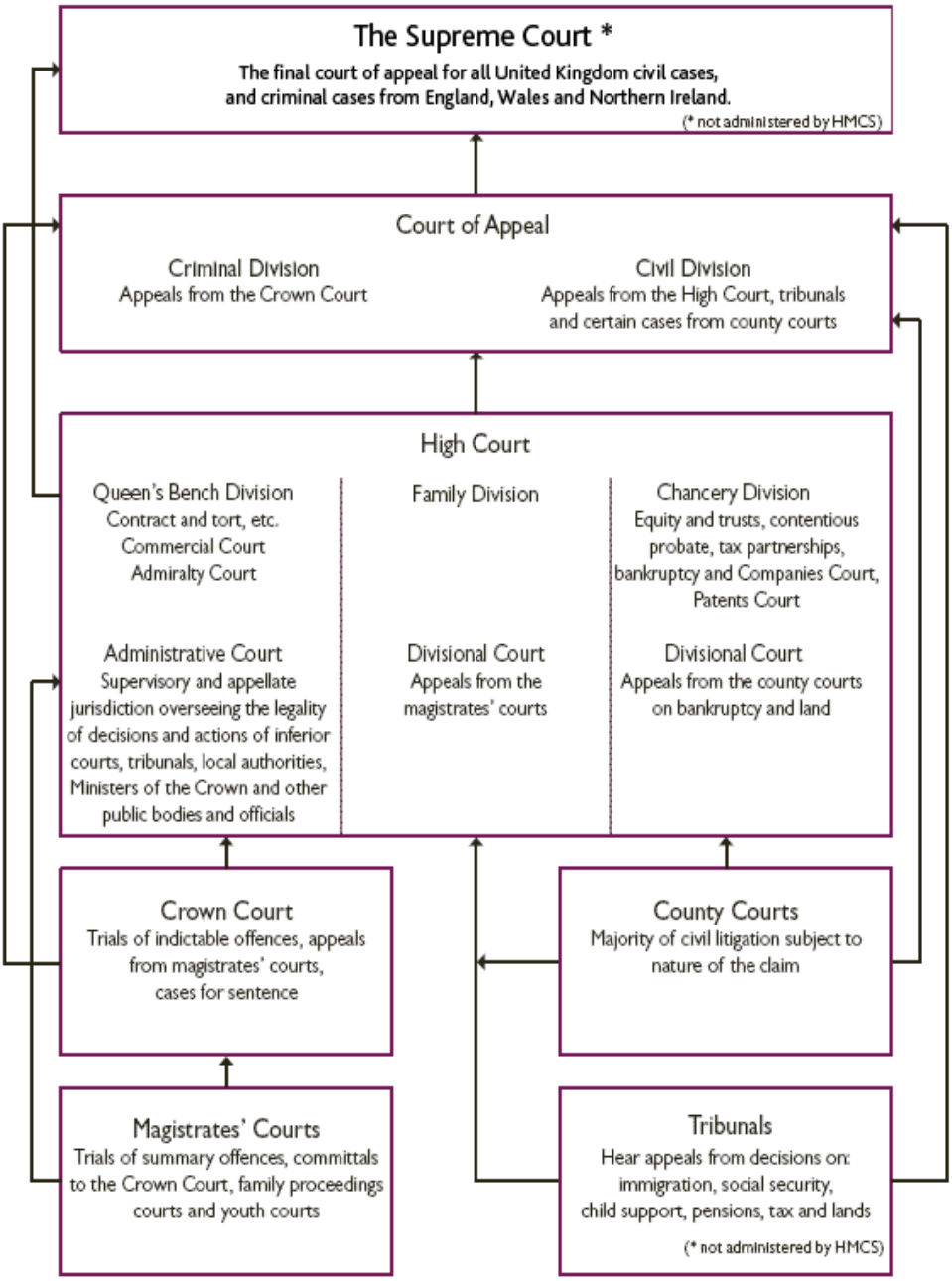
So to wrap up I would like to thank you for your time and your contribution to the thesis. I gratefully appreciate the time and effort that you have given and I hope to do your data justice.

Appendix C – Institutional Structure



Persuasive relationship ———
Direct relationship (indicative of relationship direction) ⟶

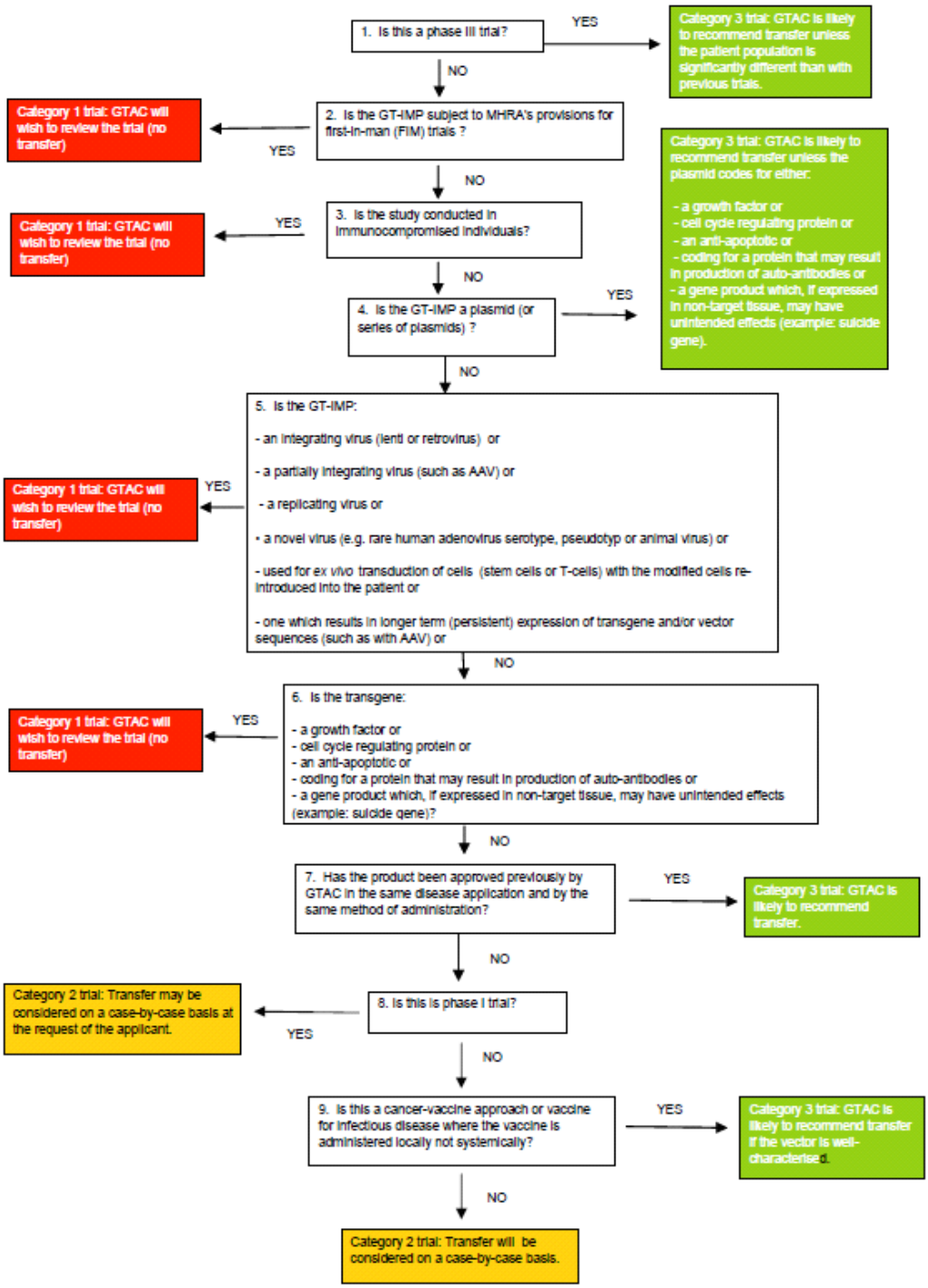
Appendix D – UK Court Structure



Her Majesty's Court Services, 2007. The Court Structure of Her Majesty's Court Services. Available at: http://webarchive.nationalarchives.gov.uk/20110218200720/http://www.hmcourts- service.gov.uk/aboutus/structure/index.htm [Accessed: 1st June 2010].

European Court of Justice and European Court of First Instance make rulings upon issues regarding interpretation of EU law. A reference can be made from any court as governed by the Treaty on the Function of the European Union 2008, Article 267. A reference can only be made to the European Court of Human Rights once all domestic remedies have been exhausted under the ECHR Article 35.

Appendix E - Decision Tree for GTAC Approval



From Gene Therapy Advisory Committee. 2009. GTAC Decision Tree. Available at http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_087984.pdf [Accessed on: 3rd July 2010]

Appendix F - List of Analysed Documents

International institutions

Council for International Organizations of Medical Sciences. 2002. *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Geneva: WHO.

Council of Europe, 2005. *Additional protocol to the convention on human rights and biomedicine concerning biomedical research*. Strasbourg: CoE.

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European Union

Council Directive 98/81/EC of 26 October 1998 amending Directive 90/219/EEC on the contained use of genetically modified micro-organisms [1998] OJ L330/0013.

Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC [2001] OJ L106/72.

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Appendix G – Glossary of Terms

Term	Meaning
Agency	The capacity to act within the world.
Agent	A being with agency.
Competing rights	Where by two or more agents are making claiming the same right but against each other.
Conflicting rights	Where two or more agents asserting different rights to the same issue.
Correlating duty	A duty arising from a positive or negative right.
Fetus	A human between the 56th day of development and birth.
FGT practitioner	Someone who works at any stage of the development of FGT.
Future generation	Any generation of genetic offspring
Germ line cell	Cells involved in reproduction such as an oocyte, sperm cell or one of their antecedent cells.
Individual	Any agent, possible or not, within a clinical setting.
Interest	Where a being has a duty or right to be considered.
Intergenerational issue	An issues has a possible or proven implication between two or more generation
Mother	A person who is currently pregnant or has given birth to a child.
Negative duty	The duty to refrain from interfering with another's right.
Negative right	The right not to be interfered with, or the right to omit doing something.
Next generation	The immediate genetic offspring of an individual including those in gestation
Patient	A agent receiving a doctors service.
Positive duty	The duty to provide assistance to another in order to facilitate their right.
Positive right	The right to do something or have an action facilitated by someone.
Somatic cell	Any of the cells of the body that compose the tissues, organs, and parts of that individual other than the germ cells.
Therapy	A therapeutically aimed intervention.

Appendix H – Sampled Matrix Query

	A : article	B : book/academic input	C : case law	D : cases from other jurisdictions	E : ECHR	F : European directive	G : european regulation	H : foriegn legislation	I : International declaration or charter	J : legislative	K : Policy documents	L : statutory instrument
1 : Directive 1998-81-ec	0	0	0	0	0	1	0	0	0	0	0	0
2 : Directive 2001-18-ec	0	0	0	0	0	1	1	0	0	0	0	0
3 : Directive 2001-20-ec	0	0	0	0	0	1	1	0	1	0	0	0
4 : Directive 2001-83-ec	0	0	0	0	0	1	1	0	1	0	0	0
6 : Directive 2004-27-ec	0	0	0	0	0	1	1	0	0	0	0	0
7 : Directive 2005-28-ec	0	0	0	0	0	1	1	0	1	0	1	0
9 : Directive 2006-86-ec	0	0	0	0	0	1	0	0	0	0	0	0
30 : European Medicines Agency guidance on quality, non clinical and clinical apsects of medicial products containing modified cells	0	0	0	0	0	1	0	0	0	0	1	0
31 : European Medicines Agency Guideline onFollo-up of Patients Administered with Gene Therapy Medicinal Products	0	0	0	0	0	1	1	0	0	0	1	0
32 : European Medicines Agency Guidelines on Non-clinical Testing for Inadvertant Germline Transmission	0	0	0	0	0	1	0	0	0	0	1	0
on Gene Therapy	0	0	0	0	0	1	0	0	0	0	1	0
50 : Boso v Italy app no 50490-99	0	0	1	1	1	0	0	1	0	0	0	0
51 : Brüggemann and Scheuten v Federal Republic of Germany (Application No 6959-75)	0	0	1	0	1	0	1	1	1	0	0	0
52 : CASE OF VO v. FRANCE[1] full	0	0	1	1	1	0	1	1	1	1	1	0
53 : H. v. Norway no. 17004-90	0	0	1	1	1	0	0	1	0	0	1	0
54 : Paton v United Kingdom no 8416-78	0	0	1	1	1	0	0	1	0	1	0	0
55 : X v. the United Kingdom no. 8416-79	0	0	1	1	1	0	0	1	0	1	1	0
56 : AG ref (no3) 1994, [1997] 3 WLR 421l	1	1	1	0	0	0	0	0	0	1	1	0
57 : AG ref no 3 1994 [1996] 2 WLR 412	0	1	1	1	0	0	0	0	0	1	0	0
58 : Burton v Islington Health Authority [1991] Q.B 638	0	0	1	1	0	0	0	1	0	1	1	0
59 : Burton v Islington Health Authority [1993] Q.B 204	0	0	1	1	0	0	0	1	0	1	1	0
Authority (2007) EWHC 48	0	1	1	0	0	0	0	0	0	0	1	0
61 : CvS [1988] Q.B. 135[1]	0	0	1	1	0	0	1	0	1	1	1	0
[2010] EWHC 178	1	0	1	0	0	1	0	0	0	0	1	0
63 : McKay and Another v Essex Area Health Authority and Another [1982] QB 1166	0	0	1	1	0	0	0	0	0	1	1	0
64 : Paton v British Pregnancy Advisory Service Trustees [1979] QB 276	0	0	1	1	0	0	1	0	0	1	1	0
66 : Peters v University Hospital of Wales NHS Trust [2002] WL 31257309	1	1	1	0	0	0	0	0	0	1	0	0
67 : Re f (In Utero) [1988] 2 W.L.R	1	1	1	1	1	0	0	0	0	1	1	0
68 : Re MB [1997] 2 FLR 426	0	1	1	1	1	0	0	0	0	1	1	0
84 : Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine	0	0	0	0	0	0	0	0	1	1	0	0
85 : Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine explantory report	0	0	0	0	1	1	1	0	1	0	1	0
86 : European convention on human rights 1952	0	0	0	0	0	0	0	0	1	0	0	0
87 : protection of the human embryo and fetus 2003	0	0	0	0	0	1	1	0	1	0	1	0
88 : Council for International Organizations of Medical Sciences international ethical guidelines for biomedical research involving human subjects 2002	0	0	0	0	0	0	0	0	0	0	0	0
89 : declaration towards future generations 1997	0	0	0	0	0	0	0	0	1	0	0	0
90 : human genome and human rights 1997	0	0	0	0	0	0	0	0	1	0	0	0
91 : UNESCO 2005	0	0	0	0	0	0	0	0	1	0	0	0
101 : Human Rights Act 1998	0	0	0	0	1	0	0	0	1	0	0	1
102 : Human Tissue Act 2004	0	0	0	0	0	1	1	0	0	1	0	1
103 : Infant Preservation Act 1929	0	0	0	0	0	0	0	0	0	1	0	0
104 : Mental Capacity Act 2005	0	0	0	0	0	0	0	0	0	1	0	0
105 : Genetically Modified Organisms (Contained Use) (Amendment) Regulations 2002	0	0	0	0	0	1	1	0	0	1	0	1
106 : Genetically Modified Organisms (Contained Use) (Amendment) Regulations 2005	0	0	0	0	0	1	1	0	0	1	0	1
107 : Genetically Modified Organisms (Contained Use) Regulations 2000	0	0	0	0	0	1	1	0	0	1	0	1