

THE BIOMEDICAL ETHICS OF DONATING BLOOD FOR  
MOLECULAR AND GENETICS RESEARCH IN SAUDI ARABIA

By

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## **Abstract**

My main thesis is that Saudi culture, in the context of the field of Molecular Genetics Epidemiology (MGE) research, poses many challenges to the currently used biomedical research regulations developed by the Saudi National Committee of Bioethics (NCBE). The NCBE regulations are informed by selected international research ethics guidelines, and they are influenced by a set of assumptions about how we ought to think about ethics. The overall focus is on a version of liberalism, where there is a strong commitment to autonomy, there is a significant focus on informed consent, the harm principle guides the justification of action, and paternalism is seen as something that is to be avoided. There are no specific guidelines that regulate MGE research in Saudi Arabia. Therefore, it was important as a first step in the thesis to analyse the relevant regulations (both the Saudi and the selected international ones) and explore the related normative issues. One of the main empirical findings of this project was an observed and reported lack of adherence to the requirements of the NCBE regulations. There are a number of different ways to interpret this finding. One way, and this was suggested by some members of the focus groups, is that this research demonstrates a clear failure of researchers to abide by the appropriate guidance, and that the relevant response is to act aggressively to correct such research practice in the hospitals where the data was collected. This would ensure compliance with the guidelines. An alternative view is that the problem emerges from a mismatch between the liberal international guidelines and the nature of the Saudi context. One possible way to address this tension is to formulate a set of guidelines and research practices that build upon the nature of Saudi social relations and norms. This may result in a focus on what we can call trust-based, rather than the currently promoted autonomy-based, bioethics.

To those who loved me unconditionally,  
who accepted me as I am,  
who felt my pain and suffered it with me,  
who believed in me even when I doubted myself  
  
to my family.

“Here's to the crazy ones. The misfits. The rebels. The troublemakers. The round pegs in the square holes. The ones who see things differently. They're not fond of rules. And they have no respect for the status quo. You can quote them, disagree with them, glorify or vilify them. About the only thing you can't do is ‘ignore’ them. Because they change things. They push the human race forward. And while some may see them as the crazy ones, we see genius. Because the people who are crazy enough to think they can change the world, are the ones who do.”

**Apple Inc.**

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## Table of Contents

ABSTRACT.....	II
TABLE OF CONTENTS.....	VI
TABLE OF TABLES .....	XV
TABLE OF FIGURES.....	XVI
1 CHAPTER ONE: GENERAL INTRODUCTION .....	1
1.1 SETTING THE SCENE .....	2
1.1.1 Informed consent .....	3
1.1.2 General introduction to DNA (the genetics material) .....	4
1.1.2.1 Genetic Epidemiology .....	5
1.1.2.2 Genetic Exceptionalism.....	8
1.1.2.3 Molecular and Genetic Epidemiology (MGE) .....	9
1.2 THE SAUDI ARABIAN CONTEXT.....	9
1.2.1 The social context in Saudi Arabia.....	11
1.2.2 The Saudi cultural and political climate.....	11
1.2.3 Health-related research in Saudi Arabia.....	12
1.2.4 The emergence of bioethical debate in Saudi Arabia.....	13
1.3 CHALLENGES OF MGE IN SAUDI ARABIA .....	16
1.3.1 Consanguinity.....	16
1.3.2 Premarital genetic testing in Saudi Arabia .....	19
1.3.3 Stigmatisation .....	22
1.3.4 Blood purity.....	24
1.3.5 Patient vulnerability.....	25

1.3.6	Conclusion of the Saudi Context.....	27
1.4	THE NEED FOR EMPIRICAL DATA .....	27
1.4.1	Normative policy- or practice-oriented bioethics.....	32
1.4.2	The is/ought fallacy .....	33
1.5	THESIS AIMS AND OBJECTIVES .....	35
1.6	RESEARCH QUESTIONS .....	36
1.7	SUMMARY.....	37
SECTION ONE: THE NORMATIVE ANALYSIS OF THE SELECTED GUIDELINES		
	.....	38
2	CHAPTER TWO: THE INTERNATIONAL GUIDELINES .....	39
2.1	INTERNATIONAL GUIDELINES ON BIOETHICS: INCLUSION AND EXCLUSION CRITERIA	39
2.2	THE CONTEXT OF THE SELECTED INTERNATIONAL GUIDELINES.....	40
2.2.1	Nuremberg Code .....	40
2.2.2	Declaration of Helsinki.....	41
2.2.3	International Conference of Harmonisation – Good Clinical Practice (ICH- GCP) .....	43
2.2.4	Council for International Organizations of Medical Sciences (CIOMS) .....	45
2.2.5	Universal Declaration of Bioethics and Human Rights of UNESCO .....	46
2.3	HOW MOLECULAR & GENETICS EPIDEMIOLOGY COULD BE REGULATED:.....	47
2.3.1	Review by local ethics committees .....	47
2.3.1.1	Accepting only properly constituted and justified research .....	48
2.3.1.2	Respecting other cultural norms .....	49
2.3.1.3	Avoid exploitation of the local research subject .....	50
2.3.2	Consent.....	55



2.3.3	Risk.....	60
2.3.4	Identifiable material.....	63
2.4	SUMMARY.....	64
3	CHAPTER THREE: THE SAUDI RESEARCH GUIDELINES.....	74
3.1	THE NATIONAL COMMITTEE OF BIOETHICS (NCBE):.....	74
3.2	THE SAUDI NCBE GUIDELINES:.....	77
3.2.1	Terminology defined by the NCBME .....	77
3.2.2	Sending Biological specimens out of the country: .....	79
3.2.3	Accepting only properly constituted and justified research .....	84
3.2.4	Informed Consent: .....	89
3.2.5	Biobanking in Saudi Arabia .....	94
3.3	SUMMARY.....	97
4	CHAPTER FOUR: THE SAUDI AND INTERNATIONAL GUIDELINES VERSUS THE SAUDI CULTURAL CHALLENGE .....	98
4.1	INTRODUCTION .....	98
4.2	AUTONOMY-BASED BIOETHICS .....	98
4.3	INFORMED CONSENT IN SAUDI ARABIA.....	105
4.3.1	Informed consent and the assumption of vulnerability .....	106
4.3.2	Informed consent and the value of trust .....	107
4.3.3	Informed consent in Saudi hospitals.....	108
4.4	STIGMA IN THE TRIBAL CONTEXT .....	110
4.5	OWNERSHIP OF GENETIC MATERIAL.....	115
4.6	SENDING SAUDI GENETIC MATERIALS OUTSIDE SAUDI ARABIA .....	117
4.7	SUMMARY.....	120

SECTION ONE: SUMMARY.....	121
SECTION TWO: THE EMPIRICAL PROJECT .....	122
5 CHAPTER FIVE: METHOD .....	122
5.1 BACKGROUND.....	122
5.2 DESIGN .....	122
5.2.1 Data Collection.....	123
5.2.1.1 Overview .....	123
5.2.2 Phase One – Observations .....	124
5.2.2.1 Recruitment and ethical considerations .....	126
5.2.2.2 Inclusion and Exclusion criteria .....	128
5.2.2.3 Sampling.....	128
5.2.3 Phase Two – Interviews with patients who had been invited to donate blood for MGE research .....	129
5.2.3.1 Sampling.....	131
5.2.3.2 Recruitment and consent process .....	132
5.2.3.3 Inclusion and Exclusion criteria .....	133
5.2.3.4 Interviews, language and translations.....	133
5.2.4 Phase Three – Focus Groups .....	135
5.2.5 Analysis .....	138
5.2.5.1 Interim analysis: .....	139
5.2.5.2 Observation Data Analysis: .....	140
5.2.5.3 Phase Two analysis:.....	142
5.2.5.4 Phase Three Analysis.....	144
5.2.6 Validation and trustworthiness .....	145

5.2.7	Ethical approvals and permissions .....	146
6	CHAPTER SIX: RESULTS .....	147
6.1	INTRODUCTION .....	147
6.2	PHASE ONE: PASSIVE OBSERVATION OF INFORMED CONSENT PROCESSES .....	147
6.2.1	Demography .....	147
6.2.2	Observations .....	148
6.2.3	Phase One findings .....	150
6.2.3.1	Describing the recruiting procedure .....	150
6.2.3.2	Coercive practices.....	154
(a)	Deception.....	156
1)	Misinformation.....	159
2)	Not informed .....	161
(b)	Who asked .....	164
(c)	Rushing.....	164
6.2.3.3	Obstacles, challenges.....	165
6.2.3.4	Patient vulnerability.....	167
(a)	Vulnerability .....	167
(b)	Sense of power .....	168
6.3	PHASE TWO: IN-DEPTH INTERVIEWS WITH MGE RESEARCH PARTICIPANTS .....	169
6.3.1	Interviewee characteristics .....	170
6.3.2	Interview lengths .....	171
6.3.3	Phase Two findings .....	172
6.3.3.1	Coercive practices.....	173
(a)	Deception.....	175

1) Misinformed .....	175
1) Not informed .....	178
(b) Who asked .....	183
(a) Rushing.....	184
6.3.3.2 Patient vulnerability.....	185
a. Vulnerability of patients recruited by their treating physicians.....	185
b. Vulnerability of patients asking if they would lose treatment privileges ....	186
c. Vulnerability of Saudis wishing to appear to be devoted Muslims .....	187
d. Vulnerability counterargument.....	189
6.3.4 Summary.....	190
6.4 PHASE THREE: FOCUS GROUPS.....	192
6.4.1 Participant Characteristics .....	192
6.4.2 Results of the first focus group.....	193
6.4.2.1 Coercive practices.....	194
(c) Deception.....	194
1) Misinformed .....	195
2) Not informed .....	196
(d) Who asked .....	199
(e) Rushing.....	202
6.4.2.2 Obstacles, challenges and responses .....	203
(a) Lack of support.....	203
(b) Distance, return trips and funding .....	205
6.4.2.3 Patient vulnerability.....	207
(a) Patient vulnerability counterargument .....	208

6.4.2.4 Responses to the presented data .....	209
(a) Oversight regarding policies.....	209
(b) The need to educate donors .....	210
(c) The need to educate the doctors .....	211
6.4.2.5 Genetic material: Its importance in Saudi Arabia .....	211
6.4.2.6 Summary.....	212
6.4.3 Results of the second focus group .....	214
6.4.3.1 Coercive Practices .....	214
(a) Deception.....	215
(b) Who asked .....	216
(c) Rushing.....	217
6.4.3.2 Obstacles, challenges and responses .....	217
(a) Lack of support.....	217
6.4.3.3 Patient vulnerability.....	218
- Suggestions of vulnerability.....	218
- Patient vulnerability counterargument .....	219
- Suggestion of the presence of some knowledge .....	220
6.4.3.4 Responses to the interim analysis .....	222
- Overview of policies .....	222
- The need for education.....	224
6.4.3.5 The importance of DNA .....	225
6.4.4 Conclusion.....	227
6.4.5 Section Two Summary: .....	227
SECTION THREE: DISCUSSION AND RECOMMENDATION .....	228

7	CHAPTER SEVEN: DISCUSSION.....	228
7.1	OVERVIEW .....	228
7.2	WHAT THE FINDINGS CAN BE TAKEN TO IMPLY .....	229
7.2.1	The discourse of failure .....	230
7.2.2	The discourse of moral relativism .....	233
7.2.3	Embracing the importance of social reality .....	236
7.3	WHAT IS BLOOD IN THE SAUDI CONTEXT?.....	238
7.3.1	Blood in the Islamic literature: .....	238
7.3.2	Blood in the Saudi context: .....	239
7.3.3	Blood as identity tool.....	242
7.3.4	DNA ownership.....	245
7.3.5	The absence of specific regulations for blood donation to MGE research in SA 250	
7.4	CONSENT IN THE SAUDI CONTEXT.....	251
7.4.1	Claim of ‘white coat’ effect.....	254
7.4.2	Trust in the organisation of health provision.....	260
7.5	ETHICS COMMITTEES AND PROTECTING TRIBAL INTERESTS: .....	265
7.5.1	The call for research committee education.....	268
7.6	CONCLUSION .....	270
8	CHAPTER EIGHT: RECOMMENDATIONS.....	272
8.1	INTRODUCTION .....	272
8.2	RESEARCH GAP AND CONTRIBUTION .....	274
8.3	STUDY LIMITATION .....	275
8.4	REFLEXIVITY .....	277

8.5 FUTURE WORK .....	278
APPENDIX 1: PHASE ONE, THE OBSERVATION PHASE, CASE 1 FIELD NOTE .....	280
APPENDIX 2: CLINIC POSTER PHASE ONE, FOR RESEARCHERS .....	281
APPENDIX 3: CLINIC POSTER PHASE ONE, FOR PATIENTS THE ARABIC VERSION .....	282
APPENDIX 4: VERBAL CONSENT CONFIRMATION - PHASE ONE .....	283
APPENDIX 5: CLINIC POSTER PHASE TWO, FOR PATIENTS THE ARABIC VERSION .....	284
APPENDIX 6: INFORMATION SHEET (PHASE TWO) THE ENGLISH VERSION .....	285
APPENDIX 7: INFORMATION SHEET (PHASE TWO) ARABIC TRANSLATION .....	288
APPENDIX 8: ENGLISH INFORMED CONSENT PHASE TWO .....	291
APPENDIX 9: ARABIC INFORMED CONSENT PHASE TWO .....	292
APPENDIX 10: FOCUS GROUPS –PHASE THREE - POWER POINT SLIDES.....	293
APPENDIX 11: FOCUS GROUP – PHASE THREE - TOPIC GUIDE .....	296
APPENDIX 12: INFORMATION SHEET PHASE THREE –THE FIRST GROUP .....	297
APPENDIX 13: INVITATION EMAIL - PHASE THREE - THE SECOND GROUP ...	300
APPENDIX 14: INFORMATION SHEET PHASE THREE –THE SECOND GROUP .....	301
REFERENCES .....	304

## Table of Tables

TABLE 1-1: VARIOUS DEFINITIONS OF MOLECULAR EPIDEMIOLOGY (FOXMAN AND RILEY, 2001) .....	7
TABLE 2-1: HOW EXPLOITATION IS DEFINED IN THE LITRETURE ACCORDING TO WERTHEIMER (2007, P248) .....	54
TABLE 2-2: SUMMARY DISCUSSED CONSENT IN THE ANALYSED REGULATIONS: .....	67
TABLE 2-2: SUMMARY OF THE CONSENT THEMES IN THE ANALYSED REGULATIONS (CONTINUE): .....	68
TABLE 2-2: SUMMARY OF “ACCEPTING ONLY WELL SUPPORTED RESEARCH” IN THE ANALYSED REGULATIONS: .....	69
TABLE 2-3: SUMMARY OF “ACCEPTING ONLY WELL SUPPORTED RESEARCH” IN THE ANALYSED REGULATIONS (CONTINUE): .....	70
TABLE 2-4: SUMMARY OF THE “RISK” THEMES IN THE ANALYSED REGULATIONS: .....	71
TABLE 2-5: SUMMARY OF SOME OTHER ETHICAL THEMES IN THE ANALYSED REGULATIONS: .....	72
TABLE 2-5: SUMMARY OF SOME OTHER ETHICAL THEMES IN THE ANALYSED REGULATIONS (CONTINUE): .....	73
TABLE 5-1: THE THREE RESEARCH SITES .....	129
TABLE 6-1: THE TWO RESEARCH SITES .....	148
TABLE 6-2: CHARACTERISTICS OF THE INTERVIEWEES IN PHASE TWO.....	171
TABLE 6-3: CHARACTERISTICS OF FIRST FOCUS GROUP PARTICIPANTS* .....	192
TABLE 6-4: CHARACTERISTICS OF SECOND FOCUS GROUP PARTICIPANTS* .....	193



## Table of Figures

FIGURE 1-1: GLOBAL DISTRIBUTION OF MARRIAGES BETWEEN 1ST AND 2ND COUSINS (BITTLES AND BLACK, 2010).....	17
FIGURE 3-1: THE INSTITUTIONAL HIERARCHY OF RESPONSIBILITY FOR RESEARCH GOVERNANCE IN SAUDI ARABIA .....	89
FIGURE 6-1: THE PI ROLE IN BOTH TEAMS .....	150
FIGURE 6-2: SUMMARY OF THE RECRUITMENT PROCESS .....	152
FIGURE 6-3: SUMMARY OF THE THEMES ARISING FROM PHASE ONE.....	153
FIGURE 6-4: SUMMARY OF THE THEMES OBSERVED IN PHASE TWO .....	173

## **1 Chapter One: General introduction**

My main thesis is that Saudi culture, in the context of the field of Molecular Genetics Epidemiology (MGE) research, could pose challenges to the currently used biomedical research regulations developed by the Saudi National Committee of Bioethics (NCBE). The NCBE regulations are informed by selected international research ethics guidelines, and they are influenced by a set of assumptions about how we ought to think about ethics. The overall focus is on a version of liberalism, where there is a strong commitment to autonomy, there is a significant focus on informed consent, the harm principle guides the justification of action, and paternalism is seen as something that is to be avoided. There are no specific guidelines that regulate MGE research in Saudi Arabia. Therefore, it was important as a first step in the thesis to analyse the relevant regulations (the Saudi and the selected international ones) and explore the related normative issues. One of the main empirical findings of this project was an observed and reported lack of adherence to the requirements of the NCBE regulations. There are a number of different ways to interpret this finding. One way, and this was suggested by some members of the focus groups, is that this research demonstrates a clear failure of researchers to abide by the appropriate guidance, and that the appropriate response is to act aggressively to correct such research practice in the hospitals where the data was collected. This would ensure compliance with the guidelines. An alternative view could, however, be taken that suggests that the problem emerges from a mismatch between the liberal international guidelines and the nature of the Saudi context. One possible way to address this tension is to formulate a set of guidelines and research practice that builds upon the nature of Saudi social relations and norms. This may result in a focus on what we can call trust-based, rather than prioritising the currently promoted autonomy-based, bioethics.

One of the original contributions to knowledge of this thesis is an empirical study of recruitment practice for MGE research in Saudi Arabia. The method used in the study is outlined and justified in Chapter Five. Data was collected in three phases. Phase One involved observation of the taking of informed consent within the context of recruitment to MGE research. Phase Two involved semi-structured interviews with individuals who had donated blood for MGE research, the aim of which was to obtain an idea about how the interviewees understood and perceived their experience as a donor for MGE research. Phase Three of the data collection included convening two focus groups to discuss the results of phases one and two, and more broadly discuss the norms that do and should govern MGE research in Saudi Arabia. The results are reported in Chapter Six.

The final section of this thesis discusses its philosophical and empirical findings, as reported in its first two sections. It sets them in context, extending and deepening the issues that were raised (Chapter Seven). Based on the tensions and problems that have been observed, reported and discussed, the thesis concludes by recommending that those responsible for Saudi medical research and generating MGE research ethics guidelines need to reflect carefully on the appropriateness of prioritising the autonomy-based model of Western guidelines and the problems that emerge when applied in a Saudi context.

## **1.1 Setting the scene**

In this section, I will set the scene by defining two important concepts used in this thesis (i.e. informed consent, and molecular and genetics research) and how they are to be understood. The thesis's main focus is on molecular and genetic epidemiology (MGE) research, which uses blood samples taken with the patient's consent for this purpose during routine clinical visits to tertiary care centres in Saudi Arabia.

### **1.1.1 Informed consent**

As the focus of this work is on donating blood for research, where research participants have consented to a specific piece of MGE research, it is essential to outline what is meant by informed consent. According to the Saudi guidelines: ‘A person gives his consent with his free will, without exploitation or coercion and upon full understanding of what is required from him and of the research objectives and potential risks as well as of rights and obligations arising out of his participation therein.’ (NCBE, 2010 p3). This understanding, as I will explain in Chapter Three (Section 3.1.1.4 Informed Consent), accords with all the international research ethics guidelines.

In order for an informed consent to withstand legal and ethical scrutiny it must have three major components, starting from the threshold elements which require competence and voluntariness, and then an information element, which includes disclosure, recommendation and an understanding of both and, lastly, the consent element, which consists of decision and authorisation (Meisel and Roth, 1981). Accordingly, threats to the process of attaining an informed consent can come from more than one direction.

The main role of informed consent is to legitimise an action that will impact on the consenting party. According to Manson (2007), consent ‘is a way to waive certain rights, and thus it allows actions to be performed that would otherwise be impermissible’ (Manson, 2007, p299). Manson argues that, in a broad sense, every successful act of consent is in fact an act of informed consent, because a level of communication (i.e. most likely communicating information) is required. However, the term ‘informed consent’ gained its standing in medical and research ethics because it is more specific than the general understanding of consent. It is more specific insofar as it requires explicit disclosure of information about a number of factors (i.e. risks, benefits, obligations, side

effects and alternatives options, if any). This disclosure is required as the basis for obtaining permission for a proposed action or set of actions from a person (O'Neill, 2002; Manson and O'Neill, 2007; Manson, 2007).

### **1.1.2 General introduction to DNA (the genetics material)**

Deoxyribo Nucleic Acid (DNA) is the biological unit that stores the essential information (genes) required for the cell to function properly (GHR, 2015). The main building unit of DNA is the nucleotide, which comprises a deoxyribose sugar, a phosphate and nitrogenous bases (adenine, thiamine, cytosine or guanine) (GHR, 2014). Two strands of the nucleotides are linked by the nitrogenous bases (adenine with guanine and cytosine with thiamine) in the form of a double helix, which is the essential form of DNA (GHR, 2015). Every three nucleotides form a codon, which is a sequence of three nitrogenous bases that code for an amino acid (the protein-building unit), a starting point, and a terminating point. Sequences of codons that generate a specific protein (a sequence of nitrogenous bases) are called a gene (GHR, 2015).

Every gene is responsible for creating a specific protein, which has a specific task, at a specific time, in the life cycle of a cell (GHR, 2015). The cell depends on thousands of proteins (GHR, 2015). However, the sequence of the nitrogenous bases of these genes can be disturbed (mutated) by factors such as exposure to radiation or certain chemicals (GHR, 2015). In view of that possibility, the cell is equipped with another copy of the same gene, called an allele. Of the two alleles that code for the same protein, one comes from each of the parents (GHR, 2015). If only one gene is mutated in a recessive disorder, then the other healthy allele takes over the process of protein synthesis; however, if the disorder is dominant even with the presence of a healthy allele, one defective gene is enough to express the disorder (GHR, 2015).

In some cases, the cell is equipped with mechanisms to correct an incidence of mutation. However, in many cases those mechanisms fail to correct the mutation and the gene is then passed on to the next generation. Based on the role of the coded protein in the cell life cycle, mutations could be life-limiting (e.g. cancer), serious (e.g. sickle cell anaemia), chronic (e.g. glaucoma) or benign (e.g. some forms of myopia) (Al Husain and Al Bunyan, 1997). Any diagnosed disease caused by one or more mutant genes is called a genetic disorder (Al Husain and Al Bunyan, 1997).

As the mutation is passed down to the offspring, siblings share similar DNA characteristics (Tallbear, 2013; Boddington, 2012). Therefore, every DNA molecule can possess a set of mutations, which can identify individuals, and sometimes families, with extremely high precision (Tallbear, 2013; Boddington, 2012). This high level of identifying ability is called the DNA fingerprint (Tallbear, 2013; Boddington, 2012).

### **1.1.2.1 Genetic Epidemiology**

The term epidemiology derives from the Greek ‘Epi’ (meaning upon or over) and ‘Demos’ (meaning population or people). Thus, epidemiology, in general, is concerned with population health. The Oxford Dictionary defines epidemiology as: ‘the branch of medicine which deals with the incidence, distribution, and possible control of diseases and other factors relating to health’ (Oxford, 2014). The Oxford Dictionary definition does not explicitly link epidemiology with public health per se, but it is assumed that the incidence and distribution are statistically calculated values dependent upon a well-defined population. There are also other definitions specific to the kind of epidemiology being defined. For example, molecular epidemiology can be characterised by two main factors:

1. the use of molecular biology techniques in order to determine the characteristics of genes and/or proteins in specific population; and

2. the study of the incidence and distribution of disease among human populations. (Foxman and Riley, 2001). Foxman and Riley (2001) provide a summary of eight different definitions of molecular epidemiology (see Table 1-1).

Among these eight, the most relevant definition is the one by McMichael (1994), because it is sufficiently general to describe the different molecular epidemiology activities currently occurring in Saudi Arabia. The recurring concept in these diverse definitions is that epidemiology is connected with understanding the ‘aetiology’ (the study of causation) of ‘disease’, that is to say, how and why disease is distributed among specific groups. But despite this emphasis on ‘disease’ or ‘aetiology’, epidemiology is not always about the people who are affected by disease. It is also concerned with healthy people, and how to prevent or control disease and its elements (so it could, for example, include studies of healthy people who are carriers of an affected gene, those who have been vaccinated, or those in a high risk group). As the Oxford Dictionary’s definition is comprehensive enough to capture the most important concepts surrounding epidemiology, it will be accepted for the purposes of this work.

TABLE 1-1: VARIOUS DEFINITIONS OF MOLECULAR EPIDEMIOLOGY (FOXMAN AND RILEY, 2001)

AUTHOR	Reference	Definition
Higginson J	Am J Pathol 1977;86:460–84	“the application of sophisticated techniques to the epidemiologic study of biological material” (p. 463)
Schulte PA	In: Schulte PA, Perera FP, eds. San Diego, CA: Academic Press, 1993:3–44	“molecular epidemiology is the use of biologic markers or biologic measurements in epidemiologic research” (p. 13)
Tompkins LS	In: Miller VL, Kaper JB, Portnoy DA, et al, eds. Washington, DC: American Society for Microbiology, 1994:63–73	“the application of molecular biology to the study of infectious disease epidemiology” (p. 65)
McMichael AJ	Am J Epidemiol 1994;140:1–11	“using molecular biomarkers in epidemiology” (p. 5)
Groopman JD, Kensler TW, Links JM	Toxicol Lett 1995;82-83:763–9	“molecular epidemiologic research involves the identification of relations between previous exposure to some putative causative agent and subsequent biological effects in a cluster of individuals in populations” (p. 763)
Hall A	Trop Med Int Health 1996;1:407–8	“the analysis of nucleic acids and proteins in the study of health and disease determinants in human populations” (p. 407)
Shpilberg O, Dorman JS, Ferrell RE, et al	J Clin Epidemiol 1997;50:633–8	“molecular epidemiology uses molecular techniques to define disease and its pre-clinical states, to quantify exposure and its early biological effect, and to identify the presence of susceptibility genes” (p. 633)
Levin BR, Lipsitch M, Bonhoeffer S	Science 1999;283:806–9	“the practical goals of molecular epidemiology are to identify the microparasites responsible for infectious diseases and determine their physical sources, their biological relationships, and their route of transmission and those of the genes responsible for their virulence, vaccine relevant antigens and drug resistance” (p. 806)



### 1.1.2.2 Genetic Exceptionalism

‘Genetic exceptionalism’, according to Murray (1997), means that ‘genetic information is sufficiently different from other kinds of health-related information that it needs special protection’ (Murray, 1997). What supports this claim is that DNA has three major characteristics:

- it can provide information about genetic mutations (i.e. disease vulnerability and mutation carriage rate);
- it can identify individuals; and
- genetic test results are more reliable than most other serology tests.

Advocates of exceptionalism claim that the prominent problem with genetic testing is that in some circumstances genetic testing provides definitive information about future (Spinello, 2004).

The notion of genetic exceptionalism has not gone uncontested. Some commentators suggest that genetic testing does not differ in any relevant way from any other clinical testing. Green and Botkin (2003), for example, argue that the notion of such exceptionalism should be rejected, since, despite the fact that genetic tests can reveal sensitive information like paternity, the same sensitive information can be inferred from the common clinical blood test the ABO<sup>1</sup> typing system, as well as by HLA<sup>2</sup> typing. The same can be said for many other serious medical indicators if not treated as confidential (for example, lack of exercise, hypercholesterolemia, and family history of heart disease are strong indicators of a risk of heart disease, which itself is sensitive information, for

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<sup>1</sup> Blood type testing A, B, AB, and O; if the parents are O blood types, offspring should be O.

<sup>2</sup> Human Leucocyte Antigen, a serology test used to determine organ transplant suitability.

instance if medical insurance is being sought). This position has been strongly embraced by many other researchers (Gostin and Hodge Jr, 1999; Hellman, 2003; Lazzarini, 2001; Suter, 2011).

### **1.1.2.3 Molecular and Genetic Epidemiology (MGE)**

‘Molecular epidemiology’ and ‘genetic epidemiology’ are used interchangeably in the medical and ethical literature (Boddington, 2012). There is no consensus as to what constitutes the difference between them, which makes precise definition difficult (Boddington, 2012). Despite the lack of agreement on their definition, they share some of the same ethical concerns. Therefore, in this work I will refer to them jointly as Molecular and Genetic Epidemiology (MGE). I will also use the definition that is most pertinent to the overall aim of this project, which looks at them as the branch of medicine that is concerned with the distribution, prevention and control of genetic diseases and genetic carriage rates (see section 1.1.2.1 Genetics Epidemiology). MGE aims to characterise the sequences of amino acids in proteins, and nucleic acids in genes. It uses advanced biomedical techniques in genetics to study how these changes affect the distribution and determination of disease occurrence, prevention or control in human populations. There are myriad other definitions (see section 1.1.2.1 Genetics Epidemiology), but, for the purposes of this research, I will only consider the aforementioned definition because it captures the most important points.

## **1.2 The Saudi Arabian Context**

Advances in technology have spurred the evolution of molecular and genetic epidemiology (MGE) research to unprecedented levels. With such advancements come the responsibility of protecting research participants from foreseen, unnecessary risks and

balancing risks in general against benefits. In the history of Western biomedical ethics, several organisations and bodies have assembled ethical guidelines for medical research that involves the use of human participants (e.g., the Nuremberg Code, the Helsinki Declaration, the Council for International Organizations of Medical Sciences (CIOMS), and the International Council for Harmonisation - Good Clinical Practice (ICH-GCP)). In the context of MGE research in Saudi Arabia, there are at least two major challenges to ongoing efforts to achieve comprehensive consensus guidelines: (i) It might be argued that most of these guidelines are written more for clinical trials than for MGE because they use vocabulary specific to clinical research that does not translate in a meaningful way in other types of research (e.g. terminology such as ‘minimum risk’, ‘side effects’, ‘adverse events’ and ‘monitor’ in the ICH-GCP). (ii) It is usually the case that guidelines developed in the West are later adopted by the less-developed world. The main challenge is that the inherited normative assumptions that are built into the guidelines might not be applicable to contexts other than Western ones.

Saudi Arabia is a particularly suitable place to test the Western normative assumptions embedded in Western bioethical guidelines, and their suitability for MGE research in general. This is because Saudi Arabia provides an environment with a different heritage, culture and norms to the West. An initial set of problems that looked potentially challenging to Western norms, such as the nature of the blood purity value among Saudi tribes, what blood means in the Saudi context, how consent is practiced and understood in Saudi hospitals, the nature of the health care system in Saudi Arabia, and the nature of Saudi doctor-patient relationships, were quickly identified during this research for further exploration. Another is stigma in tribal culture. One way of looking at MGE research in the

context of those challenges is that it could be a useful case study for conceptualising research in the Saudi context more generally.

### **1.2.1 The social context in Saudi Arabia**

Saudi Arabia is in the south-Western corner of Asia. It is a geographical link between Asia and Africa. It is the second largest Arabic country, with an area of 2.25 million square kilometres and a population of more than 20 million Saudi (CDSI, 2014). Its capital is Riyadh, and it is a monarchy. The Saudi king, currently King Salman Bin Abdulaziz Al Saud<sup>3</sup>, is the Custodian of the Two Holy Mosques. He is the sixth direct successor of the Al Saud monarch, who founded the Kingdom of Saudi Arabia. He is also the prime minister. Saudi Arabia is a Sunni Muslim country, where the monarchy rules by Sharei' Law.

### **1.2.2 The Saudi cultural and political climate**

Being at the heart of the Islamic world, literally and metaphorically, Saudi Arabia is highly significant in terms of religious leadership for Sunni Muslims internationally. It is home to two highly influential international Islamic jurisprudence councils, whose dicta and injunctions have an impact on Muslims across the Muslim world, as well Muslims in Saudi Arabia. Ethical principles used in the Kingdom are influenced by Islamic principles. Many of Saudi Arabia's Islamic norms have spread to other countries. These Islamic norms are blended with other social norms stemming from the tribal nature of Saudi society, with all the pros and cons that convictions of tribal conformity dictate. In general, these factors help to promote the culture of trust and respect over that of agency (i.e. the

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<sup>3</sup> This was not the case when I handed in the original thesis but a change brought about by the death in January 2015 of the King Abdullah Bin Abdulaziz, the elder brother of our new king.

personal capacity to act intentionally) and liberty (i.e. the ability to take decisions free from other influences).

### **1.2.3 Health-related research in Saudi Arabia**

The Ministry of Health provides free health care in Saudi Arabia to all Saudis. However, there are many health care organisations in Saudi Arabia in addition to the Saudi Ministry of Health and its primary healthcare centres such as university hospitals, tertiary care hospitals, military hospitals, and private centres and hospitals. The primary healthcare centres are fairly distributed, reaching even the small, remote areas. They handle basic healthcare needs, such as treatment for flu, colds and headaches. If a patient needs tertiary care, he/she will be transferred to one of the Ministry of Health central hospitals or university hospitals, where specialist healthcare services are available. The main problem is that there are very long waiting lists for non-emergency care, which forces Saudis to seek and fund alternatives, which will often be provided by specialist hospitals.

These specialist hospitals are usually fee-charging or provide services to a specific group of people. For example, National Guard Health Affairs (NGHA) provides services to the National Guard's soldiers and their families; they also extend their services to very specialised serious cases, such as cancer, liver transplants, and heart transplants.

Although Saudi Arabia is a young country, health-related research is very well established in a few Saudi organisations, in the form of dedicated – and often competing – Saudi research centres, notably the King Faisal Specialist Hospital and Research Centre (KFSH&RC), the King Abdullah International Medical Research Centre (KAIMRC), and the King Khalid Eye Specialist Hospital (KKESH), all located in Riyadh. These are the

three largest Saudi research centres, but they compete for research funds and official recognition.

#### **1.2.4 The emergence of bioethical debate in Saudi Arabia**

In Saudi Arabia, there is a history of putting the latest technologies into practice long before any guidelines are established to govern their use. This was the case for organ transplantation, where the regulations were inaugurated a decade after transplantation was first practised (Adlan, 2013). Similarly, guidelines for in vitro fertilisation (IVF) were announced in Saudi Arabia in 2004, 20 years after the first IVF procedure (Abduljabbar and Amin, 2009). Molecular biology is no exception. MGE research has been flourishing in Saudi Arabia for at least two decades. Indicative here is the growing number of biobanks, prompted by the surge in molecular biology research in recent years, which has been mainly clinical and oriented towards population genetics. However, this increase in biobanking has taken place with an underdeveloped consideration of the associated ethical dilemmas. Thus, paradoxically, there has been very little effort invested in studying the bioethical, legal and social challenges of such practices.

Bioethics debate was introduced into Saudi Arabia as a result of an incident in 2000. A twenty-nine-year-old woman was planning to have another child of her own but she could not. Her gynaecologist consultant suggested a uterus implant, which had never been done before. The patient found a forty-six-year-old non-Saudi donor. Dr Al Fageeh (Fageeh et al., 2002) confirmed that the donor formally consented after a hysterectomy, due to multiloculated ovarian cysts. Major Saudi newspapers, such as Al-Riyadh and Al-Sharq Al-Awsat, argued for months that the donor had 'sufficient' children and that money was most likely involved. After the uterus transplantation, the recipient had two menstrual

cycles, which was a scientific and medical breakthrough. However, due to the significant anti-rejection medications that were required, it transpired that she could not bear children (Fageeh et al., 2002). Following several newspaper articles, there was an unprecedented, cultural and ethical outcry in the Kingdom of Saudi Arabia (Fageeh, 2001). The main concern was that the procedure went against Saudi culture, and was unethical, because some Islamic scholars pronounced it forbidden (Fageeh, 2001). Some concern centred on the assumption that the ovaries had been transferred as well as the uterus. In Islam, having a child is sacred. It is contrary to religion - and therefore in Saudi Arabia also contrary to law – for people to have children unless they are married. Bearing a child out of wedlock is punishable by law and is stigmatized by the culture. The use of donated gametes in fertility research is accordingly forbidden, so only married people are allowed to have children using IVF, and then only using the egg of the wife and the sperm of the husband. In the transplanted uterus case, the assumption that the ovaries were transplanted with the uterus gave rise to the belief that donated gametes had therefore also been involved (Serour, 2008).

There was also another public debate when the donor's relatives filed a lawsuit against the surgeon, claiming that the patient had not been informed about the transplant: they claimed that she had been told that there was a tumour in her uterus requiring a hysterectomy, and only later did she learn that her uterus had been involved in a transplant procedure. In newspaper interviews the surgeon clarified that Saudi officials had investigated the claim and found that the patient had signed the proper informed consent form (Fageeh, 2001) – although, of course, signing a consent form does not necessarily mean that consent had been voluntarily given, nor that the information was understood (AlSharq, 2004).

The fact that the procedure was a medical ‘first’, with no proper training of the surgery team, was at the centre of another heated debate about the lack of regulations concerning what can effectively be considered an impermissible experimental procedure on a human participant (Catsanoz et al., 2011).

The debate between Islamic scholars and researchers became so heated that the then King Fahad Bin Abdul Aziz interjected and stopped it. He deemed that it had become more philosophical than practical (Fageeh, 2001). The king also clearly instructed all health care providers that no more unethical practices or research would be allowed. To this end, he established the National Committee of Bioethics on 7th Aug 2001 to oversee research in the Kingdom and to provide practitioners with the principles of permissible practice. This committee also has to approve any research activity conducted in the Kingdom, but can delegate this responsibility to institutional review boards within hospitals. Research can only commence after such an institutional review board approves it (Fageeh, 2001).

The National Committee of Bioethics issued its national guidelines on bioethics on 19 August 2010. These were intended to guide medical research ethics in the country. The guidelines are adapted from internationally accepted good practice, blended with Islamic Sharei’ jurisprudence. The international guidelines that inspired the new legal document were, prior to this, the only source of guidance at the disposal of policy- and decision-makers in Saudi hospitals and research organisations. The development process took about ten years from the time the committee started until it announced its findings. There is now royal approval of the new law, making the document legally binding for all research undertaken in the Kingdom.



### **1.3 Challenges of MGE in Saudi Arabia**

One of the aims of this study is to answer the question of what is the ethical impact of genetic knowledge on Saudi Arabian culture, and whether the Saudi guidelines that are in force are capable of dealing with this. In order to answer this question, it is necessary to understand the challenges that could impact on practice.

#### **1.3.1 Consanguinity**

In most Saudi tribes, first cousin marriage is not a random practice; it is a matter of honour that is diligently encouraged. The Saudi tribes themselves have different rankings, based on blood purity, history, wealth (in terms of controlling water sources and number of cattle), and stories about their generosity toward strangers, visitors and allies. The social ranking within the tribe is based on blood purity, which means that a person is linked to the tribe by the blood-line of his parents. To start with he is connected to a tribe only by his paternal lineage, while his maternal lineage determines his social class within his tribe. In the event that his mother is not from the same tribe or not from a stronger tribe, the person will be assigned an inferior ranking. Since marriage between strong tribes is very expensive and is usually used as tool for inter-political harmony between tribe leaders, the majority of tribal marriages are usually between first cousins. A person who rejects that unwritten agreement risks the future of his offspring's social position in the tribe.

In Saudi Arabia, consanguinity has been a very frequent phenomenon over past centuries. During the period between 2004 and 2005, El Mouzan (2008) reported a consanguinity rate of 56% (n=11,554) in comparison to Jordan 51.3%, United Arab Emirates 50.5%, Tunisia 49%, Egypt 40%, Yemen 40%, and Kuwait 36% (Bittles, 2001; El-Ashry et al., 2007; Jurdi and Saxena, 2003; Khoury and Massad, 1992). All of these

countries share the same Eastern and/or Arabic tribal values. Global patterns of consanguinity can be seen in Figure 1.

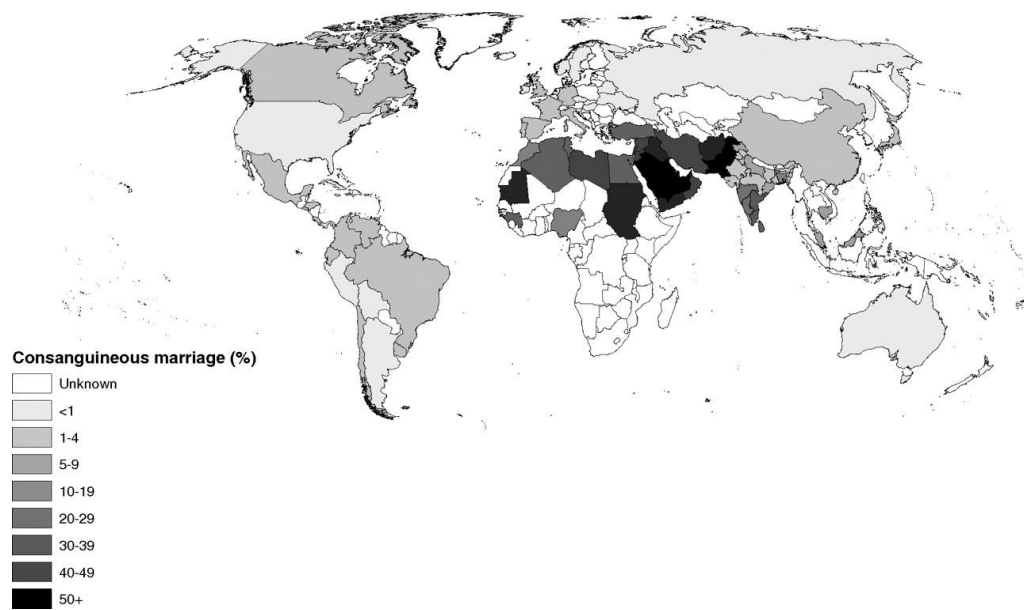


FIGURE 1-1: GLOBAL DISTRIBUTION OF MARRIAGES BETWEEN 1ST AND 2ND COUSINS (BITTLES AND BLACK, 2010).

The high rate of consanguinity in Saudi Arabia was found to be significantly associated with major congenital diseases (El Mouzan et al., 2008), the incidences of which are relatively higher than that reported elsewhere (Al Husain and Al Bunyan, 1997; Elhadd et al., 2007; Panter-Brick, 1991).

Often, MGE research is used in Saudi Arabia to link the detected mutations with demographic and environmental factors in order to control, or even prevent, their outcome. Genome-wide association studies (GWAS) perform a similar task in terms of trying to associate the DNA single-nucleotide polymorphism (SNP) that is usually present in the non-coding area of mutations with diseases. In order to do this, a group of compromised

people with genetic conditions and a group of healthy people (control) are selected, so that the differences might be compared and contrasted, and a better idea developed as to which genetic mutations are responsible. For more accurate results, GWAS usually seeks a control group from the same family as the compromised participants. One of the most challenging results of MGE in Saudi Arabia is the suggestion that a premarital genetic test should – as a matter of law – be conducted to identify carriers of the more common Saudi genetic diseases, including sickle cell anaemia, glucose-6 phosphate deficiency and thalassaemia.

The main ethical challenge in such a context is that consanguinity has been associated with various harmful genetic conditions in the published results of MGE research on blood from Saudi patients and their relatives. It is not the intention of this thesis to discuss whether or not consanguinity is good, nor whether it is accurate to hold it responsible for the relatively higher prevalence of genetic diseases among Saudis. The ethical challenge, however, is using MGE research as an epistemic authority (Al Husain and Al Bunyan, 1997; Elhadd et al., 2007; Panter-Brick, 1991; Hamamy, 2012) to undermine what could be seen as an important cultural value (i.e., consanguinity). Even if the cultural value is to be addressed and reflected upon, MGE research, as pure laboratory-oriented science, should not be used as the only tool to readdress the questioned value as it usually lacks consideration of the necessary social, ethical and cultural dimensions. MGE research should only be used as an indicator to start a serious ethical and social study to address the issue fairly, which does not seem to be the case in Saudi Arabia. Also it is unclear whether or not Saudis would participate in a research study if they were aware that the results would be used to undermine one of their cultural values. Even if an individual consents to participate in MGE research, is it right for him/her to do so given that his/her

participation may provide information about a whole family or even a tribe (if enough individuals chose to participate)? This challenge will be further explored below.

### **1.3.2 Premarital genetic testing in Saudi Arabia**

The Saudi Royal Cabinet issued the Saudi Royal Decree No. 3 dated 11-7-1424H (7 Sept 2003), mandating that all Saudi couples have to undertake a pre-marriage test to be declared genetically suitable for each other, as well as being free from sexually transmitted diseases (El-Hazmi, 2004).

The test itself is a legal requirement for issuing a marriage certificate, but there are no legal restrictions to marriage implied by the results, and the couple can elect to go ahead with the marriage plan without legal sanction, even if either or both of them test positive. However, some Saudi legislators have proposed that marriages should be legally prevented if both persons are carriers of the same recessive gene. Leading Islamic scholars have rejected this suggestion because Sharei' laws does not accept adding conditions to what already exists; but this issue is still the subject of public debate in academic circles and on television, radio, and news print media (Al-Aama, 2010; Al-Mendalawi, 2011; El-Hazmi, 2006; Ibrahim et al., 2011; Memish and Saeedi, 2011).

A similar debate took place in Cyprus during the 1970s when trying to control the high rate (15% of the population) of patients with autosomal recessive  $\beta$  Thalassaemia. Three arguments were used to campaign against marriage between two  $\beta$  Thalassaemia mutated gene carriers:

- the first argument concerned the burden of the disease for society: the aim was mainly to draw attention to the idea that Cyprus's small society could not

bear the financial cost of treating the disease. Even if it could, the relative costs would jeopardise other health services,

- the second argument was the burden of the disease for the family: this argument highlighted the emotional distress that parents, family and friends have to deal with;
- the third argument was the burden of the disease for the patient: in this argument, an appeal was made to the norms of good parenting and parents' electing to have children that would live in pain and die prematurely, when they could take early preventive measures. (Hoedemaekers, 1998)

Hoedemaekers (1998) argues that this programme, and others that followed, were purely motivated by the desire to reduce costs. It was underpinned by the presence of budget stress, which could be seen as a conflict of interests (e.g. health professionals asserted that they were planning to stop receiving new cases in order to reduce health care costs, on the grounds that "it is imperative to be successful [in reducing disease incidences]") (Hadjiminas, 1994 as cited in Hoedemaekers, 1998).

In Saudi Arabia a similar approach was pursued, which opens up the same objection as that considered by Hoedemaekers (1998). It prioritised reducing the number of affected children over giving care and support to compromised families. The public campaign in Saudi Arabia promised to eradicate 'genetic diseases' for the better health of future children, which is misleading on a number of counts: (a) the test being promoted is only for Thalassaemia, Sickle Cell anaemia and G-6-P; and these are not all the 'genetic diseases'; (b) to 'eradicate' genetic diseases is a process that would take massive public education to change established cultural practice. It is unfortunate that there has been no

in-depth study of the impact of the premarital test on Saudi culture, as this would enable a valuable assessment of how Saudis are dealing with the clash between the burden of genetic incompatibility and the value of consanguinity.

The ethical challenges could be summarised in the following three points:

- A- In the Saudi cultural context, premarital tests could be seen as a proxy to limit consanguinity due to the established assumption that it is responsible for the relatively higher prevalence of genetic diseases in countries that value consanguinity in the same way (see the previous sub-section 1.3.1 Consanguinity.) Premarital tests should not be used as an epistemic authority to prevent or control consanguinity, for the same reasons that MGE research results should not be used alone either (see an example in Al Odaib et al., 2003; and Alenizi, 2014). It does not seem right to use what is claimed to be a generalizable laboratory result to label consanguinity as wrong and then take further laboratory tests to prevent consanguinity on a personal level (i.e., just before marriage).
  
- B- Another ethical challenge is the way in which premarital tests were introduced to the public. As explored earlier in this subsection, these tests were introduced with what look like overpromises, such as contributing to eradicating all genetic and sexually-transmitted diseases by the taking the test and then adhering to its results (such as by cancelling the marriage). To the best of my knowledge, there is no social support service for those who will bear the burden of such knowledge when they culturally cannot cancel the marriage or those who cancel the marriage and then must live with the

stigma (e.g., refusing to marry a cousin and/or being labelled as genetically unfit).

- C- In addition to all of the above points, the notion of premarital tests seems to be motivated by prioritising the reduction of the cost of having children who could have one of the three diseases, rather than by caring for and supporting the compromised families.

### **1.3.3 Stigmatisation**

Furthermore, as a result of decades of consanguinity, Saudi tribes are genetically homogenous, which means testing may result in tribal stigma, as well as the stigmatisation of individuals. As consanguinity has been practised for hundreds of years in the Arabian Peninsula, there is a concentration of genetic lineages amongst persons of the same tribe and a tribe can share very high rates of the same inherited genetic diseases. This is so common that Saudi geneticists can often identify an individual's tribe or the region where their tribe is traditionally based solely by knowing the genetic disorders they have. It is very well known, for example, that the Saudi Eastern Province has more carrier rates of  $\beta$ -Thalassaemia and Glucose-6-phosphate dehydrogenase than the rest of the Kingdom. Although medical cover is now free for all Saudi citizens, the government is in the process of legislating (Decision No. 71, Council of Ministers) for the provision of private insurance for Saudis, where the premium may vary, based on individual risk factors. This could mean that people from the Eastern region (i.e. already characterised by higher rates of  $\beta$ -Thalassaemia) will have higher premiums than people from the rest of the Kingdom.

In Saudi Arabia, if a family were to become known as being carriers of a genetic disease, their daughters' chances of getting married would be very slim. The main reason

for this is the process of arranged marriage, in which the mother of the groom looks for a suitable bride for her son. It has become common for mothers to ask whether the proposed bride has been previously engaged and then had the engagement broken due to the premarital test, or whether she is from a branch of the family that is known to have a particular disorder. If the answers to such questions raised doubts over the proposed bride, the mother would move on to other families to find someone more genetically suitable (Al Sulaiman et al., 2010). It is unfortunate that the cultural paradigm of this practice has not yet been studied; however, a study from Israel reported a similar case, where the father of a Arab Bedouin tribe refused to test his daughter, as it would decrease her marriage chances (Raz and Atar, 2004). Although the result would stigmatise both the male and female in the engagement should they turn out to be carriers, women are more stigmatised than men in tribal cultures (Raz and Atar, 2004).

To summarize the challenges for MGE research in the Saudi Arabian cultural context, stigma is ethically problematic in three ways:

- A- Blood donated by an individual, even with that person's explicit consent, may provide information about the whole tribe, which might open the door to the stigmatization of far more people than the individual who originally consented.
- B- Women in Saudi Arabia are likely to be the most stigmatized because of the arranged marriage practice, in which the mother of the groom looks for the most 'suitable' bride.
- C- Stigma in general creates and perpetuates an unfair disadvantage.



### 1.3.4 Blood purity

As explained earlier, blood purity determines the rank of a person in his own tribe. If the person's genetic lineage is connected to the tribe from both of his parents' sides, or from his father's side, while his mother is from a stronger or similarly ranked tribe, he would be in the highest rank among his peers.

The notion of blood purity has been used by the government to determine the veracity of non-Saudi individuals' claims to belong to one of the strong tribes in the border regions, either on the northern border (for example, the tribe of Onaizi) or on the southern (the tribe of Nahdi). This was an attempt by the Saudi government to stop illegal immigrants from getting permits for citizenship through tribal leaders.

It is noticeable that participants in the Arabic online forums have started to gain an interest in online analysis services for identifying DNA genealogy, for example, [www.familytreedna.com](http://www.familytreedna.com) (Arab-DNA, 2012; Howitat, 2012). There are heated debates on these Arabic forums about tribal belonging. This is a new form of genetic identity that has gone unaddressed by the Saudi government.

It appears that the MGE technology, in some reported cases, has started to infringe on the main fabric of the tribe's identity. For example, there was a highly publicised case recently when two brothers won a verdict to divorce their sister from her husband and the father of her two children against the couple's will because the brothers claimed that the husband was not as 'pure blooded' as their sister. The couple appealed the decision to a higher court, where they were able to reverse the divorce and authenticate their marriage after a three year court battle (Arabian Business, 2012). This is not an isolated case: *Al Sharq Alawsat*, a Saudi news website, claimed in September 2013 to have found at least

sixteen divorce cases based on blood purity incompatibility between Saudis, including nine cases in Riyadh, six cases in the Eastern province, one case in Medina and one case in Jeddah (Al Sharq, 2013). The Al Madinah newspaper reported that during the first two months of 2014, there were 13 cases of blood purity incompatibilities (2014). Another case concerned a woman who tried to kill herself after her family received a court ruling that her future husband was not from an equivalent pure bloodline (Alwatan, 2013).

To summarise the challenges in this context, MGE consumer-oriented services are introducing what could be regarded by some Saudis as a more reliable epistemological tool to verify lineage than the traditional way (looking towards shared culture, language, religion, history and interests) as a way to promote or demote families among specific tribes. This could be problematic in situations such as when couples are divorced against their will just because the tribe's elders regard one of the spouses as not genetically pure. Thus, utilising of such technologies, in this specific way, has the potential to infringe on established-families' stability. Also, consumer-oriented services appear to introduce a whole new paradigm of genetic identity that will be discussed below (section 7.2.3 Blood as identity tool).

### **1.3.5 Patient vulnerability**

Saudis generally like to be regarded by each other as conservative, generous, kind, supportive and religious. According to some Western physicians who have worked in Saudi hospitals, those claims are not completely wrong. Western physicians affirm that Saudi patients trust the physician who treats them (Lacey, 2011), and confer on the physician an authoritative status (Abolfotouh and Adlan, 2011). In some cases, Saudi patients even try to personalise the relationship by attempting to engage on a social level.

Saudis also like to be perceived as believers (Halligan, 2006). If misfortunes occur they are attributed to God's will as it is part of the Islamic creed that God sometimes tests people's beliefs through either doubt or hardship (Al-Shahri, 2002, Rassool, 2000). Good Muslims should be patient, accepting and tolerant, and surrender to God's will, basing their every action on Islamic rules. Therefore, if they were convinced that donating blood is a good deed rewarded by God in the hereafter, it is difficult for them to say no, given perceptions about what it is to be a good Muslim.

In the past, in the Western context, it was normal to expect a level of paternalism to be practiced in medical decision-making. Physicians thought that they were the most qualified to take difficult decisions. In contemporary medical practice, the doctrine of informed consent is believed to counter such paternalism and promote autonomy (Manson, 2007). Some of the factors explained in this section may suggest that Saudi physicians are still leaning towards some level of paternalism, even though paternalism is largely dismissed in contemporary medical ethics (Manson and O'Neill, 2007; Manson, 2007; Adlan, 2013)

Saudi patients usually look up to the doctor who treats them. They rate him/her as a healer or, more precisely, as an authoritative figure (Mobeireek et al., 1996). It could be argued that such authority makes the physician feel paternally responsible for his patients' care. Despite the debate over the appropriateness of paternalistic behaviour, when it comes to inviting patients to participate in health-related research, the matter takes a more critical turn, as is unlikely that any patient would say 'no' to a physician in Saudi culture just because of their professional role (Mobeireek et al., 1996). Even though informed consent is mandatory, in Saudi Arabia informed consent is rated as mere paperwork (Jamjoom et

al., 2011). It appears that among Saudi patients and their doctors, verbal commitments that everything will be fine are more powerful than any signed documents (Abolfotouh and Adlan, 2011). This would suggest that paternalism is not the choice of the physician; it could be the result of prioritising other values, such as trust between the caregiver and the research subject. This claim will be further discussed later in this thesis.

The ethical challenge in this specific context is considering Saudis as vulnerable to not providing what is held to be an appropriate level of consent. For example, they could be seen as not being good Muslims if they refuse to perform a good deed that would cost them only a few blood drops. If they said no to the treating doctor, they would fear they would lose some of the treatment privileges, and some physicians choose not to provide full information to patients.

### **1.3.6 Conclusion of the Saudi Context**

In conclusion, the aforementioned challenges are not unique to the Saudi Arabian context, but, I argue, they are particularly important due to the complex nature of the Saudi culture. I have argued that due to the nature of the tribal hierarchy, religion, and the stress on healthcare in Saudi Arabia, values such as trust and respect are much more applauded than commitment to individualism and free choice, this claim will be discussed in detail in this thesis. MGE research has the potential to be harmful, insofar as it can intertwine with challenges such as stigmatisation, and patient vulnerability and produce negative effects. This claim will be discussed in detail in Chapter Four.

## **1.4 The need for empirical data**

This thesis investigates whether the research ethics guidelines for MGE research, constructed from Western regulations, are appropriate within the Saudi context. Therefore,

I will argue in this section that empirical bioethics and more specifically the *normative policy- or practice-oriented bioethics* (NPOB) approach, that uses both normative analysis and empirical data to inform the analysis of each other (Ives and Draper, 2009), is the most suitable approach to achieve the aim and objectives of this thesis.

The importance of normative analysis in this thesis stems from the complex nature of the normative challenges surrounding MGE research and the specific Saudi Arabian context. However, different disciplines have different ways of identifying these challenges. Some might argue that applying ethical theory and moral reasoning are enough to answer the question in hand. There are two reasons why this is not the case and why there is a need for empirical research as well as normative reflection. Firstly, my overall research question starts with posing a normative question about how MGE research ought to be regarded in the Saudi-specific context. Such a question calls for studying the context empirically to understand Saudi culture and attitudes to donating blood for MGE research as a first step to reflecting upon the policies and investigating those policies' appropriateness. Secondly, philosophical reasoning and intuition are among the most important tools in moral philosophy; for decades these tools have led moral philosophers to come up with highly respected moral theories. However, relying on these tools alone would not be enough to resolve conflicts between two or more principles if those principles are equally justified in the philosophy literature, but contradict each other. In such situations, disagreements between theories would enrich further debate and reasoning but would be of limited applicability and value for someone trying to identify which one is more suitable within a specific context (Hoffmaster, (1992). For example, some writers support genetic exceptionalism, arguing that genetics ought to be treated differently to other research disciplines because it generates unique medical data that may be a greater

risk to participants than other kinds of health information (Green and Botkin, 2003). Genetic exceptionalism is, then, used to justify exceptional measures for the regulation of genetics research. Others argue that genetic information is not exceptional and that the same risks can be associated with any personal information and, therefore, require no exceptional treatment. Using only a philosophical analysis approach would add to the body of knowledge and might contribute to one or both of these positions on genetic information. Philosophical analysis could be rated as a necessary contribution to the field of applied ethics but of little benefit to the discussion of the policies in question, as the outcome should be more inspired by the culture (Moorlock, 2013).

Concentrating exclusively on the philosophical debate would be problematic because philosophy as a discipline is not a part of any Saudi education curriculum, including the higher education systems (Goucha, 2007). It is, therefore, extremely rare to find a normative analysis or rigorous philosophical debate about values in Saudi Arabia. Most bioethics papers are either practice-oriented or propose an Islamic version of bioethics, where authors try to find a connection between medical/research practice and Islamic law. Therefore, philosophical analyses alone would be of limited value because it risks being alien and might not be acceptable. Knowing how Saudi stakeholders in the context of MGE argue for their normative values and what seems important to them, one can provide potentially less resistible advice that is more likely to be followed which cannot be identified by looking at philosophical literature, and so must be done empirically.

For centuries, normative analyses, through moral reasoning and reflection, were among the most important tools that enabled moral philosophers to produce their moral theories. In the same vein, but with a twist towards empirical bioethics, Hedgecoe (2004) suggests the importance of introducing a '[r]igorous normative analysis to the lived moral

experience in addition to critical empirical work which is usually the best way to assess the lived moral experience' (Hedgecoe, 2004, p120-122). In this same paper, Hedgecoe (2004) argues for the need for empirical work to inform philosophical reasoning and intuition. The social science critique describes traditional applied ethics as: a) abstract, b) rooted mainly in rational and formal argument, c) being based on the assumption that moral norms are prescriptive and binding through rationality, d) believing that solving problems relies on the application of moral theory, and e) overlooking cultural differences (Hedgecoe, 2004). Those criticisms have influenced my aims to provide a contextual understanding of MGE research in Saudi Arabia as an essential step to conducting a culturally sensitive normative analysis. Based on Hedgecoe's (2004) work, I considered that, if any work attempts normative analysis with appropriate cultural understanding in the way that this work promises, it cannot afford to neglect the need for empirical data that shed light on the intuitions and experiences of stakeholders in the analysed context. To the best of my knowledge, no work has yet investigated the intuitions of stakeholders in health research in Saudi Arabia. This means that such important intuitions can be easily overlooked if this work based its methodology only on traditional ways of reasoning in moral philosophy. The social science critics believe that morality would not make sense if the solution to an ethical problem did not consider empirical understanding the nature of the problem to which the solution was offered. To be effective, any solution to an ethical problem must pay close attention to the potential problem that this solution might address. For example, one might suggest that Saudi MGE research ought to be regarded in a specific way that empowers full autonomy through informed consent documentation; this suggestion would be of limited value if in Saudi Arabia it would be regarded as an example of undermining tribal cultural systems. Those imposed suggestions potentially could, at the least, create

adherence issues that could be circumvented if the context were considered for the suggested solution.

Over the last twenty years, there has been a significant increase in the use of empirical data and its analysis in bioethics, as well as numerous references being made to data collected and published by others (Sugarman et al., 2007; Borry et al., 2006; Leget et al., 2009). Despite that, there is no consistency on what is meant by empirical bioethics either theoretically or practically (Molewijk & Frith, 2009). Therefore it is important to outline in the beginning what I mean by empirical bioethics which is in general terms conducting both ethical analysis and empirical analysis and allowing each analysis to inform the other

In the previous paragraphs, I illustrated the importance of the empirical bioethics for this thesis and stated how Molewijk & Frith (2009) criticised a lack of consistency in how empirical bioethics is approached in the literature. To detail this claim Molewijk (2004) suggests three different ways in which authors use empirical bioethics: a) Prescriptive applied ethics - the data collected by the empirical investigation are only used as a premise in an argument or to measure how people are behaving. In prescriptive applied ethics priority is given to the theory over any data collected empirically. b) Theory building - the main aim of a theorist is to produce a theory, thus they need the data to refine the theory in a one-way relationship, from theory to empirical finding but not the other way around. c) Critical applied ethics - this mainly uses both the empirical analysis and the philosophical analysis in two-ways relationship and neither is prioritised. This means allowing the data to inform the theory and vice versa (Leget et al., 2009). There are many different and equally valid methodological approaches and the important thing is to employ that one that best addresses one's aims. In the context of this thesis, the main promise is to provide an



understanding of what is going on in the field of Saudi MGE research ethics as a necessary step to providing answers to more important normative questions like how Saudi MGE research ought to be regulated. In order to do that, it is important to follow the methodology that would allow the context to inform the theoretical analysis and visa versa in a critical way.

Hedgecoe (2004) outlines a concept of ‘critical bioethics’ which uses social science techniques as tools to better inform normative analysis. This approach to bioethics can be regarded as critical of common bioethics practice (i.e., not using empirical data) from a social scientist point of view. It calls for the development of a methodology that would have stronger potential to bring the empirical data into ethical analysis and theorising. Such a call has paved the way for the suggestion of a different methodological empirical approach which ‘is important in two significant ways: to achieve a contextual understanding, and to understand meaning’ (p251); this methodological approach is called empirical bioethics (Ives and Draper, 2009).

#### **1.4.1 Normative policy- or practice-oriented bioethics**

As Ives and Draper (2009) see it, a policy must be in harmony with the community that will be expected to follow it. Empirical work is a means of uncovering what the stakeholders think about, and how they react to, those policies. Stakeholders’ input cannot, however, be taken as the sole authority for the regulation of MGE research in Saudi Arabia. Giving such authority to such views could lead to the ‘defence of the indefensible’, or at least face the difficulty of justifying conflicting points of view (Moorlock, 2013, p4). Instead, stakeholder views will be combined with philosophical reasoning so as to come up with a better understanding of the MGE research practice in Saudi Arabia. It is essential to provide the needed ‘encounter with experience’ (Ives, 2008) which has yet to be assessed

in the MGE research in Saudi Arabia. This, Ives describes as ‘[b]ringing philosophical ethical analysis to the ground, and rooting it in real people and in real problems’ (Ives, 2008, p3). Thus, for the sake of providing a better critique of policies in Saudi Arabia, it is important to employ empirical analysis in addition to philosophical analysis. Accordingly, the most appropriate research approach is the NPOB approach, as this will help to understand the normative assumptions of the Saudi MGE-regulating policies, as well as to determine what value is attached to MGE research in Saudi Arabia (i.e. whether people think it a valuable thing to do and why) by combining both normative analysis and empirical analysis. Another important reason for why NPOB seems the most suitable approach for this thesis is the importance of both intuitions in moral philosophy and the empirical data in gaining a more accurate understanding of the Saudi MGE research context. NPOB’s main promise is ‘to integrate empirical data and philosophical bioethics is to utilize empirically gathered lay intuition as the foundation for ethical reasoning in NPOB...[this]... involves a modification of a long-established tradition on non-intervention in qualitative data gathering, combined with a form of reflective equilibrium where the demands of theory and data are given equal weight and a pragmatic compromise reached’ (Ives & Draper, 2009 p 249). Thus it was the best approach that would fulfil this thesis aims.

#### **1.4.2 The is/ought fallacy**

Some might argue that such a work, if undertaken lightly or uncritically, would fall foul of the is/ought fallacy. The is/ought fallacy refers to accepting the descriptive value (what is usually practiced by people) to be a prescriptive value (a statement of what they therefore ought to do or value). According to David Hume you cannot derive an ‘ought’ from an ‘is’ because the ‘is’ statement is descriptive while the ‘ought’ statement is

prescriptive. In other words we cannot have a moral conclusion based on premises that do not have at least one moral claim among them. Consider, for example, society X prefers doing Y, therefore doing Y should be regarded as morally acceptable. The fallacy here is accepting a moral claim Y based solely on what society X prefers, without seeing that we need at least one premise that ‘bridges’ the descriptive and the normative, such as: ‘where a society prefers an action it is what we ought to do’. To avoid the is/ought fallacy, I will not use the empirical data in the embedded study to make moral claims, but rather they will be used to inform my moral reasoning. Thus, using data will help provide better analysis insofar as data are used in the same way that intuition uses example and scenarios; it is mainly by informing the reasoning for moral theories and by respecting the idea that facts and values are not distinct in practice (Ives & Dunn, 2010). In the context of the empirical project in this thesis, to ensure that it will not fall foul of the is/ought fallacy, it is essential not to advocate any moral conclusion based on the data analysis alone without critical moral reasoning. The plan is to use the data as well as personal reflexivity to ensure an “encounter with the experience” (Ives & Draper, 2009) of the stakeholders and use the understanding gained to help develop a more encompassing normative analysis without claiming that because in the Saudi context, X action is happening therefore X should be an accepted moral practice.

In conclusion, the empirical part of this research aims to explore the current practice of MGE research in Saudi Arabia, not in order to provide a sociological understanding of how social actors react with each other, but to provide an overview of the normative assumptions that tacitly guide donors, researchers, and policy-makers with regard to MGE research. The Saudi stakeholders’ normative assumptions will be compared with the normative assumptions explored in the Chapters regarding the guidelines that are supposed

to guide MGE research practice in Saudi Arabia. Accordingly, this work can be understood as an empirical study in bioethics, specifically normative policy-oriented bioethics (NPOB), as described by Ives and Draper (2009). NPOB refers to the blending of normative bioethics analysis and empirical data analysis in the examination of normative principles underlying policies (Ives and Draper, 2009). This approach will better serve the overarching aim of this research, which is to contextualise ethical theories related to the ethical issues of relevance to thinking about genetics for policy-makers in Saudi Arabia.

### **1.5 Thesis Aims and Objectives**

The aim of this thesis is to explore the ethics of collecting and using donated blood for MGE research in the context of Saudi Arabia, as a preliminary step to enabling policymakers to generate specifically Saudi oriented guidelines for MGE research in the Kingdom. Accordingly, I have studied the current regulations governing the collection and use of blood for MGE research in Saudi Arabia against the background of the international policies that informed the development of the Saudi general bioethics guidance (NCBE 2010). This enabled me to determine whether the reviewed international policies' embedded norms that anticipate ethical issues in MGE research. Accordingly, the thesis objectives were:

- 1) To outline the international ethics guidelines for the collection and storage of blood samples from adults for the purposes of MGE research. This was achieved through desk-based research, reviewing the literature and applying critical analysis to the selected international guidelines to determine their appropriateness in this context.

- 2) To explore how the current Saudi guidelines regulate the collection and storage of blood for MGE research and reflect the principles and norms distilled from the international guidelines. The Saudi guidelines were distilled and compared to those driving

the international guidelines. In order to determine how appropriate they are for the regulation and collection of blood for MGE research in Saudi Arabia, the Saudi context in terms of culture, religion and politics was explored to gain insight into how a blend of these factors interacts with complying with the selected international bioethics regulations regarding the donation of blood for MGE.

3) To illustrate how the official Saudi guidelines and ethical norms are implemented in current practice in relation to the collection and storing of blood, with reference to samples taken from adults who have given prior consent to a particular type of MGE. This was achieved by field observations (i.e. recruitment of blood donors for MGE research sessions in one of Saudi Arabia's tertiary care hospitals) and interviews with people who had been invited to participate in MGE research in Saudi Arabia.

4) To explore, using focus groups, how the results might be perceived by those charged with generating and applying the Saudi guidelines and norms for research.

## **1.6 Research questions**

1. What are the influential international guidelines for the collection and storage of blood, with reference to samples taken from adults for MGE research purposes?

2. What are the Saudi guidelines for the collection and storage of blood for pre-approved MGE research, and to what extent do they reflect the international guidelines already identified?

3. To what extent are the Saudi or the international guidelines followed in practice in the Kingdom?

4. What, if any, are the challenges of collecting blood from Saudi donors for MGE research, as perceived by the stakeholders?

5. What is the feedback of those charged with generating the Saudi guidelines and norms for research to the results of the investigation into current practice in relation to blood collected for genetics research?

6. What recommendations would help to promote better and more culturally sensitive guidelines with respect to the donation of blood for MGE in Saudi Arabia?

## **1.7 Summary**

In this chapter, I introduced the overarching aim of this thesis and its objectives. The primary aim is to explore the ethics of using donated blood for MGE research in the context of Saudi Arabia, as a preliminary step to enabling policymakers to generate specifically Saudi-oriented bioethics guidelines for collecting and using blood for MGE research in the Kingdom. Accordingly it was essential to start by introducing the Saudi context, which puts the MGE research in its Saudi context, to cast a light on what could be the challenges that ought to be considered when writing specific regulations for MGE research in Saudi Arabia.

This chapter also introduced some of the Saudis' values and provided the context in anticipation of tensions that will emerge in Chapter Four between cultural norms in SA and the international guidelines. This introduction outlines how the thesis has explored the ways in which MGE research in the Saudi context, by contrasting what the policymakers expect with what is going in the field. Based on this, I have also argued for the use of empirical bioethics, by showing that a combination of empirical data and philosophical analyses are the best way to answer the overarching aim of this study.

### **Section One: The normative analysis of the selected guidelines**

This section will be dedicated to the normative analysis of the selected international guidelines (Chapter Two), the Saudi NCBE guidelines (Chapter Three) and how the Saudi context would pose challenges to MGE research regulated by those guidelines (Chapter Four).

In the first two chapters of this section (i.e. Chapters Two & Three) the policies are analysed in three main steps. The first stage involved in-depth reading and familiarisation, looking at the selected policies in the historical and regulatory context. This helped to understand the motivations behind these policies and paved the way to the second stage. Secondly, I familiarised myself with the policies and tried to look past the words to the normative assumptions at work, to gain the necessary richness and depth (Bowen, 2009). Thirdly, after I familiarised myself with the data, I used a mixture of content analysis (arranging the text's content in a way that answers the research questions) and thematic analysis (in the sense of pattern recognition in the text) (Bowen, 2009). I then engaged in philosophical analysis of the relevant themes in the light of the issues uncovered in the literature.

The final chapter in this section (Chapter Four) will be dedicated to normatively analysing and describing how the Saudi culture and its contexts outlined in Subsection 1.5 above poses challenges to how MGE research is currently regulated in Saudi Arabia.

## **2 Chapter Two: The international Guidelines**

This chapter will be mainly dedicated to answering the first research question of this thesis, namely identifying the international guidelines governing the collection and storage of blood samples taken from adults for the purpose of MGE research. In order to do so, I will justify the selection of the guidelines that will be interrogated, to determine how they can be used to regulate the collection of blood for MGE research in general. The main points that can be applied to MGE are summarised in Tables 2-2 to 2-5. I will also argue that there are three key points here. The first is that the current selected and analysed guidelines were written largely with Randomised Controlled Trials (RCTs) in mind. Secondly, the lack of guidelines specifically intended to regulate MGE research resulted in the adoption of some elements of the ones analysed in this chapter, which is problematic because of the different nature of MGE research, and results in gaps that lead to strange conclusions, such as the way that risks and harm are understood. Thirdly, looking at MGE as an area of research also allows us to see that the international guidelines might well be problematic, because they fail to take local culture and context sufficiently into account. Although the guidelines explored in this section are not legally binding unless adopted into national law, they are nevertheless important because they set out internationally recognised norms. The extent to which they have been cited, which will be demonstrated in this chapter, has reinforced their role in the ethical regulation of research.

### **2.1 International guidelines on bioethics: inclusion and exclusion criteria**

There are myriad international bioethics guidelines; selection for inclusion in this thesis was based on the international regulations that are used specifically as references for the Saudi national bioethics guidelines. Those selected guidelines are the Nuremberg Code, the Declaration of Helsinki, the International Conference of Harmonisation – Good



Clinical Practice (ICH-GCP), the Council for International Organisations of Medical Sciences (CIOMS), and UNESCO's Universal Declaration of Bioethics and Human Rights. The Saudi NCBE guidelines mention in a very general way that the references are based on Islamic Sharei' laws and the international guidelines (NCBE, 2010). Further consultation with experts from the committee confirmed that the above selected guidelines were agreed by NCBE members to be the most influential and that they were often appealed to in the most respected Specialists Saudi hospitals (KFSH&RC, 2013; NGHA, 2013).

## **2.2 The context of the selected international guidelines**

In the following subsection, I will briefly summarise these guidelines and identify to whom they apply. This step is important for three reasons:

- It helps to place these guidelines within their historical context.
- It helps to understand who is expected to read and comply with them.
- It gives an insight into many Western ethical perspectives and priorities.

All of these points, I argue, are essential for assessing the suitability of the guidelines for regulating GME research in Saudi Arabia, which will be more fully discussed later in this study.

### **2.2.1 Nuremberg Code**

The Nuremberg Code is the oldest set of guidelines for acceptable research involving human participants. Conceived in Nuremberg, Germany in August 1947, it consists of ten principles, presented by mainly American judges at the trial of Nazi doctors charged with conducting murderous and torturous human experiments on those detained in concentration camps (Utley, 1992). Although it was not originally intended to provide

guidelines for clinical trials, this code is considered to be the cornerstone of international research ethics (Utley, 1992). In its development, judges considered specific cases of unethical and inhuman research perpetrated by the defendants. The Nazi doctors' main line of defence was that there were no laws to distinguish legal from non-legal research activities at the time, and that similar research had been conducted elsewhere (Manson and O'Neill, 2007). The Nazi doctors' lawyer specifically mentioned the malaria trial conducted by the United States upon prisoners of war. Some commentators think that the Nuremberg Code's main contribution was merging the Hippocratic Oath (in which the physician is responsible for protecting the best interests of his or her patient) with the contemporary notion of protecting human rights (Shuster, 1997).

### **2.2.2 Declaration of Helsinki**

In 1947, the World Medical Association (Bowman and Hui, 2000) was established. It continues to grow and gain increasing respect; to date, it represents more than eight million physicians worldwide (Carlson et al., 2004). In 1964, the WMA published the Declaration of Helsinki (DoH) (Carlson et al., 2004; Puri et al., 2009). They incorporated the ten principles of the Nuremberg Code with the 1947 Declaration of Geneva, which was also authored by the WMA as a statement of physicians' ethical duties. During the last 46 years, the DoH has been revised six times; the last revision was in October 2013. Among these revisions was one in the year 2000 that did not support the idea of testing drug efficacy by using placebo control in clinical trials when an alternative treatment is available, which was the main reason that many countries, such as the USA, stopped using it as reference for its research ethics bylaws.

As the Saudi bioethics bylaws were announced in 2008 as binding law articles, a subcommittee was formed in 2009 to publish the guidelines that explained the bylaws. In

those guidelines the version used as reference was the 2008 version of the DoH. Therefore, in the context of this thesis I will use the 2008 version, not the 2013 version.

This declaration consists of three parts. The first is made up of points introducing the general concept and the statement of the declaration. The second part is made up of twenty points concerning general principles of all medical research. The third part consists of five points concerning the combining of medical research with medical care. According to Williams (2008), the Declaration of Helsinki is primarily concerned with public health research, as it differentiates between individual and public health; this idea can be refuted by the fact that the DoH does not mention any non-clinical research in its guidelines, which suggests it is more focused on clinical trials, particularly RCTs, than public health research.

This declaration clearly defines its audience: ‘Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles’ (DoH, 2008, p1). This might give the impression that these guidelines are more applicable than the Nuremberg code to scientists (who are the most likely to do laboratory work in MGE research). However, elsewhere the Helsinki Declaration also states that scientists should be under the supervision of a clinically competent medical person when they are conducting research that involves human participants (DoH, 2008, p3). Thus, it can be argued that the document considers physicians as its main audience, which Millum et al. (2013) and Emanuel (2013) consider to be a mistake because ‘a statement of ethical principles does not require a mandate from the people who ought to follow those principles’ (Millum et al., 2013, p2143). Similarly, it could be argued that scientists adhering to the code may regard themselves as both obliged to work with a clinician and themselves be bound by the precepts. However, it can be

understood that if anything went wrong, it is the physician who is held responsible (DoH, 2008). This suggests that although it is written for physicians, it also applies to scientists, but all the liabilities fall to the physicians.

The fact that the document does not define what it means by the involvement of human participants, as different types of involvement might call for different measures, may have contributed to ambiguity surrounding to whom this document is addressed. For example, the nature of the involvement of a patient who is asked to fill out a questionnaire is wholly different from that of a patient who is asked to join a Phase One clinical trial (i.e. asking a healthy person to take an investigational drug in order to assess its safety profile). This can be justified in clinical trials or RCTs but mandating the physician to assume major responsibility is to protect participant's interests. It fails, however, to acknowledge that not all research is as risky as clinical trials (Williams, 2008). The point of having a physician assuming responsibility for a questionnaire could be sometimes unjustified.

### **2.2.3 International Conference of Harmonisation – Good Clinical Practice (ICH-GCP)**

The original mission statement of the International Conference of Harmonisation (ICH) was to regulate clinical trials in America, Europe, and Japan (Dixon, 1999). Now, Canada, Australia, European Union and the World Health Organisation (WHO), as well as many other countries (including Saudi Arabia), have adopted these guidelines (Alahmad et al., 2012). Their main goal is to achieve a consensus on the guidelines that dictate how clinical trials should be performed, investigated, sponsored, and audited for the final step of approving a pharmaceutical product or a new medical intervention (e.g. a medicine, device, or new operational manoeuvre). With harmonisation it is possible to conduct clinical trials across national borders.

Since its announcement in 1996, the GCP system has provided a unified system for exchanging clinical research data between the countries that have accepted it. This means that drug companies can target populations outside their geographical area as long as the GCP guidelines are accepted and enforced in the targeted country. In other words, a single set of guidelines governs clinical trials internationally, rather than different guidelines for different countries. The main audience for the GCP is principal investigators. The GCP guidelines define the principal investigator as ‘[The] person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator’ (GCP, 1996, p5). Given that the GCP is meant to regulate clinical trials, the clinical site in question is usually a hospital or other health centre. In a hospital, it is less likely that a non-physician would be allowed to lead a clinical trial, as the safety of patients is the responsibility of the attending physician. This is especially true in research-orientated Saudi hospitals, because of the lack of research training amongst non-physicians. Based on this, Saudi policy makers inferred that the GCP policy did not specifically address physicians, but that the context of clinical research dictates that the person addressed in the guidelines should be the one responsible for patient safety (i.e. the physician). Conversely, this could mean that all researchers have to take responsibility for the safety of participants: the PI takes overall responsibility for the site’s conduct and the coordinating investigator takes overall responsibility for running the trial across sites. The latter, an EU designation, could very well not be a physician but an epidemiologist or genetic scientist, for example, but the site PI should be a clinician.

#### **2.2.4 Council for International Organizations of Medical Sciences (CIOMS)**

The WHO and the United Nations Educational, Scientific and Cultural Organisation (UNESCO) together established the CIOMS as a non-profit and non-governmental organisation in 1949. By 1991 CIOMS issued a set of guidelines oriented to regulate epidemiology research. In 1993, CIOMS disseminated a set of 15 principles regulating the involvement of human participants in health-related research. Later, in 2002, the CIOMS guidelines were updated to regulate clinical research. CIOMS started the revision of these Guidelines by forming a multidisciplinary group, which resulted in the 2008 CIOMS principles that will be used in this thesis which is known as the International Ethical Guidelines for Epidemiological Studies as well as clinical research (CIOMS, 2008).

CIOMS originally targeted the assessment of the suitability of the 1964 Helsinki Declaration (Emanuel et al., 2008). In the 1980s, there were many clinical trials occurring in the developing world that were responding, not to the most urgent problems of the developing world, but to the sponsors' needs. Problems such as malaria, HIV, respiratory infections, tropical diseases, and many others were neglected despite the need for solutions. The vulnerability of less developed nations posed many ethical challenges to multinational research, such as the recruiting of participants from low income populations and the protection of their particular interests (Emanuel et al., 2008). Some might say that such contexts and debates enlivened the CIOMS and gave it a more sensitive grounding with the developing world through its understanding of cultural diversity. Nevertheless, it was still far from being sufficiently specific address all research activities in the less-developed world (e.g. MGE).

### **2.2.5 Universal Declaration of Bioethics and Human Rights of UNESCO**

UNESCO is trying to move from mere recommendations and guidelines to internationally agreed declarations at the state level. In 2005, UNESCO announced its Universal Declaration of Bioethics and Human Rights. This was a result of two years of deliberation by 36 members of the International Bioethics Committee (IBC), which served as a transparent, independent committee of bioethics experts. The declaration was then discussed by member states as a non-binding agreement, in the hope that it would be incorporated within the member states' legislation. The IBC includes bioethics experts from different backgrounds, including scientists, lawyers, philosophers, and medics (UNESCO, 2005). Efforts were made to include spiritual and religious groups as well, but despite this, some academic groups, specific branches of scientists, and some interested politicians still claim that their voices were not properly represented or consulted during the drawing up of the declaration (Langlois, 2011). In addition, many countries, including the UK, did not ratify the declaration. However, it has been introduced and accepted in Saudi Arabia, and the chairman of the ICB is the chairman of the Saudi National Bioethics Committee.

Its initial aim involved clinical research. Some say it is essential as a step towards unified international bioethical guidelines (ten Have and Jean, 2009), while sceptics believe it lacks strength because some articles are vague and lack clarity (Levitt and Zwart, 2009).

Having summarised the context of the selected guidelines, in the next subsection I will analyse how MGE research could be regulated using these selected international guidelines. This step is important because MGE research is not mentioned per se in these

particular regulations, but some general guidelines can be used in the MGE research regulations context.

### **2.3 How Molecular & Genetics Epidemiology could be regulated:**

Of the different areas covered in the guidelines, only five items were relevant to the regulation of the collection of blood for MGE. These are:

- The importance of ethical committee review: The committee main tasks would be:
  - Accepting only properly constituted and justified research, and rejecting research where the methods cannot achieve the aims, where the aims cannot be justified, and where there is an absence of equipoise in defining the aims.
  - Rejecting any research that does not respect the local cultural norms.
  - Rejecting any research that intends to exploit local research participants.
- The need for participant consent.
- Minimising risk for the human research participants.
- Protecting participants' privacy and confidentiality.
- Declaring conflicts of interest to the research committees.

The justification for isolating each of these items and their applicability to MGE follows.

#### **2.3.1 Review by local ethics committees**

Review by an independent committee is thought to ensure that research has scientific validity and investigators are providing maximum protection to participants. With the



exception of the Nuremberg Code, all the included guidelines mention the importance of a local independent committee looking at a research proposal and deciding its scientific and ethical merit. However, if a hospital has only one committee that studies research proposals for all the hospitals subspecialties, it risks a lack of fair representation of the hospital service subspecialty. In an ideal situation, the committee is expected, according to the analysed guidelines, to reject or accept the research proposal after weighing all of its elements in a reflective process. Assuming that the research committee members are local experts, this is a way to protect local populations from exploitation in the service of internationally funded research (see Subsection 2.3.1.3 Avoid local research subject exploitation).

#### **2.3.1.1 Accepting only properly constituted and justified research**

One of the charges levelled during the Nuremberg trial was that the Nazi's trials were methodologically flawed. Accordingly, the suffering imposed could not be justified – even if at that time it was defensible to use such a justification - with reference to the potentially good ends. The problem was that the ends could not be achieved by the methods used. Moreover, the defendants, as scientists, must have realised this (Utley, 1992). This charge is reflected in the Nuremberg Code, which dictates that research should be properly constituted, and be for the 'good of society' (See Table 2-3) (N.Code, 1949). In MGE research as well as any other health related research the suitability of the method for achieving the good for society aim could be taken as a measure of research fruitfulness. Of course MGE researchers could use those regulations if it is more specifically addressed how it can be good for society. It is important, therefore, to know where the line between the MGE research fruitfulness (in the above mentioned way) and its burden (see Subsection 2.3.3 Risk).

Although the Nuremberg code is one of the most influenced international instruments, it fails to recognise that different countries may have different laws and guidelines articulating what is locally accepted as ‘for the good of society’ is used to determine what it is properly constituted and justified. Such a distinction is very important to reflect the peculiarity of MGE research in a culture like the Saudi one. This distinction was addressed in later guidelines. The Declaration of Helsinki, for instance, states ‘It [Research] must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards, but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration’ (Table 2-3) (DoH, 2008, p2). However, in the context of MGE research in Saudi Arabia, there are two challenges contained in this guideline: a) it assumes the presence of specific laws that regulate MGE research specifically. b) It can be seen that prioritising the interests of individuals over societal good is essential for the research to be justified, which might not be true in many societies such as, for example, in Saudi Arabia in the context of the health service, as I will discuss in Chapter Four.

### **2.3.1.2 Respecting other cultural norms**

It can be claimed that the local research ethics committee protects the local community by applying local cultural norms. Of the included guidelines, only the CIOMS noted the importance of respecting cultural norms ‘that are morally acceptable within the communities in which the research is carried out...’ (CIOMS, 2008, p6). Whilst Article 12 of the UNESCO Declaration of Bioethics appears to promote respect for cultural diversity, it includes the proviso: ‘However, such considerations are not to be invoked to infringe upon human dignity, human rights and fundamental freedoms nor upon principles set out

in this Declaration, nor to limit their scope' (UNESCO, 2005, p1). This suggests that local norms and values are to be respected only insofar as they are compatible with human rights, which protect the interests of individuals. Jing-Bao (2005) claims that the wording embodies a cultural assumption about non-Western values that is likely to conflict with other Western values, such as respect for human dignity, human rights, and fundamental freedoms (Jing-Bao, 2005). A discussion of moral relativism will be included in Chapter Four. The main challenge in MGE research is that the Saudi context, as explained earlier and as will be further discussed in Chapter Four, could be regarded as presenting a different context to the one in which the guidelines were written. This difference could cause some tension between the Western inherited norms in the analysed guidelines and Saudi norms. Respecting Saudi norms as simply being 'different' might not be enough if those norms are regarded as challenging the interest of individuals.

### **2.3.1.3 Avoid exploitation of the local research subject**

'Exploitation' is a complex concept variously interpreted; therefore, it is important to introduce what I mean by exploitation and how I use my understanding of exploitation in the context of this thesis.

People have different ideas about what exploitations means (see Table 2-1). In the context of this thesis, Wertheimer (2007) seems to offer the best approach to understanding exploitation, for two reasons. Firstly, his is, perhaps, the leading account in the literature of exploitation (Wertheimer, 2007), and secondly, despite the negative connotation of the word, he unpacked the actual moral problem. According to Wertheimer (2007), not all acts of exploitation are morally wrong. For example, it could be argued that any form of contract of employment is a form of exploitation because.in this case it could be related to

the claim of instrumentalisation, but such contracts need not be seen as morally problematic in themselves, especially if the concerned parties provide valid consent. However, if an employment contract contained coercion, deception or slavery, then we would deem the contract morally problematic, not just by appealing to the negative connotation of the word ‘exploitation’, but also by identifying the morally problematic action.

Based on this account, the charge exploitation is not a straightforward claim to establish, especially in the MGE research context. For example, if a patient had consented to donate a few drops of blood for research purposes in exchange for receiving a medical examination, it might seem inaccurate to describe such a transaction as unfair exploitation, because no actual harm was induced to the consenting body (Wertheimer, 2007). To accept the claim that someone is exploited in an ethically problematic way, it is important to distinguish between two different concepts: harmful exploitation that is when the exploiter gains benefit from harming the exploited, and when the exploitation results in a mutual benefit (Wertheimer, 2007). The first form of exploitation is easily condemned. The latter, however, needs closer examination to understand what actually goes on in such interactions, which is likely to be the case in donating blood for MGE research in Saudi Arabia

Based on this way of understanding of exploitation, two aspects of potential exploitation in the context of MGE research in Saudi Arabia could be discussed. The first aspect is the unfair exploitation of the research subject by the researcher. In some places in the world, research studies offer the only opportunity for individuals to be seen by health care providers, leaving patients with little choice but to agree to participate. In this context

the exploitation arises because someone is taking advantage of the lack of choice of someone else to do anything other than agree. Such a choice, or lack of it, is more relevant to the exploitation claim when compared to the level of harm in cases such as RCTs (See 2.3.3 Risk). In the analysed documents, such kinds of exploitation were mainly discussed in the context of stressing the importance of informed consent, as I will discuss in 2.3.2 Consent.

The second aspect of potential exploitation in the context of MGE research in Saudi Arabia is the exploitation of international funding agencies of less-developed countries. This seems to be covered in the way CIOMS dictates that ‘investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organisation, and the ethical standards applied should be no less stringent than they would be for research carried out in that country’ (see Table 2-4) (CIOMS, 2008 p14). In addition to the previously explained demand for well-written research, it appears that this statement was expected to deal with what could be regarded as the ethically problematic exploitation of the less-developed world. The history of clinical trials is full of such exploitation, for example, the maternal-foetal HIV transmission trials, which were approved and funded by the American NIH to perform RCTs that would not have had approval to take place in the United States (De Zulueta, 2001). It might be easier to spot ethically problematic exploitation in RCTs than in MGE research because the risks, vulnerability issues and fairness seem more obvious in the former. In RCTs the risk can be clinically assessed with a diagnosis and prognosis, but in MGE research the risk could be more general than any clinical assessment (e.g. stigmatisation). The CIOMS requirement cited above can be used to protect RCTs participants, but it is not enough to protect MGE research participants.

The challenge here is that there are no clear boundaries between research and diagnostics in molecular genetics (Nelson et al., 2001).

In summary, in this subsection I have demonstrated that normative assumptions may be made when applying the analysed guidelines to regulate MGE research in general. The most central guideline was the call for local committee review. This committee's main duty is to protect human research participants by a) ensuring that research proposals have clear reasons for justifying the enrolment of human subjects as a necessary requirement; b) accepting only properly constituted well justified research, and c) ensuring that ethics committees are representative of their communities and that they protect the interests of the research subjects within those communities. Despite the call for accepting cultural diversity, it can be sensed that the other values appear to be given a superior moral standing over the values that reflect the perspectives of other cultures. This seems to stem from a paternalistic notion of protecting research participants from potential ethically problematic exploitation, that may result from a practice or value that might contradict some of the principles supported by those internationally influential guidelines.

TABLE 2-1: HOW EXPLOITATION IS DEFINED IN THE LITRETURE ACCORDING TO WERTHEIMER (2007, P248)

Author	Definition
BUCHANAN 1985	“[T]O EXPLOIT A PERSON INVOLVES THE HARMFUL, MERELY INSTRUMENTAL UTILIZATION OF HIM OR HIS CAPACITIES, FOR ONE'S OWN ADVANTAGE OR FOR THE SAKE OF ONE'S OWN ENDS.”
BENN 1988	“EXPLOITATION [IN EXCHANGE] DEMANDS... THAT THERE IS NO REASONABLY ELIGIBLE ALTERNATIVE [FOR THE EXPLOITEE] AND THAT THE CONSIDERATION OR ADVANTAGE RECEIVED IS INCOMMENSURATE WITH THE PRICE PAID. ONE IS NOT EXPLOITED IF ONE IS OFFERED WHAT ONE DESPERATELY NEEDS AT A FAIR AND REASONABLE PRICE.”
GOODIN 1988	“EXPLOITATION OF PERSONS CONSISTS IN ... WRONGFUL BEHAVIOR [THAT VIOLATES] THE MORAL NORM OF PROTECTING THE VULNERABLE.”
FEINBERG 1988	“COMMON TO ALL EXPLOITATION OF ONE PERSON (B) BY ANOTHER (A)... IS THAT A MAKES A PROFIT OR GAIN BY TURNING SOME CHARACTERISTIC OF B TO HIS OWN ADVANTAGE... EXPLOITATION ... CAN OCCUR IN MORALLY UNSAVORY FORMS WITHOUT HARMING THE EXPLOITEE'S INTERESTS AND ... DESPITE THE EXPLOITEE'S FULLY VOLUNTARY CONSENT TO THE EXPLOITATIVE BEHAVIOR...”
MUNZER 1990	“PERSONS ARE EXPLOITED IF (ARABIC-FORUM1) OTHERS SECURE A BENEFIT BY (2) USING THEM AS A TOOL OR RESOURCE SO AS (NELSON ET AL.) TO CAUSE THEM SERIOUS HARM.”
LEVINE 1988	“AN EXPLOITATIVE EXCHANGE IS... AN EXCHANGE IN WHICH THE EXPLOITED PARTY GETS LESS THAN THE EXPLOITING PARTY, WHO DOES BETTER AT THE EXPLOITED PARTY'S EXPENSE... [T]HE EXCHANGE MUST RESULT FROM SOCIAL RELATIONS OF UNEQUAL POWER ... EXPLOITATION CAN BE ENTERED INTO VOLUNTARILY; AND CAN EVEN, IN SOME SENSE, BE ADVANTAGEOUS TO THE EXPLOITED PARTY.”
MOORE 1973, 53	“[E]XPLOITATION FORMS PART OF AN EXCHANGE OF GOODS AND SERVICES WHEN 1) THE GOODS AND SERVICES EXCHANGED ARE QUITE OBVIOUSLY NOT OF EQUIVALENT VALUE, AND 2) ONE PARTY TO THE EXCHANGE USES A SUBSTANTIAL DEGREE OF COERCION.”
HILL 1994	“[E]XPLOITATION IS A PSYCHOLOGICAL, RATHER THAN A SOCIAL OR AN ECONOMIC, CONCEPT. FOR AN OFFER TO BE EXPLOITATIVE, IT MUST SERVE TO CREATE OR TO TAKE ADVANTAGE OF SOME RECOGNIZED PSYCHOLOGICAL VULNERABILITY WHICH, IN TURN, DISTURBS THE OFFEREE'S ABILITY TO REASON EFFECTIVELY.”

### 2.3.2 Consent

Consent seems to be the most prominent value in all of the included international guidelines (Table 2-2). During the last 50 years, the Nuremberg Code has been applauded for introducing the notion of informed consent (Manson and O'Neill, 2007; Beauchamp and Childress, 2001). This is despite the fact that the term 'informed consent' is not mentioned in the document and emerged later. What was mentioned is the term, 'voluntary consent': 'The voluntary consent of the human subject is absolutely essential' (Table 2-2). Amongst the analysed guidelines, the phrase 'informed consent' did not appear in the Nuremberg Codes or the Declaration of Helsinki. With the emergence of the term 'informed consent' in the CIOMS, the word 'voluntary' did not disappear from the other guidelines, but it did become part of the definition of informed consent. For example, in the Declaration of Helsinki, the notion of consent was introduced as a 'voluntary' notion in relation to competent individuals: 'Participation by competent individuals as subjects in medical research must be voluntary' (Table 2-3) (DoH, 2008, p3). This was also true in the case of CIOMS and ICH definitions.

UNESCO's claim about when consent ought to be invoked reads as 'Any preventive, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information' (Table 2-4) (UNESCO, 2005, p6). In this context, 'free' can be taken to mean a voluntary condition, even though the word 'voluntary' is itself absent.

As these codes developed, the notion of 'consent' appeared to grow gradually, from its emphasis as a voluntary condition, to a more central concept, symbolised as 'informed



consent' in research ethics. In the Declaration of Helsinki (DoH, 2008), the requirements to meet the consent condition are as follows: 'In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study' (DoH, 2008, p3). However, neither the Nuremberg Code nor the Declaration of Helsinki offer an account of how consent should be documented, in the way that CIOMS and ICH-GCP do. Both CIOMS and the ICH-GCP explicitly explain the informed consent element which constitutes the patient information sheet (Haven and Jean, 2009; GCP, 1996). The ICH-GCP is mainly oriented towards clinical trials and, therefore, it is expected that the elements of informed consent covered in it is mainly for the use of clinical trials. It can, of course, be used for different kinds of research, but it has gaps, leading to inadequate conclusions. For example, one of the elements of the ICH-GCP guidelines for informed consent mandates that the participant should be informed if there is an alternative treatment. If an MGE researcher wants to use such a guideline, the researcher would either disregard it completely or need to explain to the patient why such a statement was in the patient information sheet, even though it is not relevant.

Almost all these guidelines stress the importance of giving the participant the right to withdraw. This idea was mentioned briefly in the Nuremberg Code: 'the human subject should be at liberty to bring the experiment to an end' (N.Code, 1949), which is an odd way to put it, as it only ends the experiment as far as that individual is concerned; it does not stop the whole study. Later, within the Declaration of Helsinki, the right to withdraw is supplemented with the reassurance to the participant that withdrawing will not invite

reprisals: ‘The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal’ (DoH, 2008 p3). The rest of the guidelines, for example ICH-GCP, went further in explaining what could be meant by ‘reprisal’ by clarifying that withdrawal should be permitted without penalty or loss of benefits. It also mentioned the right to withdrawal but with greater detail about protecting withdrawing participants and assuring them that their specific rights would not be compromised as a result of the withdrawal.

It is important, however, to see how the freedom to withdraw (as part and parcel of the process of continued consent) is put into practice in the case of MGE. The challenges of clinical trial withdrawal are different from those relating to blood donation for MGE research. In a clinical trial, it is desirable that the participant remains in the trial until the last scheduled visit. Failing to do so means that the individual’s participation is incomplete and can probably not be used in the final analysis. On the other hand, it only takes one visit to extract blood, assess someone’s lineage, and take his or her medical history. Therefore, if an MGE research participant decides to withdraw, a more transparent procedure is needed—a procedure in which the patient knows exactly what stage the investigation is at the time of withdrawal, combined with a stronger commitment from the research team to abstain from using the data. At the very least, one must be honest with the participant, by letting him/her know when the point of no return is reached, if there is such a point (for example, once data has been published or analysed in a specific way). This requirement can be frustrating to the researcher as, in some cases, genetic research is undertaken with a whole family, where every person is important in order to study a mutation. Here, a conflict of interest may arise in two ways: (i) researchers may wish to respect the participant’s right to withdraw, but it conflicts with the researcher’s desire to continue, and

thereby not lose funding and prematurely terminate the research; (ii) a single member of a studied family may not be able to withdraw him/herself without affecting the participation of the remaining family members. The participant might ask that the donated material be destroyed, but it is not possible to destroy the generated data because it is shared with other family members.

Data collection is a very important part of MGE research. The Declaration of Helsinki mandates informed consent only in cases where identifiable data is used: 'For medical research using identifiable human material [this includes tissues as well as blood] or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse' (DoH, 2008). CIOMS is more specific than the Declaration of Helsinki, in that it includes guidelines for excerpting data rather than just extracting it. 'Extract' specifically refers to texts (e.g. medical records and laboratory reports) while 'excerpt' covers a wider domain of capturing (e.g. photography, recordings, and different forms of graphs). CIOMS also goes into detail regarding the mandating of informed consent, even in the case of a reviewing a patient's medical records, although it does give the ethics review committee the right to waive some, or even all, of the informed consent elements in some circumstances, such as when the required data can be totally non-identifiable (CIOMS, 2008). The ICH-GCP specifically mandates that all stakeholders (committee members, sponsors, monitoring agencies, clinical trials organisation, and authorities who need access for verifications) reveal who would need access to the data that has been taken with consent.

Consent in relation to MGE is problematic as it is not immediately obvious what data it covers given that data from one person is applicable to some or all family/tribe members,

and also because the status of tissue as property is contentious. In the UK, in the case of biobanking, for instance, according to empirical investigation, most people who donate blood for research describe it as a gift (Barbour, 2003). The gift terminology was used quite explicitly by Titmuss (1974) to distinguish blood donation in the UK - as gifting to the healthcare system for clinical uses - from the American system, where blood is purchased from one person and sold on to another individual or organisation. However, one can only gift, or sell, something one owns in the first place (De Witte and Have, 1997; Busby, 2004). The ownership debate of the blood or tissue material as tangible property takes a different context in MGE research because the data taken from the genetic material is not as physical or tangible as the blood or tissue sample from which it is derived. The notion of ownership is one of the shortcomings of medical research ethics guidelines in general (Godard et al., 2003), as they fail to clearly demarcate data ownership. This is a major issue in MGE because many people of the same family, or even tribe, share the same genetic makeup and, therefore, the data. If we accept the premise that this data is property owned by someone, it arguably belongs to the whole tribe, not just the individuals who participate in the research. This will be discussed further in Chapter Four.

The Declaration of Helsinki and CIOMS are the only guidelines that offer the possibility of waiving the requirement to gain consent. The Declaration of Helsinki suggests: 'There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee' (DoH, 2008, p4). CIOMS suggests: 'Waiver of individual informed consent is to be regarded as exceptional, and must in all cases be approved by an ethical review committee...' (CIOMS, 2008, p16). Further, it offers an account of what those

exceptional situations might be: for example, if there is no more than the minimal risks, ‘that is, risk that is no more likely and not greater than that attached to routine medical or psychological examination’ expected of the research, and if the nature of the procedure does not require an informed consent such as taking patients’ temperature (CIOMS, 2008, p18). The importance of this point is that some researchers may know that it will be a challenge or considerable expense to gain consent, for example, to reuse surplus blood given for clinical tests. If researchers can convince the review committee that the research is minimally risky, as per CIOMS, and that it is impractical to recall patients to consent to using material that is going to be thrown away, they may receive the approval of the committee to use surplus blood for their research. The problem with such an outcome is that it reduces the concept of harm to a very narrow understanding, i.e. the one that can be clinically diagnosed. It does not take into account that harm is a wider concept than direct physical risk, for example, the harm resulting from stigmatisation. In MGE research in general, policy makers cannot afford not to look at the potential stigma experienced as a possible risk that could be, in some cases, worse than the kind of harms incurred in a routine physical or psychological examination. Thus, it is important to see how the analysed guidelines look at the concept of harm and risk in the context of MGE research.

### **2.3.3 Risk**

The risk here is taken to be the chance of harm being done. All the analysed guidelines stipulate that no major risks to human participants are acceptable. The only exception, introduced by the Nuremberg Code, is when the physician himself serves as a research participant: ‘No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects’ (N.Code, 1949). This also serves

as an indication of what a major risk is, namely something that may result in ‘death or disabling injury’, with no indication of other harms, such as stigmatisation, which is a key risk in MGE research. The regulation assumes that no amount of benefit can outweigh a certain level of harm. It appears that the Nuremberg Code expressed those levels of harm in points 4, 5, 6 and 7 (N.Code), which are mainly describing physical or mental harm (i.e., a harm that can be diagnosed medically), such as injury, disability or death. Of course, there are serious risks that ought to be mentioned considering the historical context. However, MGE research harbours other kinds of risks, such as stigma, violation of privacy, loss of confidentiality and exposure to information about susceptibility to diseases like cancer, Alzheimer’s and Huntington’s for which there is currently little available by way of remedy or prevention.

The notion of minimal risk is introduced by the CIOMS and UNESCO. This is a notion of potential significance to MGE. Bathe & McGuire (Bathe and McGuire, 2009), for example, suggest that using stored tissue does not exceed the minimum risk, and thus argue that committees ought to look at it with less scrutiny than other types of research if the samples are anonymised (i.e. no personal identifying information included). The main challenge, however, is how to define minimal risk. It is described by the CIOMS in the following way ‘In this [minimal risk] expression “risk” is taken in its common meaning of a possible but not certain adverse effect (on health)’ (see Table 2-4) (CIOMS, 2008, p89). In the context of MGE research it is not clear how minimum risk is supposed to be assessed. There is a need, when identifying risks and determining the associated levels of harm to distinguish between those arising when pre-collected data/tissue are used, those arising from obtaining the tissue and those arising as a result of using the data/tissue.

If a research risk assessment suggests only minimal risk, the researcher is in a position to ask for a waiver of informed consent such as may occur then ‘surplus’ tissue is used. The real risk, however, may be concerned with the wealth of information that the extracted data could provide.

The risk/benefit analysis is mentioned in most of the documents as a way to judge whether a research proposal is acceptable. The rule of thumb suggested by UNESCO is that ‘direct and indirect benefits to patients, research participants and other affected individuals should be maximized and any possible harm to such individuals should be minimized’ (UNESCO, 2005, p6). The main challenge for MGE research is that research participants will probably not directly benefit from the research because the indirect benefit is very vague. In contrast, indirect benefit to the participants from the research outcome could be claimed if the research contributes to a larger general purpose to provide a therapeutic benefit, from which they may benefit at some future point. Even if we accept that MGE research contributes to general knowledge, the question that ought to be asked is, at what price are we gaining this knowledge? In Subsection 1.3, Challenges of MGE research in Saudi Arabia, I outlined some risks that are specific to MGE research in the Saudi context (e.g., the genetically homogenous Saudi tribes, the use of the MGE research results as an epistemic authority to undermine local cultural values, stigmatisation and Saudi patient vulnerability). Thus, the risk/benefit ratio in the context of MGE research in Saudi Arabia might not be as straightforward as in RCTs. In current situations, it is difficult to determine who is in authority to evaluate the risk of MGE research among the stakeholders. One might argue that this is specific to the case of MGE research because of how the data in genetically homogenous populations such as the Saudi population can put more people at risk than those who originally participated. Thus, the risk assessment

should consider a wider circle than that of the people who individually decide to participate. Moreover, according to Manson and O'Neill (2007), the assumption that all the risks will be comprehended after an informed consent meeting is not realistic. Accordingly, the individualistic account of informed consent (where someone is expected to be fully informed and then make a decision) might be impossible.

On the other hand, translational research in the field of genetics is in its infancy, so any risk, however minimal, will have no tangible direct immediate benefit to outweigh it (Rosoff, 2012). This might dictate a shift in thinking from the notion of risk assessment as mentioned earlier to the idea of 'the common good', which would not be a familiar concept in the field of MGE research. Some researchers found out that some donors mentioned that they were just glad to help (Michie et al., 2011), which may be engaging with the notion of common good, albeit they used donors' recall of what is common good as a proxy for their understanding (Michie et al., 2011). Thus, even though patients stated that they just wanted to help, the statement could be a result of what they were told in the recruitment process, or that it was how they remembered the reason. Those who insist on using the idea of the common good to ignore the risks of MGE, may be promising more than MGE can currently deliver (Rosoff, 2012).

#### **2.3.4 Identifiable material**

In the context of MGE research material there are many ways of isolating the identifiers that can reveal participant identity such as: a) coding or masking: this is when the material or data is separated from, but still can be traced to, its origin (i.e. the research participant). Every sample or set of data is given unique codes that refer to the identifiers in other and usually separated databases. The access to this separated database is usually



limited, and needs a key to break the code. b) semi-anonymised: when the identifiers are totally isolated, but some demographic data is still attached. c) completely anonymised: when the material can never be traced back to its origin (i.e. the participant) (Boddington, 2012).

With the exception of the Nuremberg Code and UNESCO, the guidelines represent the concept of identifiable material differently. For example, the Declaration of Helsinki simply mentions the importance of regulating research that uses identifiable material. On the other hand, CIOMS goes a step further, trying to differentiate between the identifiable and non-identifiable and calling for more restricted measures in dealing with identifiable material. The main challenge in MGE research is that molecular material is always identifiable in the sense that comparing results could lead to an educated guess about who the data represents (Boddington, 2012). The ability to guess from where the sample has been taken translates into two factors: the issue of confidentiality and the ability to stigmatise a huge number of people (sometimes hundreds of thousands) due to the nature of autosomal genetic disorders, as explained earlier.

## **2.4 Summary**

This chapter has outlined the selected international regulations that were used as references for the Saudi ones. I have analysed them to determine how they might be interpreted as governing MGE research. This was mainly to answer the first research question of this thesis, which is a necessary step towards the overall arching aim of this work (Subsection 1.4 Aims and Objectives).

All the included guidelines point towards accepting only properly constituted and justified research, in the sense that research proposals should be rejected where the

methods cannot achieve the aims, where the aims cannot be justified, and where there is an absence of equipoise in defining the aims. However, not all of them have mention of clear guidance about who should take that decision (analysing research proposals and approve or disapprove them). Some of the studied guidelines require an independent research committee to make the judgment over whether or not a study should be allowed. The research committee review has evolved from being recommended, to being mandatory. Some of the guidelines explicitly describe how a research committee's membership should be constituted, but less is said about how it should function, what to do in cases of conflict of interest, who is responsible for ensuring that they have sufficient funding to undertake the reviews, and how to committees should make decisions.

Consent is a requirement in all the included guidelines in one way or another. All of the guidelines stress the importance of its being voluntary and the participant's right to withdraw without adverse consequences. However, the regulations are oriented towards the individual rather than families or groups. Informed consent in epidemiology research, including MGE, is not only meant to address individuals. I will argue that, for MGE, a different notion of informed consent is necessary. It is a notion that covers all the stakeholders, such as families and/or groups sharing the same genetic lineage. I will explore this argument at length and justify it at a later stage of this thesis (Subsection 7.5 Ethics committees and protecting tribal interests.)

Both MGE and clinical trials are health-related research with the potential to cause harm and ought to be regulated to protect human participants. However, each operates in a different risk paradigm. Clinical trials are more likely to result in physical or medicine-related harm, whereas MGE research, while potentially resulting in some form of harm that

can be medically assessed (e.g. psychological harm), could also harbour other community-based harms, such as stigma.

Genetic material can be identifiable if compared with other data, but this does not necessarily mean that MGE research should be regulated using clinical trials guidelines. Rather, it means that additional measures should be adopted to protect donors' identities.

The overall conclusion is that the guidelines often apparently endorse a version of liberalism: where there is a strong commitment to autonomy, there is significant focus on informed consent. This could be attributed to the historical context. However, the lack of specific guidelines to regulate MGE research in Saudi Arabia have lead to use some elements from the selected guidelines to regarded all health-related research including MGE research. However, applying them in their current state to MGE research in Saudi Arabia is problematic because they have gaps and may produce strange conclusions.

TABLE 2-2: SUMMARY DISCUSSED CONSENT IN THE ANALYSED REGULATIONS:

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
Voluntariness	"The voluntary consent of the human subject is absolutely essential."	"Participation by competent individuals as subjects in medical research must be voluntary."	"must obtain the voluntary informed consent of the prospective subject"	"That the subject's participation in the trial is voluntary and that the subject may refuse to participate"	Not mentioned
Informed consent	Not mentioned	"In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. "	Informed consent can be demanded by the ethics committee	"Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects"	Any preventive, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information.
Right to withdraw	"the human subject should be at liberty to bring the experiment to an end"	"The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal."	"that the individual is free to refuse to participate and will be free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled"	"or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled."	The consent should, where appropriate, be express and may be withdrawn by the person concerned at any time and for any reason without disadvantage or prejudice.
IC for data	Not mentioned	"For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. "	"...should not submit any identifiable data about a patient to an investigator or to a database unless the patient permits such submission of data or it is authorized or mandated by law."	"The sponsor should verify that each subject has consented, in writing, to direct access to his/her original medical records for trial-related monitoring, audit, IRB/IEC review, and regulatory inspection."	Not mentioned

TABLE 2-2: SUMMARY OF THE CONSENT THEMES IN THE ANALYSED REGULATIONS (CONTINUE):

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
IC for collecting sample	Not mentioned	"For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse."	"When collecting and storing human biological samples ... for future epidemiological research, the investigator must obtain the voluntary informed consent of the individual donor"	Not mentioned	Not mentioned
IC for using stored sample	Not mentioned	Not mentioned	"The protocol of every study using stored human biological samples (and related data) must be submitted to an ethical review committee, which should satisfy itself that the proposed use of the samples comes within the scope specifically agreed to by the subjects."	Not mentioned	Not mentioned
Explicit elements of IC	Not mentioned	Not Mentioned	"Before requesting an individual's consent to participate in research, the 1069 investigator must provide the following information, in language or another 1070 form of communication that the individual can understand..."	"be provided to subjects should include explanations of the following:..."	Not mentioned
Wave IC	Not mentioned	"There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee."	"Waiver of individual informed consent is to be regarded as exceptional"	Not mentioned	
Re-new consent - taking new IC	Not mentioned	Not Mentioned	"renew the informed consent of each subject if there are significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of subjects to continue to participate"	Not mentioned	

TABLE 2-2: SUMMARY OF “ACCEPTING ONLY WELL SUPPORTED RESEARCH” IN THE ANALYSED REGULATIONS:

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
Scientifically sound research	"to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature."	"Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature,"	"must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees."	"reviewing and approving / providing favourable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects."	Not Mentioned
Comply with local guidelines as well as international ones	Not mentioned	"It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. "	"investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organization, and the ethical standards applied should be no less stringent than they would be for research carried out in that country."	Not mentioned	Transnational health research should be responsive to the needs of host countries, and the importance of research contributing to the alleviation of urgent global health problems should be recognized

TABLE 2-3: SUMMARY OF “ACCEPTING ONLY WELL SUPPORTED RESEARCH” IN THE ANALYSED REGULATIONS (CONTINUE):

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
Local research committee approval	Not mentioned	"The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins"	"submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees"	"reviewing and approving / providing favourable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects."	"When research is undertaken or otherwise pursued in one or more States (the host State(s)) and funded by a source in another State, such research should be the object of an appropriate level of ethical review in the host State(s) and the State in which the funder is located. This review should be based on ethical and legal standards that are consistent with the principles set out in this Declaration"
Respect of different cultural norms	Not mentioned	Not mentioned	"...and that are morally acceptable within the communities in which the research is carried out.."	Not mentioned	Mentioned

TABLE 2-4: SUMMARY OF THE “RISK” THEMES IN THE ANALYSED REGULATIONS:

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
No extreme risk	"to avoid all unnecessary physical and mental suffering and injury"	"Physicians must immediately stop a study when the risks are found to outweigh the potential benefits "	"the investigator must ensure that potential benefits and harms are reasonably balanced and risks are minimized."	Not mentioned	"Appropriate assessment and adequate management of risk related to medicine, life sciences and associated technologies should be promoted."
Risk/benefit ratio	"No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects."	Not mentioned	"the investigator must ensure that potential benefits and harms are reasonably balanced and risks are minimized."	"... risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society.."	"direct and indirect ... should be maximized and any possible harm to such individuals should be minimized."
Risk	Not mentioned	"The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention"	"Minimal risk. In this expression “risk” is taken in its common meaning of a possible but not certain adverse effect (on health)."	Not mentioned	"Research which does not have potential direct health benefit should only be undertaken by way of exception,...exposing the person only to a minimal risk and minimal burden and if the research is expected ..."



TABLE2-5: SUMMARY OF SOME OTHER ETHICAL THEMES IN THE ANALYSED REGULATIONS:

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
Identifiable human material and data	Not mentioned	yes: it is mentioned that the guidelines is oriented to regulate human research that use those material	Yes: It differentiated between deniable and non-identifiable material	"The sponsor is responsible for securing agreement from all involved parties to ensure direct access (see 1.21) to all trial related sites, source data/documents , and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities"	Not mentioned
Results available to participants	Not mentioned	"At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it,"	"policy with regard to the use of results of genetic tests and familial genetic information, and the precautions in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives or to others (e.g., insurance companies or employers) without the consent of the subject"	Not mentioned	Not mentioned

TABLE 2-5: SUMMARY OF SOME OTHER ETHICAL THEMES IN THE ANALYSED REGULATIONS (CONTINUE):

	Nuremberg Code	Declaration of Helsinki	CIOMS	ICH-GCP	UNESCO
The conflict of interest	Not mentioned	Not mentioned	"Disclosure and review of potential conflicts of interest"	Not mentioned	"Professionalism, honesty, integrity and transparency in decision-making should be promoted, in particular declarations of all conflicts of interest and appropriate sharing of knowledge."

### **3 Chapter Three: The Saudi Research Guidelines**

This chapter addresses the second research question of this thesis. It discusses the Saudi guidelines, making three main points. The first is that, as they are based on selected influential international guidelines, they kept those documents' normative assumptions. The second is that the Saudi guidelines have captured some of the MGE research issues, but suffer the same level of problematic assumptions as the Western ones, which makes them difficult to apply to MGE research in its Saudi context. Firstly, I will analyse the Saudi research ethics guidelines and the extent to which it is a suitable regulatory framework for MGE in Saudi Arabia, in the light of the Saudi social, culture, and political context, The second subsection of this chapter will analyse the Saudi guidelines, using the same method employed in the previous chapter in relation to the international guidelines, to see how they can be used to regulate MGE research in the context of Saudi Arabia.

Also in this chapter I will build upon the information about Saudi culture introduced in Chapter One, to provide further context to the regulations.

#### **3.1 The National Committee of Bioethics (NCBE):**

The NCBE was initiated with a Royal Decree on 18/5/1422H (24/7/2001G). It consists of 16 members from different official stakeholders including:

- The King Abdulaziz City for Science and Technology (as the most generous Saudi Research funding governmental agency),
- The National Guard (as one of the largest health and research organisation),
- The Ministry of Defence (for their military hospitals),
- The Ministry of Interior,

- The council of Islamic Research and *Ifta'* (the official side of *Fatwa* or Islamic verdict),

- The Ministry of Higher education,
- The Ministry of Health,
- The Ministry of Education,
- The Ministry of Agriculture,
- The Saudi Wild life authority,
- The Saudi Food and Drug Agency,
- The Saudi Human Rights Agency,
- The Office of Research Monitoring,
- A selected representative from the Saudi private sector,
- An official legislative consultant.

In the early days of the national committee, there was a question of who should be the chairman. According to His Highness Prof. Abdulaziz Al Swailem, the NCBE chairman in one of his presentations, the consensus was that the chairperson should be chosen based on the idea that the committee members wanted an impartial representative. The best representative was the King Abdulaziz Medical City for Science and Technology (KACST) for reasons such as its generous funding history, which afforded KACST much respect amongst all Saudi researchers, the availability of resources in KACST, and its infrastructure, which could house and support the committee financially and logistically.

The NCBE consists of four subcommittees: the legal sub-committee, the human research sub-committee, the flora & animal sub-committee, and the education

& media sub-committee. The NCBE hopes to transform the research ethics practice to become more rigorous and better documented through the following steps (NCBE, 2010):

- The first stage is to engage with local organisations interested in research in order to encourage them to establish a local committee that reviews and oversees the ethical conduct of their research. This was supported by Ministerial Resolution number 180 dated 9/6/1425H (26/7/2006), mandating that every organisation carrying out research activity should have its own local review committee.

- The second stage is to register those Local committees: Every local review committee should be registered with the national committee, giving full information of who the chairperson and committee members are, with their credentials and positions.

- The third stage is registration of active researchers: Every researcher is expected to engage in online training about the Saudi regulations, successful completion of which licences him/her to participate in research that recruits human participants.

- The fourth step involves education programmes organised by the NCBE to educate the local committees, which is a necessary step before the last stage,

- The fifth stage is enforcement through monitoring, auditing and activating a punishment system for those who do not comply with the regulations.

The NCBE 2010 guidelines now govern every researcher recruiting donors of biological material in Saudi Arabia, including MGE. However, the overall progress of the NCBE stages is still far from complete, according to a personal correspondence with one of the policymakers involved in preparing a translated version of the NCBE regulations.

### **3.2 The Saudi NCBE guidelines:**

The NCBE has published its regulations for research involving biological material from human and/or animal donors in a booklet with 15 chapters. The most relevant chapters to this research are: Chapter 7: Informed Consent, Chapter 8: Research Using Human material, and Chapter 11: Genetic material and DNA biobanking. For consistency with the previous chapter, the Saudi guidelines will not be described in full but, rather, I will outline the main items pertinent to MGE research.

The NCBE national guidelines address scientists as well as physicians: ‘Researcher: A person academically qualified in a subject related to the research and has completed a course on research ethics’ (NCBE, 2010, p2).

#### **3.2.1 Terminology defined by the NCBME**

Like every Saudi legal document, this one commences with definitions of the terminology subsequently used to ensure clarity and unified understanding, and to avoid misunderstanding. The approach, in most of the cases, seems to be to provide pragmatic definitions rather than to engage with conceptual issues. For example, ‘informed consent’ is introduced as ‘A person giving his consent with his free will,

without exploitation or coercion and upon full understanding of what is required from him and of the research objectives and potential risks as well as of rights and obligations arising out of his participation therein.’ (NCBE, 2010, p3). It is a very broad pragmatic understanding in the sense that it is action oriented. It refrains from engagement with the bigger debate as to what informed consent is, as I will discuss in a later stage of this chapter.

Genetics material was defined as ‘Chain of nitrogenous bases that exist within the cells or are extracted therefrom and are responsible for carrying traits and characteristics from the mother cell to the sub-cell and from one living creature to its offspring’ (NCBE, 2010, p2).

**Ahliah:** It is also noticeable that the official English translation of the word ‘autonomy’ was not chosen. ‘Autonomy’ can normally be back-translated as ‘self governing’ (*Al Hokkm Al Thatti*). Rather, the Arabic word ‘*Ahliah*’ was chosen, which is usually translated as ‘capacity’. *Ahliah* has a specific meaning in Islamic literature. Historically, in the Islamic literature a person is described as having full *Ahliah* by the following specific criteria, when s/he:

- is not mentally impaired or mentally ill;
- is not a child (childhood ends with puberty), Sharei’ laws do not give a specific age as it varies from person to person because it is determined by reaching puberty; however, in Saudi Arabia a person is legally an adult, if he/she is or older than 18 years;
- is not a slave (slavery was abolished in the early 1960s in Saudi Arabia); and,

- has enough mental ability to reflect on what can be rated as a right action versus a wrongdoing.

It appears that the NCBE used the term *Ahliyah* to reinforce the use of the above-mentioned criteria focused on capacity. They did not add any further definition of *Ahliyah*.

**Definition of research designs:** the document differentiates between clinical research, non-clinical research, and clinical trials. Clinical research appears to be defined as any health related research that aims to recruit human participants directly as volunteers to collect data or research materials. Non-clinical research is defined as that which collects data that is not related directly to specific persons and then analyses it to ‘produce general knowledge or facts’ (NCBE, 2010, p5). The only noticeable difference between the non-clinical and clinical research seems to be the source of data. Clinical research seems to require the linkage of the data with its human sources, while non-clinical research collects data that is ‘not directly related to people’ (NCBE, 2010, p5). This could mean that dealing with anonymised data could be rated as non-clinical research, but the data anonymity is not mentioned directly. Based on this understanding, MGE research, if the data is anonymised, falls under the definition of non-clinical research.

### **3.2.2 Sending Biological specimens out of the country:**

In 2003, a royal decree based on NCBE guidance was issued to regulate the export of any biological research material taken from Saudis (Adlan, 2013). This was in response to Saudi researchers seeking international collaborations that included sharing biological material with collaborators in the absence of specific Saudi



guidance for how this should be done. Prior to this, it appears that the sharing of samples was regarded as acceptable practice, given the volume of international collaboration that yielded publications in international journals. It appears that the NCBE gives genetic material a high level of attention as regulating its export was the first official guideline. In 2010, when the full version of the NCBE guidelines was officially announced, they re-used the 2003 royal decree and included it in the final version (NCBE, 2010). Among the export guidelines were the following:

- Collaborations are only acceptable with internationally respected organisations, and where no local research centre has the capacity to perform the research.

- A written legal agreement between the collaborating institutions should be seen and accepted by the local review research committee.

- If there is no other way to perform the research except by exporting the Saudi samples, the biological material should be totally anonymous to the international collaborator, and patients' identity should never be revealed to any third party including, but not limited to, the international collaborator.

- The NCBE committee should be informed and approve the collaboration and the contract, its approval should be received in writing and it should be sent to the collaborator for their acknowledgement.

Anecdotally, researchers in Saudi Arabia have expressed discontent with having to gain the approval of the local committee as well as the NCBE committee, regarding this as an unnecessary waste of valuable time (Adlan, 2013).

The fact that regulating the export of Saudi genetic material was the first and earliest introduced set of bylaws is an indication of a set of assumptions regarding Saudi genetic material, as follows:

a) NCBE appears to regard Saudi genetic material as a strategic resource that ought to be protected. It is not clear from the guidelines how it was seen as strategic, but I will discuss that claim in detail in Chapter Four. Unfortunately, there is no academic evidence as to the practice before these guidelines were introduced. Nevertheless, at an official conference held by the NCBE, one of the national committee members said in a public meeting that he still remembers the days when some researchers used to transfer blood in their personal luggage when visiting their international collaborators. The motivation for the speedy announcement of the bylaws on the export of genetic material is not known, but it could be due to one or more of the following:

- The NCBE believed in some form of genetic exceptionalism. Genetic exceptionalism, as explained earlier, is thinking that DNA material can reveal more sensitive information than any other biological material. It therefore ought to be given an exceptional status and treated differently (Manson and O'Neill, 2007).

- The NCBE may have been responding to a specific (but undisclosed) occasion where Saudi DNA was exploited and/or misused by an international collaborator (or there was a perception of such a risk occurring).

- The NCBE may have assumed that Saudi DNA has commercial potential. The significant rate of first-cousin consanguinity in Saudi Arabia is associated with major congenital diseases (El Mouzan et al., 2008). This high incidence of congenital

disease may have given rise to the idea that the Saudi population could be targeted for research aimed at patenting specific DNA diagnostic tests. The NCBE committee may have sought to protect such a strategic financial resource from being exploited by other countries that may have ensured that donors, through the Saudi collaborator, waived their rights to any future commercial gain. If a patient waives his right over his genetic material, legally his state cannot regain any financial interest in the material. That, however, does not mean that the guidelines gave patients property rights over their own genetic material; to the contrary, it announced that the Saudi genetic material is a national property and belongs to the state.

- The NCBE could have feared biological threats to Saudi Arabia from biological warfare specifically targeting the Saudi or the Arabic genetic population. This interpretation could be supported by an outrage that started in October 2002 when American researchers, working in one of the highly respected Saudi research centres, published a paper in collaboration with a research centre in Israel (i.e. under the Saudi boycott laws to Israel, such a collaboration is impermissible). The views of the non-scientific commentators, fuelled by paranoid rumours, were given greater weight than the scientific evidence supported; some articles condemning that collaboration can still be found on the internet (Arabic-forum1, 2012).

b) The Saudi NCBE committee work under on the assumption that there are respectable international research centres, which could imply that there are also disreputable ones. Such a distinction is problematic, unless accompanied by the means of distinguishing between the two by using objective criteria. The problem with the word ‘respected’ lies in its vagueness. Criteria that could have helped clarify

the guidelines include peer review publication, similar processes for recruitment of donors, and the standing of the scientists it employs. The Saudi Ministry of Higher Education (MHE) faced a similar dilemma. There was a time when the MHE tried to authenticate the degrees Saudi students acquired from non-Saudi universities. To do so they announced lists of acceptable and unacceptable universities. They called it the list of authenticated universities (السعودية خارج في بها المعترف الجامعات لائحة). It appears that the MHE was advised to change the name of the list for a more politically correct one. The word ‘authenticated’ suggested a superiority that is neither accurate nor polite. The list has since been renamed ‘recommended universities’. The new term, ‘recommended’, could be misleading, as students, especially those who are self-funded, are constrained to choose only from those universities that are recommended. Thus it is not recommended, it is mandated if the student wants his degree to be authenticated through the Saudi education system. A similar situation pertains to the notion of ‘respected’ international collaborators, except that there is no list to guide the researcher’s choice of collaborators from outside Saudi.

c) As explained in Saudi health services context (Subsection 1.2.3: Health-related research in Saudi Arabia), Saudi research centres are in competition with each other. This could be the rationale behind the decision to force researchers to seek local collaborations in the first instance. International collaboration is only permissible if there is no Saudi centre that is equipped with the logistics to perform the targeted research. The assumption of aggressive competition is supported by the fact that three of the largest Saudi research centres are in Riyadh, two of them have a noticeable competition over resources, personnel, national projects, and research

funds. Further evidence of competition is that in Riyadh alone there are two competing liver transplant centres, two separate non-commercial cord blood banking facilities, and two separate bone marrow donor registries. Both sets of competing centres claim superiority over the other.

### **3.2.3 Accepting only properly constituted and justified research**

According to the Saudi guidelines, research project can be categorised as poorly constituted or poorly justified and then rejected for many reasons, including:

- where the methods cannot achieve the aims: this usually occurs when the researcher lacks understanding of different research methodologies and their limitations (e.g. someone aims to achieve generalisable data but fails to propose a randomly selected or representative sample);

- where the aims cannot be justified: this usually occurs when a researcher fails to support their aims with an equipoise. In other words only scientific aims are acceptable not political ones even if it is ideological or conceptual research;

Like the international guidelines previously analysed, the Saudi Guidelines share a zero tolerance for unjustified research. According to the national NCBE, protocols should be very well reasoned and articulated, and contain scientific aims and objectives. Local research committees, which are mandatory in every organisation recruiting human for research projects, should approve both the scientific and ethical merits of all research undertaken in that organisation.

Most of the previously analysed international regulations have mandated an independent committee to review the merits of research based on the research

proposal. This process is the mechanism by which potentially poor research is excluded as a step to protect human participants. In the same manner, the Saudi regulation mandated two measures for protecting human participants in research. The first is the local human ethics committee, its main duty being to protect human research participants and reject research that is not worthy of approval for any scientific, ethical, or legal reasons. The second is the research monitoring office, which is expected to monitor both the research in progress and the institutional committees' adherence to the NCBE regulations. The research monitoring office is the enforcement arm of the NCBE. Its main duty is to ensure that the local research ethics committees are complying with the NCBM guidelines.

Previously, in Chapter Two, I concluded that the selected analysed guidelines were written with RCTs in mind, and this seems to be the case also with the Saudi regulations. Despite a clear distinction in the early definition stage between clinical research, non-clinical research and clinical trial, the following quote appears to use the term 'research' in its general form, while specifically meaning clinical trial 'Research conducted on humans shall be for clear scientific objectives, and shall be preceded by sufficient laboratory experiments on animals if the nature of the research so requires.' (NCBE, 2010, p59).

The NCBE guidelines do, however, have a section dedicated to genetic material and biobanking, Section Eleven: Dealing with Genetic Material and its Banking, which consists of seven articles. In this section it is clear that the national committee is very determined to prohibit any unjustified research, by using review processes (i.e. the mandatory approval of a local ethics committee). Approving any

research, including MGE research, means that the local committee is legally responsible for the proper conduct of the research.

The process of local review conforms to the international guidelines e.g. those found in CIOMS, ICH-GCP, the Declaration of Helsinki, and the UNESCO documents. The Saudi guidelines offer very detailed regulation, covering 22 pages, for how these committees should work (NCBE, 2010). Such concentrated effort to regulate the local ethics committees could be seen in the context of the original call for ethics guidelines in the country. The story of the Saudi uterus transplant (see Subsection 1.2.4: The Emergence of Bioethics Debate in Saudi Arabia) seems to have had a dramatic effect on many levels. The Saudi bioethics guidelines at the time were insufficient to determine decisively whether the researcher really deceived the donor, as was claimed, mainly because a signed consent document could be produced. The signature was authenticated by officials (i.e. the donor did sign the document) but how this signature was obtained was unclear (Adlan, 2013). Opinion was, therefore, divided about whether the research was ethical or not (see Subsection 1.2.4: The Emergence of Bioethics Debate in Saudi Arabia). Had the NCBE guidelines existed, the researcher would have needed to apply for, and receive, approval before undertaking the procedure. A local committee would have been responsible for ensuring that neither the patient nor the donor was exploited and the researcher/physician would have been legally and ethically protected by their favourable opinion, assuming the protocol was followed.

The bioethics regulations require committees to have a mechanism for auditing the activities of favourably reviewed research. The office of research monitoring,

which is part of the national committee, is the body that ensures compliance with the guidelines and holds a committee liable for any lack of adherence to the guidelines (NCBE, 2010). The NCBE regulation was not very explicit, however, in the case of uncovered wrongdoing, and how the blame would be shared between the researcher and the local committee. It appears that it was left entirely to the office of research monitoring to decide. It could be argued that it is not fair that the local committee holds responsibility for researchers' actions. Alternatively, someone might read through the guidelines and conclude that the committee would be responsible in the following cases:

- If the research proposal was not reviewed according to the detailed advisory regulations.

- If the local committee gave a favourable opinion to a research proposal that should have not been approved

- If the committee failed to spot researcher wrongdoing during the mandated audit rounds that they should have carried out during the research execution.

Thus, the local committee is not punished for the researcher wrongdoing, it is punished for not following the regulations that would have helped to uncover the wrongdoing.

The researcher will be liable alone in the following cases:

- If the committee reported his wrongdoing to the office of research monitoring



- If the local committee had done everything as instructed, but the researcher was successful in covering -up his wrongdoing.

This understanding of how the liability might be distributed may work only in the case if the researcher was fraudulent. In the case of a genuine mistake, the office of research monitoring has the responsibility to assess how the liability should be distributed. As far as genetics research is concerned, responsibility for approving research concerning MGE or biobanking also rests with the local committee (NCBE, 2010).

In conclusion Figure 3-1 describes the institutional hierarchy to protect human participation in research put in place by the NCBE: the local research committees oversee the researchers and the office of research monitoring oversees the work of the local committees. I have also argued that the regulations were written with RTCs in mind, similar to the selected international guidelines. The monitoring regulation could be seen as taken from the monitoring discipline decreed in the ICH-GCP.



FIGURE 3-1: THE INSTITUTIONAL HIERARCHY OF RESPONSIBILITY FOR RESEARCH GOVERNANCE IN SAUDI ARABIA

#### 3.2.4 Informed Consent:

The Saudi NCBE regulations appear to use ‘informed consent’ in two different, but related, ways. The first is the ‘informed consent’ document that patients sign prior to participating in any research e.g. NCBE article 11 reads ‘No investigator may conduct research on any human subject prior to obtaining an informed consent from him or from his guardian in accordance with procedures specified by the Regulations.’ (NCBE, 2010, p53). The second way is the notion of ‘consent’ itself ‘A person giving his consent with his free will, without exploitation or coercion and upon full understanding of what is required from him and of the research objectives and potential risks as well as of rights and obligations arising out of his participation therein’ (NCBE, 2010, p6). The definition does not mandate the paperwork and signature to record the consent; it simply assumed it. The challenge is that the same

definition could be secured by other means of consenting (i.e. other than by signing a consent document) such as shaking one's head, saying ok, a smile of approval, and many other forms of human communications. On the other hand, it is accepted that informed consent is a species of the concept of consent (Manson, 2007).

This definition, however, is consistent with the international guidelines summarised in Chapter Two. It defines informed consent in terms of voluntary approval and sets out the criteria for voluntariness. In order to be voluntary the approval must be given without exploitation or coercion. The informed part is covered by the requirement for 'understanding' and the scope of the information that must be understood is outlined: the research objectives, the risks and consequences of participation, and the participant's rights (such as the right to withdrawal, or the right not to participate) and responsibilities (such as giving blood, taking medication, engaging in, or abstaining from, activities). The fact that this definition agrees with the international informed consent definitions suggests that it adopts the norms of the international guidelines it cites (i.e. the individualistic notion of autonomy.)

Similar concerns can be raised about this definition as those resulting from the international guidelines. One such concern is the presumption that the Saudi patient can be in a state where they could be free of coercion. This is open to challenge given the vulnerability generated by the patient's need for medical attention. The recruiting research centres are part of highly esteemed, specialized hospitals, which - unlike the free, less reputable governmental hospitals - charge high fees. Saudi patients are likely to feel privileged to have a chance to be treated in those hospitals

(Adlan, 2013). This may render them vulnerable, as they are likely to have a strong desire not to lose that privilege.

Saudi patients are reluctant to disagree with their doctors, including agreeing to invasive interventions that are more invasive than donating blood for any sort of research that the treating physician is involved in (Abolfotouh and Adlan, 2011). This could be due to either the fear of upsetting the doctor in a way that the patient thinks could lead to losing the treatment privilege, or it could be due to the culture of trust (See 1.2.1: The Social Context of Saudi Arabia.)

In Saudi culture, in common with much of the East, family influence plays a major part in a person's decisions. The assumption that a person can decide without such influence is problematic because it does not take into account factors which influence the decision. Another serious point to consider is that the nature of MGE research is such that it involves a whole family, if not the entire tribe. It is important to stress that these challenges are not specific to Saudi culture; they are also reported in different contexts, mostly recognised in non-Western academic writing such as in Arabic or far Eastern contexts (Dickenson, 1999; Tan-Alora and Lumitao, 2001; Widdows, 2009). It is fair to claim that the dominant notion in Western medical ethics is the North American understanding of the value of autonomy, which could be challenging to other norms in Europe (Dickenson, 1999), and which will be discussed in detail in Chapter Four.

The required consent documentation is fully described with a specific set of elements that must be included for the participant to read (NCBE, 2010). This specification appears to have been influenced by the informed consent section of the

ICH-GCP. ICH-GCP was originally designed specifically to regulate clinical trials; this means that the presumption throughout the Saudi informed consent regulations is that it is oriented towards clinical research. This can be noted in lines such as: ‘A description of alternative treatments available outside the scope of the research, if any’ (NCBE, 2010, p53); and ‘A description of all medical procedures and treatments related to the research or carried out only as a result of conducting the research, if any...’ (NCBE, 2010, p53).

In the first Chapter, I introduced the Saudi health context and explained how Saudi patients could be seen as vulnerable when it comes to their relationship with the treating physician (see Subsection 1.2.5.5: Patient Vulnerability). At a regulatory level, the national committee seems to presume a level of Saudi patient vulnerability when it comes to the treating physician. This can be seen in the restrictions on physician-PIs recruiting their own patients to studies: ‘If the human subject is a patient, a person other than his attending physician shall obtain his "Informed Consent," provided said person is well-informed about the research and able to answer all the patient's questions’ (NCBE, 2010, p56).

The national committee gave permission to the local committees to waive informed consent where biological samples cannot be traced back to the donor: ‘...the Local Committee may agree for the research to be conducted without obtaining Informed Consent if it is not possible to link the information in the records or from the biological or pathological samples obtained by the investigator with the source person or if the outcomes related to individuals are available to the public’

(NCBE, 2010, p58). This article is extremely vague and could be problematic when dealing with genetic research in Saudi Arabia for at least two reasons:

- In the Saudi context, it is highly likely that an individual's DNA could readily be used to identify his/her families for the reasons already outlined,

- It is already public knowledge that some tribes are known to be affected by certain inherited disorders, so where these conditions are present in the sample this will give a strong indication as to the person's tribe, which offers some level of identification, although not necessarily right down to the individual. The availability of the result, albeit not the identity of individuals, would create an argument that it should be acceptable to carry out MGE research on Saudis belonging to those tribes without their informed consent.

Due to the nature of the Saudi genetics relatedness, one could argue that the local committee has to consider potential family/tribal stigma in the balance of harms and benefits before agreeing to the waiver. In addition to that, the promise of complete anonymity has been proven inaccurate in the case of genetics information (Boddington, 2012), which also needs to be considered by the committee before any waiver is granted.

In conclusion, the Saudi National guidelines aim to make the regulations in relation to informed consent as thorough as possible. This can be seen in the amount of instruction in comparison to other topics it covers. This might reflect the notion of liberal individualism which has been inherited from the international regulations that were used as its reference point.

### 3.2.5 Biobanking in Saudi Arabia

Donating blood for biobanks is covered by article number 31: ‘A central information bank shall be established at the City to store the information pertaining to the genetic material and to organize its usage according to the procedures determined by the policies. The bank will make the information available to scientific research groups that use the genetic material in the Kingdom.’ (NCBE, 2010, p77)

The article is not clear in terms of where and how such a bank should be established. Moreover, the article does not provide information about how a national DNA bank should be regulated. There are a few vague statements about protecting confidentiality and preventing linkage of the data to its donors (i.e. anonymisation). The guideline seems to suggest that the committee regards genetic material as potentially harmful to the person, such when they suggest: ‘Scientific results shall not be leaked to the media if this could lead to promoting discrimination on the basis of race or family or tribal affiliation.’ (NCBE, 2010, p94). Thus, protection seems to be provided in two ways, the first is through avoiding linking the data to the source (anonymity), while the second is respecting the confidentiality of the donor where anonymity is not achieved.

The National Committee guidelines regarding biobanking can seem laconic when compared to the energy spent on regulating the work of local committees and on informed consent. It does not address data ownership nor answer the question of how the research centres should deal with the wide-ranging data that can potentially be derived from donated genetic material. The only limitation occurs where the local

committee believes that the results could provoke a stigmatization or lead to racial consequences. This might be seen as contradicting the wording of other NCBE regulations about waving informed consent (see the previous Subsection). By this addition MGE research is in a better position and stigma is one of the points that ought to be investigated by the local committee.

Another difficulty concerning biobanks is access to the donor's medical records and history was not anticipated in the guidance. In some hospitals these records may contain the full medical history of the donor and his parents from birth. The National Committee also did not regulate the utilization of this data, nor how anonymity can be achieved when the researchers aim to extract longitudinal data from the donor's medical history. Ignoring such challenges is to overlook a major biomedical research ethics debate that started with closing the deDECOD company, which started the Icelandic Biobank in 1998. They used two informed consent models, the opt-in for the donated material and the opt-out for the stored clinical data (Palsson, 2008). A few years later in 2003, the whole biobank was closed down after being criticized nationally and internationally (Palsson, 2008). These criticisms were centred on various challenges, namely:

- Commodification: deCODE Genetics is a company (i.e., profit-oriented) which raised concerns about selling the Icelandic heritage data for material gain (Berger, 1999). Moreover, deCODE Genetics signed a contract with another giant Swiss pharmaceutical company to finance research on twelve genes specifically (e.g. those thought to be linked to congenital heart disease and Alzheimer's disease) (Palsson and Thorgeirsson 1999).



- Privacy: In January 2000, deCODE Genetics announced that they were in the process of completing the 'Book of Iceland' and were going to publish it on the internet. This announcement raised the level of attention and started to attract an increasing number of activists who were against the exclusive rights given to deCODE Genetics (Annas, 2000). Among the strongest opponents of deCODE Genetics was the Icelandic Medical Association (IMA). The IMA's opposition was based on 'concern about inadequate measures to protect privacy, the lack of access to data among academic researchers, and the belief that individual consent should be required before inclusion of medical records in the data base' (Annas, 2000, p1830).

The main idea of biobanks challenges the individualistic notion of a moral agent (i.e. an independent individual who can decide on his/her own best interests) insofar as it sees the person as part of a larger genetics picture and not as isolated genetically from his family or tribe. The Saudi biobanking regulations appear to confuse biobanking with collecting genetic materials for preapproved research. This claim can be supported by looking at the following article: 'A central data bank shall be established within KACST for the purpose of maintaining information related to genetic material and regulating use thereof in accordance with procedures specified by the Regulations. Said bank shall provide information for research, using genetic material in the Kingdom' (NCBE, 2010, p87). However, in the following article the regulations appear to suggest a model of individual informed consent where the participant needs to be approached and agree to any usage of his material, as article 32.1 tried to illustrate (NCBE, 2010). The challenge with such confusion is that, with

a large number of stored samples, it is very labour consuming to keep contacting individuals about their material every time someone wants to use it.

In conclusion, the biobank regulations in the National Committee guidelines are not sufficient for regulating biobank in Saudi Arabia and they ignore the major international debate about the regulation of biobanks and its challenges, for example, informed consent, data access and ownership, and the lack of any opportunity for donors to withdraw from the banking system.

### **3.3 Summary**

This chapter has demonstrated two things. The first is that the Saudi NCBE regulations appear to have inherited the main normative assumptions of how Western researchers think about ethics. For example, the overall focus of the individualistic informed consent, where there is strong commitment to autonomy. The second argument is that the Saudi NCBE regulations can be used to regulate MGE research but, because of the previous two points there are still some gaps which need to be addressed. We are now in a position to further illustrate the Saudi context in terms of culture, religion and politics to set out how a blend of those factors may pose a challenge to complying with the selected international bioethics guidelines and the Saudi NCBE regulations regarding the donation of blood for MGE.

## **4 Chapter Four: The Saudi and International Guidelines Versus the Saudi Cultural Challenge**

### **4.1 Introduction**

In this chapter, I address the following research question: To what extent do the Saudi and the international guidelines meet the Saudi cultural challenges? I answer this research question by providing a normative analysis of the extent to which the current Saudi guidelines, sources and reference points (i.e. the selected international guidelines) meet the cultural challenges that are associated with specific Saudi Arabian norms and values by examining and discussing potential tensions between them. For this purpose, I critically review the related literature, as well as draw on personal reflections. To the best of my knowledge, very few papers in the literature discuss Saudi Arabian bioethics context and provide an account of the cultural challenges to the implementation of the international guidelines in the field of medical research in Saudi Arabia.

### **4.2 Autonomy-Based Bioethics**

As I argued in the first two chapters, the principal overarching assumption of the analysed international guidelines is the individualistic notion of informed consent. The broad overview suggests that this concept originates from the liberal political and moral philosophy that flourished after World War II in North America and Europe. The idea that an action could be ethical only if the concerned person was informed and agreed to conducting it freely and without coercion or inappropriate influence. Gillon (2003) for example rated autonomy as the most critical of the four principles or what he termed 'the first among equals'. On the other hand Manson &

O'Neill (2007) argued that autonomy is an extremely vague concept and that it is used inconsistently in the literature to promote highly contested views.

The term 'autonomy-based bioethics' reflects notions of respect for personal autonomy and respect of the person in the clinical and research contexts by accentuating freedom of choice and self-determination (Azétsop and Rennie, 2010). Despite the differences among them, the numerous definitions of autonomy tend to include an emphasis on agency (i.e. the personal capacity to act intentionally) and liberty (i.e. the ability to take decision free from influences) (Gillon, 2003; Manson and O'Neill, 2007; Beauchamp and Childress, 2001; Azétsop and Rennie, 2010). The Nuremberg Code, which is among the most highly regarded international biomedical ethics guidelines and one of the principal references that have crystallised the new Saudi bioethics guidelines, is one of those documents leaning towards autonomy-based bioethics based on the criteria agency and liberty (see Subsection 2.2.2: Consent).

Individualism is pivotal to the autonomy-based model of bioethics as it is mainly orienting its attention to obtaining the informed consent of 'individual research participants' with less attention given to what is best for the community where the research will be conducted (Azétsop and Rennie, 2010).

To summarise the agreement on the autonomy-based bioethics model, it seems that it is built on two principal assumptions: 1) the liberal commitment to decision-making: in the Western societal context, this makes sense because liberal values are prized within that society. They even constitute the principal theory of international relations, which assumes that the election of leaders is an individualistic act that is

independent from the state's direct influence and based on free choice through the operation of democracy; 2) Agency: the ability of an agent to make decisions free from external influence.

In Chapters Two and Three, I argued that the Saudi regulations and the international selected research ethics guidelines were oriented toward promoting individualistic notions such as promoting informed consent. Accordingly, and based on autonomy based bioethics, the Saudi guidelines and the international ones are mainly autonomy oriented guidelines. I will further, in this section, assess the suitability of such an approach to the Saudi context.

Autonomy-based bioethics would not be the best framework to regulate MGE research in general because the participant is not an individual in the sense that his/her genetic material is shared with his/her kin, (Widdows, 2009) nor considering the genetically homogenous nature of the Saudi population specifically (See Subsection 1.2.5.3 Stigmatisation). The Saudi NCBE regulations made it clear that the national committee's main job is to insure that informed consent was properly given. Informed consent is pivotal to the autonomy-based bioethics model, and is problematic because the individualistic decision of the research participant has ramifications for the information of other individuals who chose not to participate or do not want to know the results of MGE 'tests'.

Another challenge that ought not to be neglected is the level of education of the average Saudi. The autonomy-based bioethics model seems to shift the responsibility for decisions to the patient in the clinical setting and to participants in the research setting. Such responsibility requires a full awareness of the ramifications of any

decisions. One of the requirements of informed consent is to provide full information to the consenting person to enable an informed decision to be made by them based upon what they want to do. The Saudi guidelines devote many articles and sub-articles to describing the content of the consent document as a means of educating the patient. There are many challenges in this approach (i.e. expecting the form to be the ultimate tool of disclosure) like the assumption that patient will read carefully, a document that is neutrally written, with a level of disclosure that does not omit any information, and contains all the facts s/he needs to have, and most importantly do all of this in a small window of time. To start with, Manson and O'Neill (2007) argued that it is impossible to provide such a document (i.e. neutral, explicatively disclosing and with no omissions). However for the sake of argument I will assume that someone could provide such a document or process. Even so it requires a certain level of education to absorb that information, weigh it against his/her own interests, family interests, and tribe's interests in the case of MGE research in Saudi Arabia, and then decide. The nature of the Saudi political cultural climate does not support such assumption. As I explained in Chapter One, Saudis tend to accept the physician's decisions with no objections (Al-Jumah and Abolfotouh, 2011; Jamjoom et al., 2011; Adlan, 2013).

Saudi patient vulnerability (see Subsection 1.2.5.5 Patient Vulnerability), suggests that they will not decide free of a physician's influence which was discussed earlier. The autonomy-based bioethics model gives more weight to the informed consent practice, therefore any challenge to the informed consent would also challenge the autonomy-based model, and this is certainly the case in Saudi

Arabia. The hospitals that have the capacity to recruit for MGE research are the highly specialist hospitals (See Subsection 1.2.3 Health-related Services in Saudi Arabia). Those hospital are not part of the free Saudi MOH services, they are usually the most expensive services in Saudi Arabia. However, Saudis can ask for the support of a Royal Prince Order to wave the health cost charges according to strict eligibility criteria; this means that the bills will be transferred to the Crown Prince to pay (Adlan, 2013). Giving the impression that a very expensive service is going to be given for free would create a sense of gratitude that might impinge on the patients' ability to say no. The long waiting lists even inside these specialist hospitals places patients under stress because they are on waiting lists for months or, in some cases years, before their follow-up visits.

In addition to all of those features, Saudis, like most people in the Eastern world, are oriented to thinking about decision-making within the context of and benefit to the extended family, not just what is wanted by or is best for any one individual (Tan-Alora and Lumitao, 2001; Barr, 2002). This is a point taken up by some Western commentators who argue that health ought to be perceived in a more general way than just as the right of several individuals to decide (Ter Meulen et al., 2007). In Western ethics, on the other hand, there is nothing to stop an individual regarding his/her interests as being inseparable from those of his/her family or community. But individuals are not presumed to be subjugated to the interests of the family as a whole. However, according to Dunstan (1994) individualistic autonomy presupposes the right to decide what to do based on one's own preferences about what matters in one's life without interference by others. This view is dominant in

Western liberal bioethics literature (Stirrat and Gill, 2005). Dunstan (1994) contrasts this with non-Western cultures, where ethical norms do not require having the right to choose as individuals. Most decisions are not made with a sole focus on the individual themselves; rather, they concern how decisions would affect not only one's spouse and children but also one's parents, siblings, and, in some cases, one's wider family. The core difference, I therefore argue, is in how the policymakers see the patient, not the grounds on which the individual's decision is taken. The policymaker regards the patient/participant as an individual who has the right to decide individually according to his own beliefs even if the decision would infringe on others' interests. Alternatively, someone might say that the policy-maker ought to look at the participant as part of a community, tribe, or family that could be harmed by that individual's decision. MGE research in Saudi Arabia is regulated based on the autonomy-based bioethics where an informed consent document records the consent of participants as individuals rather than as part of bigger families, or even tribes.

In the Saudi context individualism might not be the most appreciated value; family however is considered to be extremely valuable for Saudis, and it lies between the levels of individuals and governments. The marriage between two people, for example is about family decision-making, it is the union between two families or, in some cases, two tribes, not just two individuals. Thus, the approval for the marriage should originate from a circle of people that is larger than the two persons who wish to get married. Such practices provide a cultural safety net, if something goes wrong. For example, if someone has children, the whole extended family is morally



responsible for taking care of them in the event that their parents are unable to do so. In the extreme case, people take the value of family to mean that when a father dies, it would be the duty of his brother to marry his widow and raise his children. In such a culturally rich environment (i.e. where even marriage decisions are taken by the entire family and brothers feel obliged to raise their nephews and nieces) promoting an individualistic autonomy-based can be regarded as untenable (Alsuwaigh, 1989).

Despite these complex cultural forces, the current Saudi guidelines suggest that consent should be gained from individuals. The concern is that in Saudi Arabia, MGE research is still in its early stages (Adlan, 2013; Abolfotouh & Adlan, 2011), although because of massive investments, MGE research is advancing rapidly. The common practice, however, seems to be international collaborations, which help researchers to advance their knowledge and publish in higher impact journals. That in turn depends on research with global impact thereby encouraging further international collaborations (Alwattan, 2015).

Notwithstanding the cultural norms of family decision-making there is the additional issue that MGE research may have an impact on whole families rather than individuals. For instance, according to Saudi policies, collecting blood from a few members of a family who have individually consented is sufficient to conduct family-based genetic research. Depending on the type of investigation, a research team can obtain information about a whole family, including those family members who did not consent. This is a general issue raised in genetic research, not only MGE research in Saudi Arabia (Hallowell et al., 2003; Forrest et al 2003). However, what makes such texts in Saudi Arabia more controversial is that the genetic information

from one family can give substantially reliable information about the whole tribe because of the genetically homogenous tribes in Saudi Arabia that was described earlier (See Subsection 1.3 Challenges of MGE research in Saudi Arabia).

One of the principal objections to the current Saudi guidelines is that individualism seems to undermine the value of groups, family and/or community. This encourages the idea that when a critical medical decision must be made, health providers look for people to decide what is best for them individually, which, in some cases, comes into conflicts with the potential good of families or communities (Wolpe, 1998, Lindemann, 1995, Bowman and Hui, 2000, Glass and Rud, 2012, Etzioni, 2011). Despite all the challenges described in this subsection, autonomy-based bioethics is a main characteristic of the Saudi NCBE regulations. It seems to adopt the idea that signing the individual informed consent form is the main tool to protecting a participant's interests.

### **4.3 Informed consent in Saudi Arabia**

As explained previously (see Subsection 1.1.1 Informed Consent) the consensus among research bioethics commentators is that voluntariness (assuming competence), disclosure (assuming full understanding) and decision (accepting or refusing) characterise informed consent (Meisel and Roth, 1981; Beauchamp and Childress, 2002). Disclosure, for example, was argued to be an unrealistic expectation; and the paradox is that if it is not fulfilled a question would be raised about the legitimacy of informed consent (Manson and O'Neill, 2007). The main disclosure assumption is that an explicit amount of information should be disclosed to participants, which includes all the relative information about the research, the

choice, the alternatives, the risks with their likelihood and any information that might affect the final decision in a way that is comprehensible to the participant. The list of details is growing to the extent it would be impossible to comprehend the whole amount (e.g. a 30 page consent document and/or information sheet) (Manson and O'Neill, 2007). Due to the complex nature of MGE research where information is very sophisticated the disclosure would be even more difficult.

#### **4.3.1 Informed consent and the assumption of vulnerability**

The other challenge to the way in which informed consent is gained, is the assumption of voluntariness. I will take voluntariness in the same way intended by the Saudi NCBE regulation as being free to act without exploitation or coercion (NCBE, 2010). Beauchamp & Childress (2009) argued that coercion requires a genuine actual threat of force to 'displace a person's self-directed course of action' (Beauchamp and Childress, 2009, p133). The problem is that both physician and patient/participant come to the consent interview with a set of norms and values that drive specific assumptions about the relationship between them (Corrigan, 2003). Therefore, it is problematic if a person genuinely thought that upsetting her physician by saying 'no' would threaten her treatment privileges or might cost her access to that physician.

An informed consent is intended to prevent overt coercion (Corrigan, 2003), but covert coercion also needs to be taken into account. For example, in the Saudi context as I explained (see Subsection 1.2.4 Patient Vulnerability) patients are under the influence of two strong forces. The first is their feeling towards their physicians as their healer who should be trusted without question. Second, the fact that MGE

research is running in most sophisticated hospitals where only those who have the support of a Crown Prince can be treated (see Subsection 4.1.1 Autonomy-Based Bioethics). One can argue that this is especially the case because there were no clear unified Saudi research ethics guidelines before 2010 to address the risk of coercion among Saudi patients. This means that physicians were acting according to the environment of trust rather than a dictated specific imported ways of understanding coercion.

#### **4.3.2 Informed consent and the value of trust**

This environment of trust is not alien to the Saudi cultural context explained in subsection 1.2 The Saudi Arabian Context. The reality of the tribal culture is built on trust. The tribe members come to trust a specific person in the tribe, either one of their elders or the most religious tribal member. This person is trusted to protect the interests of his people under the tribal cultural laws. This culture is even reflected in the Saudi political system. The Saudi monarchy is mainly a tribal monarchy. In this system the king represents the family wise person, the elder who make decisions on behalf of the tribes that agreed to obey him. Based on this, it can be said that the value of trust is deeply rooted in the Saudi culture. Therefore, it is not strange for Saudis to try and find an authoritative figure in health-related services to trust and obey.

This, however, should not mean that Saudis must trust their physicians to the extent that they will donate blood for MGE research even when this is something they do not want to do. Consent must be crucial; the problem is that a signed document is all that is needed to extract patient blood for MGE research.

### **4.3.3 Informed consent in Saudi hospitals**

Saudi hospitals used to use their own local hospitals' regulations to regulate research and, specifically, informed consent long before the Saudi National Committee announced its new regulations in 2010. One of the central goals of the national committee was to provide unified regulations for all the hospitals and research centres that legally bind every researcher who uses human participants. In numerous cases, informed consent in Saudi Arabia is no different than many other places that reduced the informed consent process to the technicality of a signed informed consent document on official paper (Abolfotouh and Adlan, 2011; Adlan, 2013).

Another point that might affect the consent process, as understood by Western policy-makers, is that there is a clash between the regulations (i.e. expecting Saudi patient to choose based on explicit informed consent) and the Saudi culture (where a patient trusts his physician to uphold his best interests I have already published the results of a quantitative cross section survey that suggests that patients are dependent on their physicians and fear upsetting them (Abolfotouh and Adlan, 2011). It was a survey of 162 patients designed to assess the quality of informed consent for invasive procedures at a tertiary hospital in Riyadh, Saudi Arabia. The majority of the patients (87.7%) who agreed to sign the informed consent form thought that they were fairly well informed, despite 66.5% reporting that they were told that signing the form was simply routine paperwork. We doubted the claim that patients were informed, they might think that they were informed because they were told that the signature on the informed consent form is just paperwork (Abolfotouh and Adlan, 2011). In addition,

approximately 35% of them thought that the information given as part of the process of gaining consent was insufficiently explained to them. Another interesting finding was that the mean score of the overall experience and satisfaction is almost  $54 \pm 17.88$ , which reflects lack of satisfaction. Sixty-six percent of the surveyed sample reported that they were told that the informed consent is just paperwork. This could mean either that the Saudi doctors are breaking the law or it could support my overarching argument that autonomy-based bioethics framework need to be reviewed to regulate bioethics in Saudi Arabia. Among these survey participants it seems that patient-physician relationship was more regarded than the right of patient to decide individually because the overall quality of informed consent is better when the doctor is the one who is taking consent as oppose to any other member of the research team (Abolfotouh and Adlan, 2011) which reflects the importance of patient-physician relations.

Another cross-sectional survey of 528 persons attending Saudi outpatient clinics at a tertiary care hospital investigated patients' attitudes towards the idea of using their medical files in retrospective research without their consent and using their surplus tissue in research (Al-Qadire et al., 2010). They reported that patients are more likely to accept researchers using data from their medical records (MR) than non-patient (companions) who attended the same hospital. Most importantly, they found that Saudis perceived MR differently to surplus tissue-based research, which is strong indication, that blood, even surplus blood, ought to be treated differently than MR.

It is also important to note that Al-Qadire's (2010) findings in term of people who wish to be consented contradicts the work I published in 2011. They reported that only 38% and 37% of their sample would accept use of MR and Tissue-based Research (TR) respectively without consent. It is important to bear in mind that the sample population is different but more important than the population difference is that both are cross sectional studies using surveys. The main limitation of cross sectional studies is that they only provides specific information about a specific time in a specific context described by the researchers which means it is not generalizable (Sugarman et al., 2001). Another way of looking at it is that in our 2011 published work we found a positive correlation between the overall satisfaction and quality of the informed consent when physicians are the ones who gain consent. The 2010 study did not specify the consenting context (for example who asked the patients to consent).

#### **4.4 Stigma in the tribal context**

As I explained earlier (see Subsection 1.2.2 The Saudi Cultural Context & Subsection 1.3.3. Stigmatisation), in the Saudi tribal context, stigma is one of the most substantial risks in MGE research. This is because of the genetically homogenous composition of most of the tribes in Saudi Arabia. In the international guidelines, I could not find any specific regulations that could be used to protect people from stigma in this context (when information derived from family has the potential to stigmatise their tribe.)

However, Article 36.2 reads 'Scientific results shall not be leaked to the media if this could lead to promoting discrimination on the basis of race or family or tribal

affiliation' (NCBE, 2010, p94). This can be seen as a strong indication that Saudi policymakers understand the risks of MGE research in the genetically homogenous Saudi context.

Another article in the NCBE puts a clear restriction on any research that is intended or can be perceived to be intended to promote discrimination: 'Research with negative impacts on society may not be conducted, especially research reinforcing racial discrimination' (NCBE, 2010, p94).

The main challenge in the two articles is that they did not mention stigma, in fact the NCBE did not regulate to avoid stigma specifically in its regulation. These two articles are the closest it gets to discuss stigma in the NCBE regulations. Genetic discrimination could be seen as the unfair deprivation of the rights of a person, family, ethnic group, or tribe solely based on information derived from their genes, that indicates an apparent or perceived variation from what is deemed to be the normal or healthy human gene (Kenen and Schmidt, 1978; Billings et al., 1992). In other words, it could be taken as treating people unfairly. On the other hand, stigma has been the centre of many definitions and debates because mainly it is perceived differently based on the complexity of what is alleged to be stigmatising or discriminating (Parker and Aggleton, 2003). Space does not permit me to enter into a lengthy debate about what stigma is. Rather I will adopt a simple and pragmatic definition offered by Boddington (2012): 'An individual who suffers stigma is disqualified from full social acceptance.' (p.99). The word originates from the Greek practise of marking the body of slaves or criminals in a way that makes it visible to everyone else that those marked people are of an inferior status (Boddington, (2012).



Stigma has mainly been discussed as a sociological practice. Therefore, one can conclude that what can be regarded as stigma is based on system of beliefs, values, and behaviour.

For a long time, people who were most stigmatised in Saudi Arabia were those who had contracted sexually transmitted diseases—the assumption was that they became infected from engaging in forbidden sexual activities (Badahdah, 2010) — and those with psychiatric disorders (Shahrour and Rehmani, 2009). In the case of genetic information, stigma can be assigned to a person even if he or she is perfectly healthy, but is known to be a carrier. Some researchers suggests that people have refused to undergo genetic testing, even for diagnoses (i.e. not research) where physicians wanted to test for genetic susceptibility to epilepsy (Obeid, 2008; Koura et al., 2012) or to autism in Saudi Arabia (Alqahtani, 2012) because in both cases society treats carrier families for such mutations as defective. Genetic research presents a new challenge, where the results of genetic testing could be used to deem a person as “defective.”

It is fair to say that not every molecular abnormality is regarded as stigmatising. For genetic information to be stigmatising, it must first be placed in the public domain and then perceived by people as demeaning. For example the claim that a majority of people from the X tribe are carriers of G6PD disorder (See Subsection 1.3.3 Stigmatisation) could be a fair description of an epidemiological finding. It can be described as stigma only if people from tribe Y starts to rate tribe X as inferior to them. It could be argued that such stigma could then lead to discrimination either in cultural domain (i.e. social ranking) or at a personal,

economic level (i.e. medical insurance). In the Saudi context the consequences of stigma have reached the level of discrimination in the cultural domain (See Subsection 1.3.3 Stigmatisation) and soon, with the introduction of health insurance, will extend to the personal economical level.

The important question is whether, if we had the NCBE regulations 30 years ago, the current level of stigmatisation would be less than it is now? It could be argued that the NCBE guidelines' lack of mentioning stigma, suggests the answer is 'No'. It is impossible to stop MGE research results reaching the public domain. This is because as soon as advances are published, even in the purely academic domain, the chances are that it would reach the public eventually, and some tribe members could find out and then use that information to stigmatise others (see the way MGE research has been utilised for proof or disproof blood purity Subsection 1.3.4 Blood Purity).

MGE research is advancing rapidly the world over and not just in Saudi Arabia. Therefore, it is important to address potential stigmatisation as a problem with two dimensions: a) to deal with existing stigma and remedy its consequences; b) to prevent further stigmatisation which is more general than its consequences.

It could be the case that the Saudi policymakers wanted to be pragmatic in responding to stigmatisation and discrimination by bolstering the importance of participant confidentiality, defined, for instance, as 'Non-disclosure or passing of any data, information or results related to the research or the human subject, to any third party not connected with the research.' (NCBE, 2010, p8). 'Set ethical controls and monitor implementation thereof to safeguard rights of human subjects during

research and ensure confidentiality and security of research information' (NCBE, 2010, p19). The challenge, however, as I argued earlier (see Subsection 2.2.4 Identifiable material) is that genetic material, even if fully anonymised still harbours the risk of providing the basis for guessing family names by simply marrying data in different databases (Gitschier, 2009). Gitschier (2009) demonstrated the possibility of making an educated guess about the family names of participants in the HapMap project, which began in 2002 and included numerous countries with the aim of identifying human genetic variations. The HapMap project included a large Mormon population. By using data triangulation (i.e. by correlating information from different available sources), Gitschier could make educated guesses about the family names. Because of her work, the HapMap project re-consented all the participants to ensure that they understood that such identification might be possible (Boddington, 2012). Accordingly, in Saudi Arabia, you can know the region where a person comes from and his family name due to the genetically homogenous nature. The NCBE guidelines seemed to aspire to further protection from stigma by announcing that the state owns the National Saudi genetic material and its data.

#### 4.5 Ownership<sup>4</sup> of Genetic Material

Because Article 31.4 did not elaborate on the Saudi policymakers' reasons for protecting the Saudi genetic material as a national property, I will offer three potential explanations: 1) genetics essentialism, 2) monetary interest, and 3) national security, and discuss each in turn.

The first possible reason is that Saudi policymakers might entertain a level of genetic essentialism, which is the reduction of human beings to DNA (Boddington, 2012). It could be the case that Saudi policymakers think that the core of Saudi identity is incorporated in the Saudis' DNA. The fact that Saudis are culturally tribal could support this assumption, because every tribe has preserved its blood purity. Therefore Saudi genetic material assumed the status of national heritage to be protected and not to be commodified. However, the genetic data that MGE research has generated presents a similar problem. Such guidelines raise a more critical question of what can become a commodity, whether it is the DNA material itself or the data that was generated by it. The guidelines tried to avoid distinguishing between the genetic material and the data that is generated from it by declaring that the material itself is owned by the state to prevent the causal sequence of having

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4 The term 'ownership' has several different, precise meanings and connotations within philosophy and again in law. As it was used in the NCBM guidelines' (translated English version), however, the term 'ownership' was not meant in either of these senses. Rather, it means something more akin to 'control' or 'authority' and was simply intended to prevent sending genetics material outside the country in international collaborations that do not respect the Saudi patient rights over any future patents. Therefore, it seems that NCBE did not attempt to look at ownership through commodification, or through contracting rights, or in any way that sees the body as mere property (De Witte & ten Have, 1997; Thomasma, 1997; Gillett & McKergow, 2007).

genetic data out of Saudi legislative control. The guidelines, however, did not draw a clear line between the individual's right to his or her genetic material and the state's right to Saudi genetic materials. For example, if someone wanted to contribute his own blood to an international organisation, the policy does not provide clear guidance as to whether the person can be prevented by the state or whether there would be sanctions if he could not be prevented but went ahead anyway. In another scenario, if the person does not want to donate his blood, does the state have the power to force him because the material that he refuses to give is not his, it is for the state? Between these two extreme scenarios there are many other problematic situations like hundreds of samples already sent to other international collaborators who received each one of those sample with individually signed informed consent gained by the Saudi collaborator.

The second possible reason is that Saudi policymakers might consider protecting Saudi rights in any patents that could emerge from using Saudi genetic material because they believe that patenting it could be financial beneficial. It could be the case that the Saudi policy makers wanted to prevent what happened in the famous case of Moore versus Regents of the University of Los Angeles which was won by the defendants who used a tissue line that was successfully harvested from James Moore but they denied him any financial benefits (Lavoie, 1989). Due to the nature of the Saudi tribes' genetic material and how it concentrates genetics variations from hundreds of generations as described in the first Chapter, the committee seem to think that the Saudi DNA attracts particular interest in relation to the study of rare diseases. Such interest could result in either cure or a patented test

where even the DNA donor organisation cannot use the test for its own patients without incurring inflated charges imposed by the patent-holder.

A third possible reason could be that Saudi policymakers are very conscious of the possibility that its enemies could use the Saudi genetic material to manufacture specific biological weapons that target only Saudis.

One, two or all of these three could be the reasons for the existence of Article 31.4. The wording of the article does not suggest which one of the three possibilities is more likely, therefore it was important to ask stakeholders in the empirical arm for their opinion on this. To the best of my knowledge this is the first attempt to try to understand this article in its context. In the following Subsection I will explore whether the NCBE regulations are enough to protect Saudi genetic material. Regardless of what is the most likely explanation, the NCBE regulations seem to regard Saudi genetic material as in some way special.

#### **4.6 Sending Saudi genetic materials outside Saudi Arabia**

In this subsection I will try to contrast the claim of special rank bestowed upon Saudi genetic material with actual practice. I will demonstrate two avenues by which Saudi genetic material can reach an international research centre. These two avenues could be seen as a challenge to the regulations insofar as these unregulated practices challenge the NCBE regulation normative assumption regarding the duty to protect Saudi genetic materials.

Someone might argue that under the assumption of special rank bestowed on Saudi genetic material, the NCBE regulations tried to minimise sending Saudi

genetic material abroad for research. However, it cannot prevent the export of Saudi genetic materials, as it does not address these two avenues. The first avenue is the sending of blood samples to international laboratories for clinical reasons. This will often happen when hospitals have a contract to carry out some laboratory tests in an internationally approved organisation or when the technology required to perform the tests is not available in Saudi Arabia. Usually, these organisations seek informed consent that either waives a right to ownership by the patient or gives permission to the organisation to do as it pleases with any surplus blood (Tutton, 2002; Godard et al., 2003). The more serious challenge is sending blood abroad for genetic diagnostics. In some cases, the physician is not sure what test to run as he is not sure of a diagnosis; thus the blood is sent for what can be regarded as full genomic analysis, such as microarray or even synopses analysis (i.e. both tests are from the most sophisticated genetic analysis used for both research and clinical reasons). It could be argued that some researchers from the private sector could exploit this avenue to facilitate research collaboration without seeking any prior approvals. The Saudi policies seem to control the export of genetic materials (see 3.2.2 Sending Saudi Genetics Material Outside Saudi Arabia), but to the best of my knowledge, they do not explore the divide between research and clinical investigation, which would, in theory, leave open a back door by which genetic material could leave the country.

The second avenue is the sending of buccal cells (swabs from inside the mouth taken for DNA extractions) to websites by private individuals who wish to obtain information about paternal lineage. This avenue could be problematic for two main

reasons. First, if the Saudi policymakers think that genetic material ought to be protected, this avenue leaks valuable material without any kind of control. This is a real test of the claim of the Saudi policymaker regarding the ownership of Saudi genetic material by the state. In this case, individuals or groups of people express their autonomy taking advantage of services that are beyond the reach of Saudi research governance. This raises the question of the relative weight to be attributed to personal autonomy versus the state claim of rights to genetic material which will be discussed under the light of the collected data. The second reason is the nature of the Saudi tribal culture, where the better proof of pure blood means greater respect and thus a higher rank in society. Some online services, those offering individual-oriented genetics lineage testing, seem to encourage a level of biological or genetic superiority claims among Saudis.

In a tribal culture like the Saudi one, the quest to prove superiority by genetics testing could be seen as problematic, because genetic research has empowered individuals to claim a higher status in society as well as to stigmatise whole families for not being truly the descendants of those they have claimed all their life. For many reasons like those I argued earlier (see Subsection 1.2 The Saudi Arabian Context), such genetics testing empowers a whole new social ranking system among Saudis (Arab-DNA, 2012; Howitat, 2012) (see also Subsection 1.3.4 Blood Purity).

Keeping in mind those two unregulated avenues of sending Saudi genetic material abroad and contrasting it with the NCBE regulations, NCBE regulations risk being inconsistent.



#### **4.7 Summary**

This chapter has outlined three main normative challenges that pose a tension between the current NCBE regulations and Saudi culture. The first tension was between the autonomy-oriented ethos adopted by the NCBE regulations and the cultural nature of Saudis. I suggested that Saudis tend to be more trusting of the healthcare provider due to the nature of Saudi tribal and political culture, and thus providing a signed consent form may be regarded as just paperwork.

Also, in regard to the concern of how stigma is treated in the NCBE regulations, I argued that it is not enough to regulate discrimination, which could be seen as one of the harms resulting from stigma, without addressing the source (i.e. the risk of potential power of the genetics research to stigmatise not only individuals but also tribes).

I then discussed the assumption that the Saudi genetic material has been afforded a special position, and challenged the consistency of that assumption. The NCBE seems to think that it ought to protect Saudi genetic material but it does not explain why. In this chapter I suggested three different explanations, and then provided two examples where practice remains unregulated.

In conclusion, at a normative level the NCBE's regulations, despite its best effort to include some of the cultural concerns, can be seen to conflict with some Saudi cultural values. This could be due to the fact that most of the normative assumptions inherent in the Saudi NCBE regulations are inherited from the Western

normative assumptions found in the international policies used as reference points for the Saudi ones.

### **Section One: Summary**

In this section I provided a normative analysis in three levels: the first was the international guidelines that were used to inform the Saudi ones, the second was Saudi NCBE regulations, and the third level was assessing tensions between the NCBE regulations and Saudi culture and values, drawing on descriptions provided in the introduction about the nature of Saudi culture and its social, political and religious values. I concluded that Saudi culture poses many challenges to the recently developed NCBE regulation.

I concluded that the set of assumptions about how ethics should be considered was inherited from the international selected guidelines to the NCBE regulation. Such assumptions posed tensions in many domains when MGE research is considered. I argued that the Saudi NCBE is dominated by values derived from liberalism, or more precisely a vision of liberalism where there is a strong commitment to individual autonomy. As a result the concept of informed consent was empowered, the harm principle guides the justification of action, and paternalism is seen as something that is to be avoided.

I contrasted those values to a normative analysis of the Saudi culture drawing on personal experience, and literature reviews. I am now in position to test these challenges and tensions using empirical data to explore how stakeholders in MGE research in Saudi Arabia operate around these issues.

## **Section Two: The Empirical project**

### **5 Chapter Five: Method**

#### **5.1 Background**

This chapter will explain the empirical study's design and justify the choice of method (the tools used to collect and analyse the empirical data), its methodology (the theory behind the selected method), and the challenges faced in the fieldwork.

#### **5.2 Design**

In the empirical study for this thesis, it was important to focus on the participants' words and perceptions in order to uncover the tacit meanings and set of norms with regard to donating blood for MGE research in Saudi Arabia. Qualitative methods could best achieve this (Silverman, 2005; Denzin and Lincoln, 2011). Three different established methods of qualitative data collection were used and the choice of each is justified below. Quantitative methods were not appropriate as they are mainly concern with the measurement of variables in controlled settings (Denzin and Lincoln, 2011). Quantitative research facilitates the calculation of relationships between variables that are collected by pre-prepared instruments (Becker, 1996). Based on this understanding of the nature of quantitative research, it is a useful tool to measure proportions of individuals with specific beliefs or attitudes and statistically to calculate associations, significant differences, or predictions between them, their demographics, or their socio-demographics factors, aimed at generalizable findings (Hull et al., 2001). Therefore, quantitative research was not suitable for the purposes of this empirical study as, to meet its aims, it needed to

explore the meanings, values, concepts, experiences, and reasons used by Saudis in the context of MGE research.

## **5.2.1 Data Collection**

### **5.2.1.1 Overview**

Phase One: data were collected through observation of patient recruitment for MGE research. The intention was to view individuals' behaviours in their natural settings in order to determine the extent to which there was adherence to the current Saudi bioethics guidelines governing recruitment.

Phase Two: data were collected through semi-structured interviews with individuals who had recently donated blood for MGE research. The aim of the interviews was to explore how the interviewees experienced donation and recruitment for MGE research and the extent to which they understood what they were agreeing to in their consent interview.

Phase Three: data were collected using focus groups comprised of researchers (group 1) and bioethics policy-makers (group 2). The intention was to explore how the participants thought MGE research in SA was and should be governed, and to gain participants' reactions to the practices and experiences encountered in phases one and two.

Having provided an overview of the methods chosen for data collection I will now describe and justify each phase in detail.

### 5.2.2 Phase One – Observations

A useful and pragmatic definition of observation as a research method is given by Marshall and Rossman (1989) as cited in Kawulich (2005): ‘the systematic description of events, behaviors, and artifacts in the social setting chosen for study’ (p79). Observation is associated with ethnography, as it enables ethnographers to observe phenomena in their natural context using their own five senses to provide what can be described as ‘written photograph[s]’ (Erlandson, 1993; Kawulich, 2005). However, ‘it is important note that the two [participant observation and ethnography] are not synonymous’ (Ives & Damery, 2014, p109). In other words, ethnography is not only participant observation and, most importantly, not every participant observation is ethnography (Ives & Damery, 2014).

There are two main methods of observation: direct observation (Kawulich); (Bernard, 2011; Hull et al., 2001) and participant observation (when the researcher assumes an ‘insider’ role and becomes part of the observed setup) (Hull et al., 2001; Kawulich, 2005). The main goal of observation in this phase was to directly view both those who were giving consent and those who were receiving it in MGE research recruiting sessions. Observation was used according to Mays & Pope (1995) account namely as ‘it can help to overcome the discrepancy between what people say and what they actually do.’ (p3) Passive observation, or what Bernard (2011) and Hull et al. (2001) called direct observation was chosen because of the risk of going ‘native’ which is described by Mays & Pope (1995) as ‘becoming so immersed in the group culture that the research agenda is lost, or that it becomes extremely difficult or emotionally draining to exit the field and conclude the data collection.’ (p3).

Observation enables non-verbal communication, including how the participants acted in the study situation, as well as how the recruiting process time was spent (Schmuck, 1997) to be recorded. Observation enables the uncovering the tacit aspects of values or culture that remain out of our awareness (DeWalt and DeWalt, 2010).

I was a passive observer and did not participate in the observed consenting procedure in any way (Robson, 2002). The observations were not video or audio recorded, but extensive field notes were taken. No identifying information was recorded in the field notes. Prior to the observations, I read the observed organisations specific clinical policies related to research consent interviews. This was to determine whether these conformed with the NCBE guidelines. This also enabled me to observe the extent to which the practices I observed conformed to the organisations own guidelines.

I, as a researcher, was aware of the challenges around observation as a qualitative research methodology. The most important two challenges were the observer effect and the robustness of the data collection. Observer effect usually refers the potential for changes in people's behaviours when they are under the impression that they are being observed. To overcome this challenge, or at least minimise its effect, it is usually advisable to spend the time in the natural setting (i.e. not to be perceived as a stranger by observed participants) (Hull et al., 2001).

I planned to minimise the observer effect by trying to habituate myself as much as possible with the research sites and clinics. However, I did not dismiss the

possibility of the observer effect therefore I planned to look sceptically at the data as it could be the best practice that would echo the regulation in details.

I resisted taking notes during the observed sessions in order not to disturb the normal flow of events in the recruitment. All the field notes were recorded immediately after the observed sessions ended. In order to ensure the robustness of the data, I planned to be as systemic as possible, i.e. by conducting each observation using the same routine and, immediately after each session, by writing up all the details that I could remember while they was still vivid in my memory (see Appendix 1: example of the field notes).

#### **5.2.2.1 Recruitment and ethical considerations**

The original intention of this phase was to observe both prospective donors and researchers in recruiting sessions for potential blood donors for MGE research in three major hospitals in Saudi Arabia. Although these hospitals were all in Riyadh, they can be regarded as representative of the whole kingdom because they all receive patients and referrals from across the country.

A poster (Appendix 2) was displayed in staff areas informing staff of my name, contact details, and the purpose of the study. When a consent interview was booked, relevant staff members were approached in person and in a private space, reminded about the study and asked if they were willing to be observed. All of the approached staff members verbally consented to participate. A similar poster (Appendix 3, translated into Arabic) was displayed in patient waiting areas. Patients were asked for permission for me to observe the researchers gaining their consent by the

researchers themselves, using a process of verbal consent as they entered the consultation room (Appendix 4) after checking that they had read the poster (Appendix 3), understood it, and had no objections to its content. I decided not gain the patients' consent myself for the following reasons:

- It was important to ensure that the observed researchers had the opportunity to veto an observation if the patients were unwilling to agree. My presence may have made this more difficult as it was socially more comfortable not to invite me into the room than it would have been to ask me to leave.

- Although the patients were part of the observation, the researchers were the target participants as they were the ones responsible for adhering to the NCBE guidelines.

- The poster that was displayed, before the observations, was designed to draw the attention of the research team (who were observed) to verbally consent the patient.

- I wanted to observe the process passively with no interaction whatsoever with the patient during the recruiting process – gaining consent myself would have inserted me into the interaction and potentially influenced behaviour, which would be detrimental to the study.

- Asking patients to provide written consent had the potential to confuse patients about what they were consenting to (i.e. to my study and blood donation for MGE research). Accordingly, it seemed more ethical to downplay my research so as not to distract their attention away from the more serious decision about participating in the MGE research.



The researcher-participant was given the opportunity to withdraw within 48 hours of being observed.

#### **5.2.2.2 Inclusion and Exclusion criteria**

All consent interviews were planned to take place in the three-targeted hospitals that were recruiting adult blood donors for MGE research during the period from February 2013 to May 2013. As the age of consenting in Saudi Arabia is 18, being an adult was defined in this project as any person who is 18 years old or older. Mental capacity was assumed when a participant appeared able to rationalise his or her decision to participate. All researchers were assumed to have mental capacity by virtue of their job. Those who did not wish to have their interview observed (researcher or patient) were excluded.

#### **5.2.2.3 Sampling**

Convenience sampling technique was employed. Convenience sampling was deemed to be the most suitable technique as it helps facilitate recruitment in a manner that matches the overall timeframe of the project. Observations were planned at three different institutes, all of which have active, busy research departments and multiple genetics studies involving international collaborators.

TABLE 5-1: THE THREE RESEARCH SITES

	First hospital	Second hospital	Third Hospital
Specialty	Ophthalmic–specialised	General-specialised	General-specialised
Reference	Ministry of Health (MOH)	Military hospital <sup>5</sup>	The Royal Court
Capacity	400 beds	600 beds	500 beds
Branches in other cities	Yes	Yes	Yes
Researchers’ education	Weekly grand rounds	Many education programs	Many education programs
MGE specialised laboratory	Yes	Yes	Yes
MGE research international collaboration	Yes	Yes	Yes
Strict patient eligibility system	Yes	Yes	Yes

### 5.2.3 Phase Two – Interviews with patients who had been invited to donate blood for MGE research

The main reason for using interviews was to gain an understanding of the potential subtext of the interviewees’ statements (Kvale, 2008). Follow-up questions can be used in interviews to reveal tacit meanings within interviewee comments. The interviews were used to explore participants’ understanding of values and norms around MGE, and their experience of being invited to participate in MGE research (Bryman 2004). Interviews have been described as ‘conversations with a purpose’ (Taylor, 2005). Interviews were chosen to enable me to explore the donors’ thoughts on the experience using their own words, beliefs, hopes, attitudes, fears, and agendas.

This kind of in-depth understanding, guided by follow-up questions about what the donors really meant to say or how they understood their participation, would not

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<sup>5</sup> This hospital treats not only personnel and their families, but also other Saudi and non-Saudi people based on specific eligibility criteria.

be as effective if we used another approach, such as a survey. Other qualitative approaches, like focus groups, could have been used. However, the level of information sought was personal, asking donors to recall their own experiences, rather than a general discussion about donation, for which focus groups may have been better suited. I elected to use interviews for this phase, for several reasons:

- Interviews have greater potential to tease out personal accounts that are not influenced by any collective debates or contaminated by others' opinions.

- Personal conversations are more acceptable in Saudi culture than, for instance, surveys. Human contact builds up trust and not all Saudi adults are literate. Interviews were therefore thought more likely to yield reliable data

- Some informants might not understand or appreciate the safe environment that is promised by focus groups and, as a result, may not have been comfortable sharing their experiences with others.

- The nature of interviews would provide a more flexible tool to be applied than the logistics of focused groups (i.e., coordinating times, places, and venues suitable to all participants) (Sugarman et al., 2001; Taylor, 2005; Sugarman et al., 2007; Creswell, 2012).

The observations in Phase One set the scene for Phase Two by providing more realistic field interview expectations. They also informed the topic guide that was used in the intended in-depth interviews during Phase Two.

The first version of the topic guide was completely informed by the literature. It addressed MGE research challenges in general. As a result of the interim analysis of results from Phase One, questions were redesigned to be simpler and to ask about

participants' general understanding, and whether or not this understanding was gained during the recruiting process. Another change was to include the themes of patient deception and patient vulnerability, in order to tease out patients' reflections on those points in an indirect way.

It was also important to know what the patients' overall perceptions were and what they recalled from the recruiting interviews. The intention was to have in-depth, semi-structured interviews with patients within a few days of their donations while they were more likely remember as many details as possible thereby avoiding recall bias. People tend to forget crucial details of their experience over time (Hutson and Blaha, 1991). Recall bias refers to when a patient's recollection of an experience might be different to what actually happened (Fortun et al., 2008; Shields et al., 2010).

### **5.2.3.1 Sampling**

The main sampling strategy was purposive sampling. Creswell (2012) suggested that purposive sample 'means that the inquirer selects individuals and sites for study because they can purposefully inform an understanding of the research problem and central phenomena of the study' (p.165). The intention was to recruit from the three institutes in which patients had recently been invited to donate blood for MGE research. Some might argue that this sampling strategy can also be categorised as stratified purposive sampling, as defined by Miles and Huberman (Creswell, 2012), to '[I]llustrate subgroups and facilitate comparison' (p158). Although I tried to look for informants from different institutes, I did not aim to

compare the resulting data. Thus, the sample strategy best categorised as purposive sampling.

The recruiting period was from March 2013 to May 2013 which was the best time before the summer vacation when usually all clinics and research activities slow down for the summer season. The target population was all patients who were asked to donate blood for MGE research in the three selected institutes during this time period. It was anticipated that 20 interviews would be needed to reach saturation, but due to time pressures it was foreseen that it would not be possible to conduct more than 20 interviews even if saturation was not reached. The plan was flexible and would have allowed me to make amendments if recruiting a purposive sample was proven to be impossible (e.g., moving from a purposive samples to convenience samples). Convenience sampling is a more flexible sampling strategy, mainly because it is opportunistic or non-systematic in its nature and is best used when time and funds are limited (Creswell, 2012). The main disadvantage of this strategy is that it is not as rigorous in the sense that it could be rated as less objective than other sampling techniques, which might impact the quality of the collected data. Such a shortcoming would not be accepted as the first choice in this phase, but it would be tolerated in a pragmatic alternative plan to the purposive sampling strategy. The purposive sampling, however, worked fine because I was able to maintain recruitment from the intended centres, as I will explain in the results chapter.

#### **5.2.3.2 Recruitment and consent process**

At the end of the consent interviews in Phase One, the patient was asked if they were willing to agree to be interviewed about the consent process for the study.

Those who were willing were given more information (which was translated into Arabic and read to those who were not literate) (see Appendix 6 English version and Appendix 7 Arabic translation) and asked for their contact details.

I then contacted them the following day to arrange an interview if the patient was still willing to participate. In addition to that, the recruiting clinics were given my contact numbers in order to contact me when a recruitment session was scheduled, so that I could approach those patients about the study after their consent interview. This process was planned to be repeated until data saturation was reached or 20 interviews were recorded (whichever was soonest).

#### **5.2.3.3 Inclusion and Exclusion criteria**

Included in the study were adult (aged 18+) patients with capacity who had recently invited to donate blood for MGE research. Excluded from the study were:

- those unwilling to participate;
- and those for whom it was not possible to organise an interview at a mutually convenient time specifically during the first week after the consent interview.

#### **5.2.3.4 Interviews, language and translations**

The interviews in this phase were carried out in Arabic. All interviews were audio-recorded, transcribed, and translated. Every participant was given a number as part of a general anonymisation of transcriptions.

The plan was to translate the Arabic interviews into English using two different, independent translators. The two translations would then be compared to assess their quality and accuracy. If any differences found were major, a third independent translator would be asked to provide a third translation. I was unable, however, to find someone with the right expertise in terms of qualitative research transcription and translation. I was able to identify someone who understood the importance of data accuracy through her activities in quantitative research data collection. She was given a quick tutorial of what was expected. I consulted a colleague, who is bilingual and had participated in qualitative research, to assess the accuracy of both the transcription and the translations. Based on my colleague's and my own assessment, the transcriptions were revisited many times to make sure they were as accurate as possible. Also, my colleague and I were convinced that those who were given the chance to translate failed to capture the essence of what was said in the original Arabic language. Therefore, in order to progress, the study had two options: the first was to do analysis in Arabic and then translate quotations into English. This was considered a good solution, but it also meant that my supervisors would not have access to the raw interview data, which would make it impossible for them to verify my analysis. Another disadvantage of this potential solution was that the lack of Arabic software that can assist with qualitative data coding. The second potential solution was to provide a more trusted, accurate, verbatim English translation despite the major time and financial investment. To do that, a multi-phase plan was initiated:

- Revising large portions of the English texts provided by the inaccurate

translations and transforming them in order to ensure that they matched the Arabic text.

- I then asked a bilingual consultant with qualitative research expertise to comment on the accuracy of the final version of the translations.

My supervisors and I agreed that this solution would be the most appropriate given the availability of resources and time permitted for this project.

An interim analysis of this phase's data was used to inform the topic guide for Phase Three (for details of how this was done, see Subsection 4.5.2 below).

#### **5.2.4 Phase Three – Focus Groups**

The purpose of this phase was to discuss what the norms of MGE research in Saudi Arabia should be in general, as well as reactions to the initial findings in phases one and two specifically. In general, the main aim of focus groups is to encourage the collection of data through discussion and debate and through discussing the participants' perceptions. Focus groups are considered a particularly suitable tool for exploring people's opinions, wishes and concerns (Kitzinger, 2005). Focus groups work best when they create the perception of being among people who are most likely to share the same way of thinking, which, in theory, would encourage the exchange ideas and the discussion of those ideas in an environment perceived to be safe (Jourard, 1964). One of the main reasons for collecting data using focus groups in this phase was to explore how the participants perceive, and feel about (Krueger & Casey 2000), MGE research in Saudi Arabia. Thus, focus groups would be more appropriate than interviews or survey questionnaire insofar as they create an environment where individuals would feel safe expressing ideas or responding to



other people's perceptions. Also, part of my study was to learn more about the different opinions and experiences that the researchers had (Morgan & Krueger, 1993) and the ways that they influence and are influenced by other researchers' input.

In this phase, the mixture of the data collected by the previous two phases would generate a mixture of opinions driven by different experiences, behaviours, and perceptions; a focus group would provide the best data collection tool to investigate those complex reactions and ranges of opinions (Morgan and Krueger, 1993). In addition, focus groups provide access to different kinds of data than that obtained by interviews. They are more suitable for assessing the richly textured normative influences on our behaviours (Bloor et al. 2001). It, also, enables data to be collected in such a way that people's behaviours, beliefs, and attitudes can emerge (Kitzinger, 2005). In focus groups ideas are generated based on discussion where the ideas are filtered through the participant's discussion. Morgan and Krueger (1993) believe that the level of interaction in focus groups provides the ability to study motivations and reasons tested through the group's discussion. Above all, this phase was mainly intended to tease out complex levels and the rich textures of the normative values held by the group, which makes focus groups the most suitable method of data collection in this phase (Bloor, 2001).

Two focus groups were organised. The first focus group targeted individuals employed to recruit and consent patients for MGE research (e.g., research nurses, research coordinators, and research assistants). The second focus group targeted bioethics policy-makers in Saudi Arabia. The intention was that this group would

include a human research ethics committee chairman, a research director, a legal advisor, and a religious expert. The main reason for separating the two groups was that the second group would contain high profile research leaders in Saudi Arabia who might unwittingly intimidate the less powerful individuals who carried out the consent interviews. A focus group typically gathers in a safe, stress-free environment in which participants can feel at ease among peers who share similar experiences (Jourard, 1964). The intention was to recruit six to nine participants in each group.

A topic guide was used to focus the discussion (Finch and Lewis, 2003). It also provided some consistency between the two groups, potentially enabling the results to be compared. It was used to steer topics and guide discussion rather than ask very specific questions (Finch and Lewis, 2003). The topic guide was based on an interim analysis of the qualitative data from phases one and two, combined with the analysis/synthesis of the international guidelines.

The meetings were divided into two parts. In the first half, I provided a few minutes of introduction in the form of PowerPoint presentation slides (see Appendix 10). The main aim of this introduction was to set the context for the discussion by giving participants an idea of the research and its objectives. It was carefully structured so as to not give any information about the interim results nor my own views on what the issues were, so as not to bias or lead the discussion. The topic guide for this phase was structured to concentrate discussion on the Saudi regulations, and on how the participants thought MGE research should be governed in the light of the existing regulations. The main topics addressed were the participants' perceptions of the challenges of MGE research in Saudi Arabia, how

the policy addressed those challenges, how the participants thought the donors for MGE research regarded their participation, and who they thought owns the collected genetic material. The second half of the meeting was designed to obtain the participants' reactions to the interim findings of Phase One and two (see Appendix 10). Discussion was preceded by a short presentation of the results and guided by a series of open questions and prompts (Appendix 11)

Group 1: Twelve potential participants were approached in each of the three clinics by senior coordinators who set up meetings with the potential participants so they did not feel any pressure to express themselves. During these meetings, an invitation to participate in the study was extended, and information sheets with the researcher's contact information were provided for the staff members who wished to take part (Appendix 12).

Group 2: Twelve potential participants were approached. As the potential participants were all high-profile leaders, their contact information was already in the public domain. I initiated first contact via phone as per Saudi cultural tradition (a telephone conversation is much more valued than any other means of contact). After the initial contact, an email with an invitation letter and information sheet was sent (see Appendix 13 & 14). The invitee would then decide whether or not to participate in the study by replying to this invitation.

### **5.2.5 Analysis**

The analysis plan in qualitative research should match the main research purpose (Krueger and Casey, 2000; Miller and Crabtree, 1992). My analysis strategy

was oriented towards informing the normative claims related to the research question (Maxwell, 2012; Caudle, 2004).

During the early stages of the data collection process I started to develop certain thoughts about the study's emerging themes and coding process. I considered this early stage of familiarisation as essential to keep a strict rigour and not to jump too quickly into the comprehensive analysis, as this might drive the data collection away from an acceptable level of objectivity. This was also a very essential step in developing early interim analysis.

#### **5.2.5.1 Interim analysis:**

In each phase, and after in-depth familiarisation, an interim analysis process was used to inform the subsequent phase by enhancing the topic guide and adjusting my expectations of the knowledge of MGE research among the research participants in each phase. Interim analysis was used in the early stages to gain an initial understanding of what could emerge as themes from the collected data after Phases One and Two. In general, Interim analysis provides qualitative research with the ability to generate preliminary hypotheses about collected data, the ability to go back and refine the questions and pursue inquiries in more depth. Interim analysis in the context of this thesis was used strictly to empower the empirical arm of this project by giving the ability to check and interpret the data to develop general, more realistic expectations for further data collection from phase to phase. (Pope et al., 2006).

### **5.2.5.2 Observation Data Analysis:**

It is important to acknowledge that in observation work the data have already been reflected upon through the process of writing up the field notes. Despite the best efforts to report only the concrete facts, ideas are generated and impressions are gained during the observation stage itself. These early interpretations of what is witnessed have been perceived by some commentators to complicate the relationship between data collection and analysis (Ives & Damery, 2014). To overcome that challenge, as I described in Subsection 5.2.2 Phase One- Observation, I remained focussed on the main aim of the observations, which was to witness the actual behaviour of the stakeholders in their natural environment in a rigorous way. This dictated writing the field notes using dispassionate description as much as possible, as described by Allen (2010), (as cited in Ives & Damery (2014)).

The analysis approach was selected to answer specific research questions. The strategy was to use data coding, which enables normative claims to be assessed and analysed. Therefore, the approach, in general, was very pragmatic insofar as it was aimed at exposing the normative values from the interpretation of the observed practice. In this phase, I used Wolcott's (1994) approach of describing, analysing and interpreting the collected data. Creswell (2012) recommended such an approach to analyse observations, field notes or ethnography reports, because this approach gives the researcher the ability to better understand the culture dynamics. Although my thesis is not based on pure ethnographic methodology, Phase One was designed to include passive observations, to understand how MGE research takes place within the Saudi culture.

The first step was describing the data to allow the reader to see the events through my eyes by way of narrating, in as much detail as possible, both the setting and the events (Wolcott, 1994). In this step, I produced the field notes from what I could remember after each observation session (see Appendix 1 for an example) with the limited help of very few but, as I thought during the observation, essential preliminary field notes. These limited preliminary field notes were written during the observation in Arabic language with only codes and abbreviations. They were only used to help drafting as detailed as possible field notes and were shredded after the final field notes were produced. The field notes formed the data that were analysed. It was important to be fact-oriented rather than interpretive at this early stage.

The second step was analysing the data through a sorting procedure (Wolcott, 1994; Creswell, 2012). This included highlighting patterns and events in the observed setting in a way that provided answers to the research question concerning the adherence of Saudi researchers to the Saudi research guidelines. The highlighted patterns were then coded in preparation for interpretation.

The third step was interpretation, which was a means to going beyond the scope of the collected data in order to understand what the data were actually saying (Wolcott, 1994; Creswell, 2012). In this step I used Wolcott's (1994) interpretation stage to make sense of the coded patterns and to suggest themes to explain those patterns.

### 5.2.5.3 Phase Two analysis:

The final, more comprehensive analysis for Phase Two was a pragmatic reasoning through inductive-deductive logic (LeCompte and Schensul, 1999; Hatch, 2002; Marshall and Rossman, 2010, Creswell, 2012). The inductive, or bottom-up, approach was used after each phase. It allowed the data to develop suggested themes without the influence of any theory-testing approaches in a way similar to that described by Notley, Green & Marsland (2014). Such an approach revealed the need to work extensively with the data to abstract the inherited normative assumptions in the forms of themes; this also meant that I had to go back and forth between the data and the emerging themes until a thorough and robust set of themes was developed. Deductive reasoning was mainly employed in Phases Two and Three. A top-down approach was used to test emerging themes against the collected data, in the sense that themes that emerged from the interim analysis of Phase One were used to explore data collected from Phase Two, and the interim themes that emerged from Phase Two were used to explore data collected from Phase Three (Creswell, 2012).

In Phase Two, the most appropriate approach, given the nature of this phase, was to engage in data interpretation to allow a data-guided analysis or bottom-up approach, following the pragmatic approach of thematic analysis, as suggested by Notley, Green & Marsland's (2014) approach. This was done as follows:

- Familiarisation: Reading and rereading the data was the first step. During this extensive familiarisation process, I tried to gain an overview of the study that was broader than any interviews. I sought to understand what the participants were trying to say while considering the normative assumptions that may

guide their responses. Examining the data in this way gave me a sense of the richness, depth and diversity of the data and guided the process of conceptualising, which helped prepare for the coding step.

- **Coding:** After this familiarisation step, I started to organise a coding system. The coding was done so as to reflect the meanings in parts of the data (Coffey and Atkinson, 1996). In certain cases, the same portion of text was coded in two different ways depending on what the participants stated and how I understood what was stated, which might give more weight to a statement than what was intended (Miles and Huberman, 1994). I started first with free coding - coding the data as I read through them. I then transferred the codes into NVIVO software version 10.
- **Theme development:** The codes and concepts were allowed to emerge into themes by grouping codes and concepts in a way that provided explanations for the data segments.
- **Thematic networks:** The themes at this stage were starting to take a more mature shape, by connecting them and trying to find similarities and differences for better understanding of what was said in the interviews.
- **Integration and interpretation:** interpretive approach allows explanations of those themes through the 'reflexive stage of thematic analysis' (Notley, Green & Marsland, 2014, p333).

During the analysis progressing stage, I managed to 'shuttle back and forth between conceptual speculation, reflection, reading, data collection and analysis'



(Williams, 2004, p77), especially in the steps of ‘thematic network’ and ‘integration and interpretations’ steps for a more thorough and reliable data analysis.

#### **5.2.5.4 Phase Three Analysis**

At this stage, it was very important that I looked at all the data from each phase as a complete set before beginning to sort through it for the analysis of Phase Three. At this point, I read and reread the field notes, listened to the interviews and focus group recordings several times, read the Arabic and the English versions of the interviews and read the focus group transcriptions. This process of in-depth familiarisation helped to remind me of the bigger picture as the starting point before the detailed analysis of Phase Three.

It was important to analyse this phase of the data in a similar way to Phase Two to maintain consistency for better understanding of the themes from the previous stage and from the discussion in the focus groups. The only difference at this stage was the coding step. I used a two stream strategy similar to Ives (2007). In the first stream, the coding was done in an unstructured way, or free coding, as the data were taken at face value without any attachment to the previous phase’s data set. The qualitative software analysis NVIVO software version 10 was used for the second stream and ‘aimed at standardising the codes so that the groups could be compared and analysed using the same conceptual framework’ (Ives, 2007, p167-168).

The first stream’s code numbers were not changed or altered, and during the second stream, the codes that were removed were those that had been replicated or that could be merged into an existing code. Although the two stream coding was labour-

intensive, it was deemed to be the most advantageous approach for the following reasons (Ives, 2007):

- It provided sufficient conceptual flexibility to ensure that the analysis was not developed in a way that was conceptually committed to the previous phase's outcomes. Nevertheless, it was rigorous enough as a pragmatic framework to ensure consistency.
- It helped to decrease the chance of bias by maintaining a level of objectivity by thinking, rethinking and considering other, more objective coding.
- Coding in this way reduces the temptation of forcing data into codes that did not actually fit.
- It provided a chance to evaluate and re-evaluate my codes by starting with a free list of codes and then looking at them thoroughly to keep, merge or discard them during the second stream.

NVIVO software was used as a tool to manage and organize the data, but it did not do the analysis. The researcher in qualitative research is the one who is fully responsible for asking the right questions and for extracting the answers that the data best provides through interpreting and choosing the segment of data that is to be coded (Bringer, Johnston, & Brackenridge, 2006).

### **5.2.6 Validation and trustworthiness**

As qualitative data analysis is interpretative in nature (i.e., it depends on my own interpretation and understanding of what the participants said) at every stage, I made sure to challenge the findings of the study's earlier stages whenever possible. The study was designed to allow each phase to inform the phase that follows it in

order to challenge the data's validity. Therefore, the three phases themselves were a form of validation in the sense that I observed one group, interviewed another group, and then ran focus groups. These are three different ways of gathering information in the practice, which can be seen as a form of triangulation in the sense that I used multiple sources of data (Richards and Morse, 2012).

Peer review was also employed in two stages, the first during the translation process by a bilingual qualitative research expert and again after the data analysis by my project supervisors, who independently coded the interviews and checked the analysis of the focus groups. The main goal of the peer reviewers was to '[keep] the researcher honest; [ask] hard questions about methods, meanings, and interpretations; and [provide] the researcher with the opportunity for catharsis by sympathetically listening to the researcher feelings' (Creswell, 2012).

### **5.2.7 Ethical approvals and permissions**

This project was approved by the following research committees:

- The Science, Technology, Engineering and Mathematics Ethical Review Committee, University of Birmingham, Reference Number: ERN\_12-1394, Date of Approval: 06/02/2013,

- Human Ethics Committee/Institutional Review Board, King Khaled Eye Specialist Hospital, Reference Number: RP 1319-P, Date of Approval: 10/03/2013

- Institutional Review Board, King Abdullah International Medical Research Centre, Reference Number: RC12/090/R, Date of Approval: 26/03/2013.

## **6 Chapter Six: Results**

### **6.1 Introduction**

This chapter will present the findings from the three phases of empirical work. The first subsection presents my interpretation of what was observed in Phase One. In the second subsection, I present the results of the Phase Two interviews. The third and fourth subsections of this chapter were built on the same coding, quoting and correction techniques used with Phases One and Two. These subsections show the results of the first and second focus groups.

### **6.2 Phase One: Passive observation of informed consent processes**

The original intention during this phase was to observe the interviews during which potential blood donors for MGE research were interviewed, in the three major hospitals that do the majority of the recruiting for Saudi MGE research. Although these hospitals are all in Riyadh, they can be regarded as representative of the whole kingdom because they receive patients and referrals from across the country. Two of the three hospitals' research ethics committees approved the research. However, the third hospital's committee procrastinated, and no final approval was forthcoming. Some of those who participated in Phase Three had experience working there. They confirmed that the practices reported in Phases One and Two reflect practices in the third hospital.

#### **6.2.1 Demography**

All observations took place in two different institutes, both of which have active, busy research departments and multiple genetic studies involving international collaborators.

TABLE 6-1: THE TWO RESEARCH SITES

	First hospital	Second hospital
Specialty	Ophthalmic – specialised	General – specialised
Reference	Ministry of Health	Military hospital <sup>6</sup>
Capacity	400 beds	600 beds
Branches in other cities	No	Yes
Researchers' education	Weekly grand rounds	Many education programs
MGE specialised laboratory	Yes	Yes
MGE research international collaboration	Yes	Yes
Strict patient eligibility system	Yes	Yes

### 6.2.2 Observations

In the Saudi culture, as explained in Chapter One, people usually attend their clinic appointments as families. Therefore, it was part of the natural sequence of events that the research teams held these interviews with families rather than with individuals. In the methodology subsection, I proposed that my involvement at this stage was very passive, meaning that I did not interfere with the natural sequence of events. When the research teams called for the patient, I followed the family but waited outside while the research team made sure that the patient had seen the poster and that he or she did not mind my presence, as noted previously as part of the verbal consent of Phase One.

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<sup>6</sup> This hospital treats not only personnel and their families but also other Saudi and non-Saudi nationals, based on specific eligibility criteria.

The research teams from the two hospitals requested verbal consent for me to observe the process of donating blood for MGE research. Of the total of eleven patients/families, only six agreed to be observed for this study. Of the five who refused to be observed; only two families eventually donated blood.

Six families were invited to participate in the first hospital, and four accepted. All four agreed to donate blood, to two different MGE projects. These research projects were managed by two different PIs with two different Western international collaborators. Of the two families who did not agree to be observed, one family eventually donated blood, and the other refused because they needed to catch a plane back to their village. As I explained, I was not in the room with the research team during the process of gaining verbal agreement to have the consent interviews observed. However, I saw the families being greeted in the corridors before they went inside the rooms. The appearance of the families who refused to participate in my research suggested that they were relatively affluent. For example, they wore expensive, clean clothes, and the expensive and strong Arabic oil perfume called Oadh. Both families spoke with the nurses in very clear English with American accents.

In the second hospital, five families were approached regarding observation, and only two accepted; both donated blood for two different MGE research projects. Only one of the two observed donations went toward a project that had a PI with a Western international collaborator. Of the three families who did not agree to be observed for this research, only one family eventually donated blood. Unlike the

other hospital, the three families did not look significantly different to the observed patients.

### 6.2.3 Phase One findings

#### 6.2.3.1 Describing the recruiting procedure

With minor exception, the recruiting procedures were the same in both institutions.

In all the observations of this phase, I noticed that the PIs or the MGE research were the treating physicians. This means that technically each of the PIs managed both teams: the research team and the medical team. To avoid confusion in this section, I will refer to research team personnel as ‘research team representatives’ or ‘researchers’. The researchers usually report to the PI, who assumed responsibility for conducting the research. The PI was usually patients’ first point of contact.

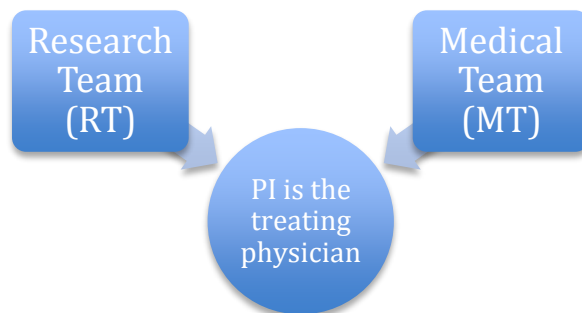


FIGURE 6-1: THE PI ROLE IN BOTH TEAMS .....

In all my encounters, research teams had access to the list of outpatient appointments and knew in advance which patients would be targeted for recruitment. Printouts of the appointment lists were typically prepared a day before each clinic. It

was also the usual practice that on the day of a clinic, research teams would make the medical teams aware of which patients were of particular value to them. At that stage, patients had not yet been contacted. The research teams also reminded treating physicians to expect patients of particular interest for research in that day's clinics. In addition to that, the patients' files were flagged to remind the treating teams (i.e., doctors and nurses) to confirm each patient's presence to the research team, and serve also to remind treating physicians of the patient's importance.

The research teams then waited for the doctor's signal that a patient is ready for recruitment. I noted a general assumption among the waiting research teams that the doctors had informed the patients about the research and invited them to participate in it. Subsequently, I have confirmed with the research teams that this was usually the case. When the doctors contacted the research teams with the patients' agreement in principle to participate, the research teams went to the outpatient clinics with a prepared set of documents, mainly national and international bilingual consent forms.

In all the observed interviews, after the treating doctor contacted the research teams, the researchers brought the patients and their medical charts from the clinic in which they were seen to a nearby clinic in the same facility. They then began by confirming the patient's name and date of birth. See figure 5-2.



FIGURE 6-2: SUMMARY OF THE RECRUITMENT PROCESS

One day before patient's arrival	During patient's clinic	After patient's clinic
<ul style="list-style-type: none"> <li>•RT anticipates patient by reviewing outpatient clinic's records</li> <li>•RT accesses targeted patient's medical records and flags them with a note to the MT to contact the research centre when patient arrives</li> <li>•RT contacts the PI with a list of the anticipated patients</li> </ul>	<ul style="list-style-type: none"> <li>•RT visits the clinic and makes sure that the PI and his MT are aware of which patients are expected</li> <li>•Records of patients who arrive are immediately checked by the MT for a flag requiring RT contact upon their arrival</li> <li>•MT contacts RT letting it know that a targeted patient has arrived</li> <li>•When the RT is contacted, it starts preparing the paperwork for the patient's enrolment</li> <li>•PI opens the donation subject and agreement in principle to donate blood</li> <li>•The MT informs the RT that the patient is ready to be recruited</li> </ul>	<ul style="list-style-type: none"> <li>•RT rushes to the clinic with the consent form and enrolment papers</li> <li>•RT interviews the patient to confirm the patient's identity and that approval was given to the PI during the clinic</li> <li>•RT finalises the informed consent process and arranges for blood extraction</li> <li>•RT updates its records and sends the collected blood to be processed</li> </ul>

All patients were asked to sign consent forms during their interviews with the researchers. This fact makes it relevant to recall the consensus in the literature about the validity of informed consent. In very general terms, for informed consent to be ethically and legally valid, the person who gives it must meet three main conditions. He or she must be:

- Capable: the consenting person should have legal capacity to decide for him- or herself,
- Acting voluntarily: consenting persons should freely decide without coercion, and
- Informed: consenting persons should be given sufficient relevant information.

It is also important to mention, as I argued in the first Chapter, that those elements seem based on Western normative assumptions about autonomy, individualism, free choice, free will, and liberalism. In this phase, in the instances I observed, data emerged that seem to contradict each of these three elements of informed consent. These contradictions seem to stem from a difference in the overarching normative relevant assumptions due to cultural differences.

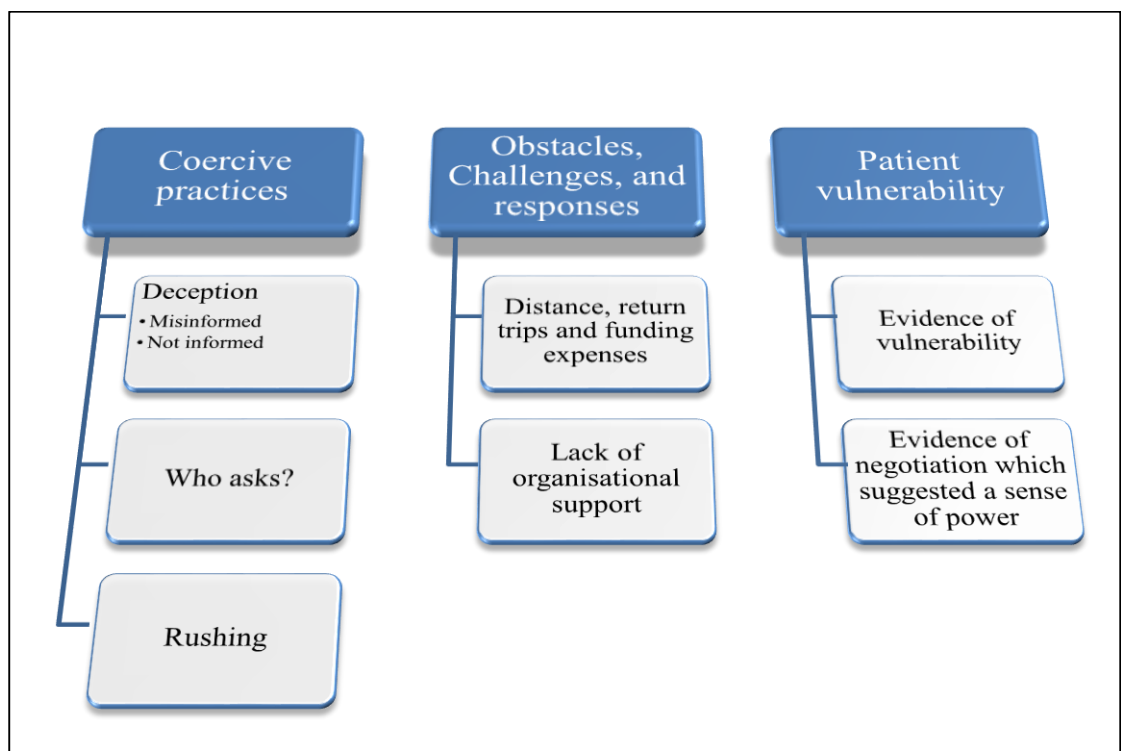


FIGURE 6-3: SUMMARY OF THE THEMES ARISING FROM PHASE ONE

### **6.2.3.2 Coercive practices**

The main challenge in interpreting the concept of coercion in the context of this work was that the concept of coercion, as opposed to its application, is culturally bound. There may be a mismatch between what Saudi patients perceive as being coercive and what, for example, UK patients might perceive as being coercive (as in SA patients expect greater direction, and paternalism is not necessarily regarded as a bad thing (see Subsection 1.2 The Saudi Arabian Context.)) People from different cultural backgrounds might, therefore, understand the term to mean the same thing, but if asked whether or not it would be appropriate to apply the term to the same set of scenarios, they might not all apply it to the same scenarios, depending on their cultural background. Equally, they might understand the term to mean the same thing, but some people might say ‘Its coercion and that’s bad’, and others ‘Its coercion, but what’s wrong with that?’. So, the normative meaning of the term might also be culturally different. According to the Saudi guidelines, and therefore the law, the donation of blood for MGE research must be voluntary or else it is unethical and/or illegal. The challenge in the observed cases is in how our framing of the context affects what appears to be coercion and what does not. In philosophy, what constitutes coercion is not fully agreed upon (Hasken, 2007). Based on the philosophical literature, there seem to be two different means of coercion. The first has to do with the techniques that are used to coerce a person, and the second has to do with the reasons a person might feel coerced (Anderson, 2014). The coercion here was not coercion by physical force. Rather, it was through the use of techniques that could be described as actively deceptive and through tactics that would usually

coerce patients, like the choice of the people who asked for patients' consent and the speed at which patients were required to make choices regarding consent.

Some patients were not sure about giving blood. With these patients, researchers assumed a salesman-like attitude. Although they always began by stating that the patient was not obliged to give blood, they usually coupled that statement with stronger statements in support of participation, such as 'Doing this will be written to your name in the hereafter'. Patients were also told that they would be pleasing God with their donations. Researchers usually finished by giving confirmation that the patient would be the first to benefit if something positive came out of the research. On one occasion, a family member told the researcher, in a sarcastic tone, that it was obvious to him that the researcher was desperate to have the blood withdrawn. They both laughed and the researcher's reply was to tell the patient that it was not up to him; it was the doctor who wanted it this way. Assuming a hard-sell attitude, the researchers often seemed to be eager to finalize donations. It was not acceptable in either hospital to pay patients to participate in the research. Thus, the researchers used non-monetary incentives as tools to persuade patients to donate. For instance, in every interview I observed, the research team used the patient's faith or belief system to convince him or her to donate. For example, patients were told that their participation would please God. In the Saudi context, charity is a means for devoted Muslims to please God, or at least to help people look like devoted Muslims. Researchers used terminology such as 'eternally running good deeds', meaning good deeds that continue to reward the person even after his or her death. These types of deeds are some of the most respected and pursued good deeds amongst Muslims. Again, it could be the case that the researchers truly believed that

they were obliged to open the eyes of fellow Muslims to an opportunity to change their destinies in the hereafter, which is all that matters in the devoted Muslim's life. However, there is a very thin line separating persuasion from using religion as coercion. Muslims believe that on occasions where the needed charity is going to have huge impact on someone's life, the charitable action become an obligation and that if you do not do it, it is a sin. For example, if someone has plenty of food, if a starving person asked him personally for some food for his/her survival, it is not a charity any more. It becomes a sin if not done. I believe that researchers crossed that line when they allow the idea that donation would be charitable to escalate to the assumption that it would be sinful to not participate in the research as people are in grave need.

**(a) Deception**

There is not space in this thesis to provide a full exposition of the concept of deception. Instead, I will present what I take deception to mean and then apply this understanding to the data I gathered. Deception contributes to enforcing a false belief either by an active action (e.g. telling a lie) or a passive action (e.g. failing to correct an untrue belief). Some of the behaviours I observed were clear examples of lying: potential research participants were apparently deliberately misinformed. In other instances, information that may have affected their decision was withheld and/or false beliefs, that seemed to be inclining them towards donation, were not corrected. It is also important to state that I am aware that coercion and deception are two different concepts and the meaning and acceptability of both are contested. However,

in the context of this thesis, I noticed that deception was used as a tool to coerce people in to donating blood for MGE research.

A part of this work's overarching aim is to understand how Saudis perceive MGE research. This requires an understanding about what happens between researchers and research participants in MGE research in Saudi Arabia. People could donate blood for various reasons, but according to the Saudi national and analysed international regulations, there is an emphasis on the choice of research subjects to be free from undue influence and free from ethically problematic exploitation (see Subsection 2.3.1.3 Avoid Local Research Subject Exploitation). It could be suggested that the research participants were deceived in cases such as donating blood for MGE research based on misleading information, lying or the creation of a situation where patients felt that the only reasonable option was to donate.

This theme provides a means of interpreting how certain actions might lead to coercion. The main concern was to analyse at a deeper level what was said, in context and what it might mean to the patient. The notion of deception has not gone uncontested (Mahon, 2015). Mahon suggests that 'deceiving is necessarily intentional, requires that another person [i.e. the deceived person] acquires or continues to have a false belief, and must involve the agency of the deceived person; and the deceiver must know or truly believe that the false belief that the other person [i.e. the deceived person] acquires or continues to have is false' (Mahon, 2007, p181). In the context of MGE research in Saudi Arabia, the above definition can be divided into two. The first part concerns the beliefs that the donor acquires about his/her donation. Based on the observed level of communication and whether the

donor was informed about the research, the voluntariness of the participation, the risks of MGE research and how privacy would be protected, it can be claimed that evidence gathered during the observed recruiting interviews fulfilled the first part of the deception definition as per Mahon (2007).

The second part of Mahon's (2015) definition speaks of the motives and actions of the research teams and whether they intentionally reinforced the donor's false beliefs or provided misleading information about the donations. This part is not easy to categorise because in some cases it is intention-based. For example, if A allows B to believe that certain action (or lack of action) would bring about a specific unwanted outcome, and A genuinely believes that his claim is true, it could be highly contested to rate A's action as deceptive if A's claim is mistaken. However, I will assume that the research teams have been trained to know that informed consent to participate in research is an essential pre-requisite to their involvement in research. In general, the challenge in looking at the account of deception is that it indicates an intention to mislead, which is problematic. I am unable to comment on the researchers' intentions because I do not have data that enables me to make such comments. However, some of the observed cases gave a reasonable indication of deception, as I will evidence in this subsection.

It is important to differentiate between two levels of persuasion; the first could be regarded as legitimate persuasion arising from the recruitment activity and with stress upon legitimate reasons for encouraging participation. Assuming that there is ethical approval, which was the case in all the observed sessions, legitimate reasons are the ones used to justify the research in the ethically approved research protocol.

The other type is what I inferred to be problematic persuasion, which is making the decision for the research subject, as opposed to allowing the subject to decide for himself, and then to say and do only whatever makes the research participant give the blood.

I felt that some of the techniques research teams used to convince patients to donate observed during this phase could be categorised as coercion by deception, as I think patients were led to believe that they had to donate. Taking that limitation into consideration, I tried to use my judgment about where the research teams seemed to cross the line between legitimate persuasion and coercion. I used that information as a starting point to think about what would seem like coercion by deception (i.e., omitting information or giving wrong information) if it took place in UK. For example, where there are different levels of education, different levels of stress on the clinic waiting lists, and a normative presumption of informed consent based on free will. I will further differentiate between those whom I think were misinformed and those who were not informed at all.

**1) Misinformation**

On one occasion, a patient told the researchers that the PI had told her that her participation was for her own sake and would improve understanding of her own medical condition. The research team member conducting the consent interview agreed with this assertion. He added that informed consent was needed because of the extra work required for the sample and added that it was not a big deal. In that encounter, nothing was said about research, which, I believe, made the patient think that the blood was for clinical use, not research. The researcher in this encounter



failed to correct a false believe as well as providing false information. Both are problematic. The deception in this case occurred in two ways, and both of them can lead to the conclusion that patient's consent was not voluntarily given

Furthermore, no patients in the interviews I observed were given verbal information about the risks of participation. Instead, because the word 'risk' was included in the consent form, the researchers suggested that the risks referred to were those involved in extracting blood. This initiated a discussion about venepuncture. The researchers assured patients that they 'will be taken care of', and they 'have nothing to fear', as the technicians were very well trained in blood extraction. There was no mention of other risks that ought to be considered in the Saudi context such as stigmatisation. If the researcher genuinely believed that the only risks were in venepuncture, perhaps because the risk of stigmatisation had not occurred to them, then their practices fail to meet the second part of Mahon's definition of deception, namely that "the deceiver must know or truly believe that the false belief that the deceived person acquires or continues to have is false" (Mahon, 2015, p181).

Another example of misinformation occurred in the observations of over-promising the benefits of the research. In the interviews I witnessed, all patients were promised that they would be the first to benefit from research in which they participated. The main problem with that claim is that, for most of the MGE research that I witnessed, there would be no tangible, foreseeable benefit other than increasing scientific knowledge about mutations. Thus, the promise of a tangible benefit might give the patient the false hope that something would be specifically tailored to his or her needs. On the other hand, the idea that we might benefit from some particular

research is a widely acceptable motivation for participating in it, both in Eastern and Western contexts (TallBear, 2013). In the context of the observed recruiting sessions, over-promising can be rated as misinforming.

## 2) **Not informed**

The other side the deception theme that emerged from Phase One was that of lack of information. The difference between this theme and the previous one is that this one highlights a paucity of information and the previous one pointed to misinformation.

The Saudi guidelines spell out the general areas about which information should be provided. This includes information about risk, yet as we have already seen patients were not informed about all the risks.

Withholding information may influence a patient's decision to donate. The observed sessions lasted between 8 and 17 minutes. In the shortest interview, the time was spent signing the paperwork, verifying the patient's personal details and extracting the blood. The interview started and ended without mentioning any details about the research apart from confirming that the patient was there to donate as per the doctor's request (i.e., the PI's request). The exact words used by the patient were 'The doctor told me that I have to do it, so I am doing it'. The researcher and his assistant seemed relieved, and they made no effort to provide any further information. In contrast, the maximum time spent with a patient was 17 minutes. This was, however, because the researchers wanted to have some more clinical information and to trace aspects of the patient's family's medical history before drawing blood.

Though patients were donating blood for genetics research, I did not see or hear anything about genetics research in the course of my observations. This limited the range of possible interpretations available to me. One option is that patients did not need any additional information about genetics research. This seems unlikely because of the apparently low level of education among these patients. For example, one of them was not able to read the Arabic word ‘genetics’ correctly on the consent form. He was given the informed consent document after the researcher attempt to summarise it in few words with the attitude that ‘this is just the normal paperwork procedure’. To the best of my understanding, according to how the patient behaved (i.e. looking at the paper, misreading most of the words, and not helped even in the form of correcting how some of the words should be read), he was not sure what he was actually signing. After the patient signed, he was asked to come with the researcher to the lab for the blood extraction, but he seemed not sure why, telling the researcher he just gave blood a few weeks ago for his routine six month follow up. The other possible interpretation is that the information imparted was insufficient to prompt even basic inquiries. This, too, would have led to silence on the topic of genetics in the discussions between researchers and donors.

Under Saudi guidelines, researchers should provide patients with the informed consent form (which includes the needed information) with sufficient time to digest the information before the form is to be signed, and patients should receive a copy of the signed informed consent form afterwards. The use of separate information sheet is not common in Saudi Arabia, as it in the UK. The Saudi regulations stipulate that the informed consent document should contain all the necessary information in

detailed and precise elements described in details in the NCBE guidelines. The assumption is that providing the documents in advance will ensure that patients have time to read and understand the information provided. In the sessions I observed, patients were not provided with the informed consent sheet in advance, nor given a copy of the consent form to keep, bearing in mind that the information sheet and informed consent were produced as one document in all of the observed sessions. As a result, those patients were more susceptible to being deceived as they would have no means of checking what they were told against the ‘formal’ information they should have been provided with.

Given that fewer than ten minutes were allotted to patients for their clinical appointment, during which time it appears they were also asked to donate blood for research, it may be reasonably inferred that most treating physicians were merely asking their patients to provide a blood sample, without further elaboration. The researchers were the patients’ other source of information. In the interviews observed, commonly a few minutes of general information about the importance of research was provided that was not related to the patient’s participation. On one occasion I observed, the patient was visually impaired. The researcher guided his hand to the place where the signature was needed on the consent form. The patient was not able to read, and the informed consent form was not read to him. In that encounter, it seemed that having the patient’s signature was all that mattered. It is difficult to regard this person as having been informed. According to Mahon’s definition, this can be seen as deception because, I think, the deceiver knew or truly believed “that the false belief that the deceived person acquires or continues to have

is false” (Mahon, 2015, p181). In fact it is a deception on two different fronts: a) deceiving the patient when he was prompted to sign a document whose contents he could not possibly know, and b) deceiving the hospital’s efforts at quality assurance by auditing the consent forms, where the hospital would assume that the patient had at least an acceptable minimum of information about what he had signed.

**(b) Who asked**

I observed that the treating physicians seemed to be actively participating in the process of obtaining consent. I did not observe the initial contact between the patient and the physician-PI (this was the patient’s clinical consultation). In all of my observations, however, treating doctors had already made an initial request to patients that they donate blood. In five observations, patients said that the treating physician asked them to donate to research projects in which the treating physician was part of the research team. This practice contravenes the Saudi guidelines; if the treating physician is a researcher on the team, he or she should not ask patients to participate in that research. Moreover, the patients I observed were asked to donate during long-awaited medical follow-up appointments. In one observation, the treating physician appears to have told the patient to give blood for extra testing, rather than informing him that it would be used for research.

**(c) Rushing**

All of the consent interviews I observed seemed to me to be rushed. For example, researchers talked quickly, using jargon without explaining things, and some of them started the interview by saying that this should only take 10 minutes. As reported above, the interviews were indeed fairly brief (8 – 17 minutes, mean =

11). In 11 minutes on average, patients were greeted, introduced to the research team, had their identity confirmed, it was confirmed that they knew about the blood extraction, the consent document was signed, and they were escorted to a lab the blood extraction took place. From what I observed, it seemed to me that the researchers were rushing the informed consent procedure to the extent that it affected the quality of the informed consent taken.

In general, time is needed to give the research participant the opportunity to think calmly. This suggests that insufficient time to decide was given to the participants, which may have resulted in the patients feeling coerced by the stress of rushing the decision to donate. The length of time of the interviews might not indicate deliberate coercion because it could be that the researchers were working on a tight schedule to provide the most efficient and pragmatic service possible. It is also important to say that even if rushing the recruiting session wasn't deliberate, it might still have had a coercive effect. Based on that, given that the limited timeline for patient's interaction with researchers or the PI, it raises questions about coercion, in the sense that there was no room for the participant to reflect upon their decision.

### **6.2.3.3 Obstacles, challenges**

Another important theme that can be traced through my observations relates to difficulties encountered in the recruiting process. I noticed that patients mostly came from remote areas and expressed concerns about the follow-up appointment, which reflects the general characteristics I explained in the chapter about the Saudi context (see Chapter Four.) Patients were eager to secure follow-up appointments. Lack of organisational support (i.e. no specific clinics was dedicated to research recruiting

and researchers had to recruit during the clinic time) seemed to emerge as a theme mainly as a function of being poorly organised. It also seems that there were no specific, institutional guidelines for the venues in which clinical research can take place. For example, five of the six observed interviews took place in very small clinic rooms. The clinic rooms were originally designed to accommodate a maximum of three people. However, on one occasion, a room was crowded with seven people, including the researcher, a technician to take the research participants to the lab for blood extraction, the patient, the patient's relative, two children and me as the observer.

Another challenge was in the design of the rooms where consent interviews took place. These were designed as large, open spaces (about 10m by 10m) but were subdivided into smaller rooms with very thin wooden walls and no individual ceilings. This means that any discussion in neighbouring rooms could be clearly over-heard. Three of the observed interviews were conducted while other patients were in the next room. I suspect they could overhear us for two reasons. First because I could clearly hear everything said in the other room, so presumably people in that room could hear us equally well. Secondly, on the occasions where the participants refused to let me attend the informed consent session, I had the opportunity to hear the discussion if I wanted to but I decided to leave the clinic and return back to the office fearing that I might hear something that would influence my interpretations in a way that it should not. It was the case to the extent that one of the researchers was saying, as a joke, that I do not really have to be inside the room to record the conversation.

It could be the case that this was the best that could be provided by the hospital due to the lack of available resources. These were the clinic rooms, therefore presumably clinical contact also took place in this environment so it wasn't that lesser standards were in operation for research but rather the standard in general fell short of that necessary to protect confidentiality. A lack of resources is a general problem in Saudi Arabian clinical environment, and, accordingly, research funders might also suffer from a lack of resources. However, it is important to consider how best to distinguish between pragmatic solutions that are appropriate responses to current challenges, and responses that might affect the quality of the recruiting process. Large numbers of people in small places can affect research participants. It is difficult for people to make a decision that is entirely their own in front of an 'audience'. Privacy not only ensures confidentiality, it also enables potential participants to decide without the sense of being judged by others or acting on perceive peer-pressure.

#### **6.2.3.4 Patient vulnerability**

##### **(a) Vulnerability**

In this work, the definition of vulnerability as per the Saudi NCBE regulations will be used, which is "individuals in need of additional protection for being minors, legally incompetent, or deprived of freedom of choice" (NCBE, 2010, p7.) This definition seems too pragmatic insofar as it is concerned mostly with who can be described as vulnerable as opposed to what is vulnerability. In order to understand more about vulnerability, I will use the definition used by CIOMS, as follows: "Vulnerability' refers to a substantial incapacity to protect one's own interests owing



to such impediments as lack of capability to give informed consent” (CIOMS, 2008, p4.) This definition was chosen to complement the NCBE one because CIOMS (2008) was one of the main documents that inspired the Saudi regulations, as explained in Chapter Two of this thesis.

Patients seemed very submissive during the six interviews. They were very quiet and apparently had no problem accepting both to donate and the premise that informed consent is just ‘paperwork’, as the researchers kept assuring them in most of the interviewed sessions.

All the interviews started with the research team either escorting patients from the waiting area after calling for them or entering the room where patients was already waiting for them. In each of the interviews, a researcher arrived holding the patient’s medical charts and confirmed the name of the patient, exactly as a treating physician would do. This seems to have created the impression that the researchers were part of the clinical treatment team. In four out of the six interviews, patients complained to the researcher about different symptoms and expected the researcher to have answers for them. In those encounters, the researchers referred the patients back to the treating physician, but only after they had taken blood.

**(b) Sense of power**

Although some of the Saudi patients I observed manifested behaviour that I interpreted as suggesting that they were largely ignorant and helpless, this was not always the case. Some patients refused to participate, which suggests they at least knew that they were not obliged to consent. Some of them were sufficiently

confident not to allow me to attend as an observer. Among the group I observed, however, the only time a prospective participant showed signs of understanding, was when a relative said to one of the members of the research team who were pressuring the patient to donate, sarcastically, that it was obvious to the patient that the researcher is determined to get the blood. The tone and the look of the patient suggested what he thought was going on and the realization that he had something valuable to the researchers. It is difficult to generalise this observation, but it also might suggest that some patients did not feel disempowered.

### **6.3 Phase Two: In-depth interviews with MGE research participants**

The observations in Phase One set the scene for Phase Two by providing expectations for what data might be collected. They also informed the topic guide that was used in the in-depth interviews during Phase Two. As a result of the interim analysis of results from Phase One, questions were redesigned to permit me to probe for richer data in the areas of revealed by those observations. It was also important to discover what the patients' overall perceptions were and what they recalled from the recruiting interviews. The original plan was to interview 20 patients or to interview patients until saturation was reached. Most of the interviewees expressed concern about the speedy and superficial nature of the encounter, and demonstrated an apparent lack of understanding considering the fact that they had consented to participation in the MGE research. This was itself an important finding. Saturation was reached after 10 interviews.

Several themes emerged from the interviews based on my interpretation of the data. The experiences of Phase One contributed to my interpretation.

### **6.3.1 Interviewee characteristics**

The patients I interviewed ranged in age between 34 and 72 years. In the case of the two oldest patients, who were 72 and 68, the patients' oldest son and daughter respectively also attended the interview and participated in answering the questions.

The education level of the interviewees varied between highly educated and illiterate (Table (5-2)). In keeping with the Saudi culture, when a female donor did not want to be interviewed alone by a male researcher, I conducted the interview in the presence of a relative with whom she felt comfortable. Therefore, on two occasions the interview included the family member (Table (5-2)). In both cases, blood was taken from more than one family member with each individual's consent. These cases were coded with an F for family rather than a P for person. Where I use quotations from these interviews I indicate the speaker as either the patient (P), who was the participant, or the family member, who was the accompanying person (F).

TABLE 6-2: CHARACTERISTICS OF THE INTERVIEWEES IN PHASE TWO

Code	Age (years)	Gender	Occupation	Education	Interview Length (minutes)	Institute
F1	72	F&M	Housewife	Illiterate	17	1 <sup>st</sup> Institute
P2	68	M	Farmer	Illiterate	10	2 <sup>nd</sup> Institute
P3	64	M	Government clerk	High school	8	1 <sup>st</sup> Institute
P4	54	M	Military	High school	7	1 <sup>st</sup> Institute
F5	60	F&F	Housewife	Basic education	9	1 <sup>st</sup> Institute
P6	58	F	Teacher	University	10	2 <sup>nd</sup> Institute
P7	34	F	Registered nurse	University	15	2 <sup>nd</sup> Institute
P8	41	F	Private businesswoman	University	8	2 <sup>nd</sup> Institute
P9	36	F	Housewife	High school	11	2 <sup>nd</sup> Institute
P10	56	M	Military	High school	9	1 <sup>st</sup> Institute

### 6.3.2 Interview lengths

The lengths of the interviews varied between 6 minutes and 17 minutes (mean = 10.5). Although the original proposal was to spend at least an hour with each blood donor, the interviewees did not have sufficient information to share about their experiences to make interviews of this length useful. Some of the interviewees were not sure why the blood had been taken. They also expressed what seemed to be confusion between my research (i.e., the interviews) and the research for which they had donated blood. Despite efforts to eliminate that confusion—which included providing an information sheet beforehand, making sure that patients understood the information, an introduction to the current research at the beginning of the interview,

and the process of building rapport—some interviewees still thought that I had something to do with their medical care.

### **6.3.3 Phase Two findings**

In general, the data that emerged from the Phase Two interviews seemed to complement what I observed earlier. The experiences patients shared matched what I previously characterized as coercion either through deception, the choice of who asked for a donation or rushing the process. The researchers who had asked them to participate had clearly influenced their decisions to donate blood for the intended research. In addition, some of the patients seemed to understand the importance of the donation, to the point that they had attempted to bargain with the researchers. For example, they said they would agree to give blood only if the researcher agreed to do something in return, such as helping them to bypass the long queue at the pharmacy.

My analysis is based on my own interpretation of what the interviewees said. To understand exactly what the patients were trying to say, I tried to put their statements in context using my knowledge and experience in the field of recruiting patients for research in Saudi Arabia. It is also important to note that I did not observe my interviewees providing consent.

The themes that emerged from Phase Two are summarised in figure 6-4.

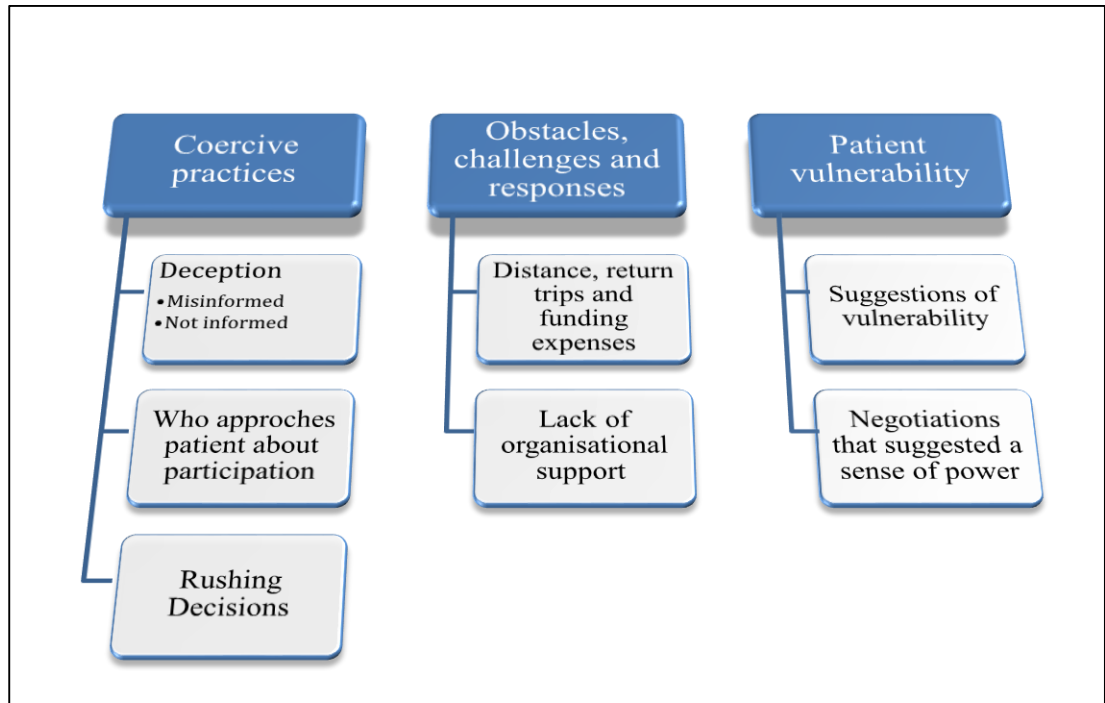


FIGURE 6-4: SUMMARY OF THE THEMES OBSERVED IN PHASE TWO

### 6.3.3.1 Coercive practices

Interviewees did not use the word coercion. However, they described practices that can be identified as at least potentially coercive. It is not common for Saudis to give negative, or what can be regarded as negative comments about their physician (Abolfotouh & Adlan, 2011; Adlan, 2013). This cultural consideration influenced my interpretation as to whether or not coercion was being suggested in the data. The difference between persuasion and coercion is blurred. In Subsection 6.2.3.2a Deception I differentiate between what I called legitimate persuasions and problematic persuasions. Therefore, I tried to analyse not only the words said by the interviewee but also its deeper meaning in the Saudi context. It is questionable whether the participants' consent process followed the recommendations that ensures the three conditions of capacity, voluntariness, and information are met

Among the most important aspects of informed consent is that patient should make his or her decision freely and without coercion or undue pressure after given the needed relative information. The condition of being informed requires some level of two-way communication. Despite the fact that each culture has its own communication norms, there is limited tolerance for variation in the literature regarding how communication should be carried out in the context of providing information about research participation. Such limited tolerance in the literature, as well as in the analysed international regulations (see Subsection 2.3.1.2 Respecting other cultural norms), reflected strong commitment to liberal individual autonomy as opposed to other cultural values such as the values of community and family; such a strong commitment was perceived to be moral imperialism or neo-colonialism (Newton, 1990; Tan-Alora & Lumitao, 2001; Widdows, 2007). This could be one explanation for most of what has here been themed as coercion—coercion was initially defined within other cultural contexts (i.e., non-Saudi contexts) see Subsection 6.2.3.2 Coercive Practice.

Patients' perceptions of what was going on accorded with the notion of deception resulting from misinforming or lack of information. Two of the interviewed patients were among the six observed recruiting sessions in Phase One. In these specific two cases, as well as others, the theme of coercion by appealing to religion (i.e. they were lead to believe that blood donation is Godly rewarded) was reported. Those patients, however, did not say anything that implied coercion. This could be because they did not necessarily feel coerced because they might not have realized that they had been misinformed. In these specific cases, it could also be suggested that coercion was practiced subtly by the research team.

**(a) Deception**

During the interviews, several patients made comments about the way the informed consent sessions were conducted. These comments can be interpreted in terms similar to those that emerged from Phase One. In Phase One, the concept of deception was introduced based on what was observed and how I understood it (see 6.2.3.2 a. Deception). In this phase, the patients' narratives of what they thought happened during the recruiting process were carefully assessed. It is difficult to make accurate claims about the intentions of the research teams; therefore, what will be suggested as deception was based on my own perception, based on patients' reported perceptions.

**1) Misinformed**

Some of the interviewed patients seemed to be confused about the distinction between research and clinical interventions. However, the interpretation of deception emerges from their understanding of what they were told. This interaction with P8 illustrates the confusion between his participation in research and the clinical examinations he needed as part of his regular appointment:

Res: Do you have any idea about the differences between your appointments with your doctor and this research?

P8: I feel that both are related, meaning they research to cure me and other patients.

This person appeared to demonstrate a substantial lack of understanding as to the reasons for extracting the blood. Given his answer, as well as my own experience of observing a similar patient been consented by the same team that consented this patient, I am in a position to infer that the person was, even after the donation,



misinformed that the donation had nothing to do with her illness, diagnosis or treatment. In this particular case, the interviewee was a middle-aged businesswoman with a degree. My interview with her took place just one day after she had donated blood and signed the donation consent form, which means that memory fade may not be a factor in her ability to recall events. The patient's failure to differentiate between her donation for research and her clinical intervention suggests that she was misinformed. In response to follow up questioning, the patient did not seem able to give a clear account:

Res: How did you hear about this research?

P8: I came to the clinic first. A woman came, greeted me and introduced herself saying that she was from the research department and asked me a number of questions, and I answered her, and then we went down to the lab and they took a blood sample, and she said it is for a study or a test or something...

Compared to the level of information and understanding suggested by the guidelines, this particular patient did not appear to have been sufficiently informed to provide an informed consent. This was the case with most of the patients I interviewed, regardless of educational background.

There is literature about how education levels might influence the informed consent process; literacy increases understanding of informed consent (Cassileth, 1980; Abolfotouh & Adlan, 2011; Adlan, 2013; Khedhiri, 2013). However, among the people I interviewed was a registered nurse, and I assumed that, through her basic nursing education; her general knowledge of genetics and of the research should have made her more informed. She, too, expressed the belief that her participation in the study was related to her treatment.

‘No, in my case it was a therapeutic intervention.’ (P7)

However, all of the interviewed participants were selected based on the fact that they had recently donated blood for genetics research and not therapeutic intervention. The time gap between the interview and the donation is less likely to suggest that such an important detail could be forgotten. Adding this to what I witnessed some researchers say in recruiting for MGE research in Phase One, it could be suggested that in this specific context there was an element of deception through misinformation.

Informed consent is highly dependent on what the patient understood, not only on what the researcher said. However, in some cases the use of language can be ambiguous. For instance, the Arabic word '*tabarou*' means donation in general, which could include money donations or any other charitable work. When the word is used with blood, it usually indicates a blood donation for therapeutic use in other patients. Another word is usually used when blood is donated for research, '*musharakah*', which literally means participation. So if the research team used the word '*tabarou*', it created the impression that the blood would be donated to other patients as a charitable act. This confusion was apparent in some interviews, where patients thought that they were doing '*tabarou*' rather than research '*musharakah*'. For example, P8 in response to my question about her willingness to suggest participation in MGE research for which blood would be withdrawn to a friend or relative replied:

'Of course I will tell him to do '*tabarou*' [donate blood], because '*tabarou*' [blood donations] do not harm; my husband give '*tabarou*' [donates blood] here in the hospital every six months, and that is a habit of ten years.' (P8)

Another participant mentioned that he would donate blood every month if his health would permit him to do so. According to the collected data, it appears that

some of the research participants were confused about the nature of the donation. This could be attributed to many factors, such as patients forgetting some of the given information to them, or being misled into thinking that they were doing *tabarou* as oppose to *musharakah*. However, it is also plausible – based on my observations for Phase One – that the researchers (also) bear some responsibility. My impressions based on those observations to seem to have been borne out in the interviews for Phase Two.

**1) Not informed**

The second way in which patients may have been deceived is by omitting to tell them key information. As I am drawing the picture based on what the patients remembered, I tried to explore their understanding about their donations. The data collected in Phase Two suggests a noticeable level of ignorance within the group I interviewed. Arguably, the level of ignorance was too high to have satisfied the Saudi bioethics guidelines or the international guidelines in relation to consent to participation in research being properly informed.

Among the most common forms of deception that I witnessed in the previous phase, was the lack of information provided to the participants, neither a copy of Participant Information Sheet (PIS) nor a copy of the consent form were given to any of the observed participants in Phase One. In SA the practice is to include the information on the consent form (as opposed to the UK where there is a separate PIS and consent form). In this phase some of the patients remembered that they had only signed a one-page consent form with no information sheet. They also claimed that they had not received a copy of the signed papers.

Res: All right, the papers that you have signed, do you remember how many pages?

P10: One page?

Res: OK, one page. Did they give you a copy?

P10: No.

Given the amount information provided verbally (based on what was observed in Phase One), given that the process did not permit prior reading/time for consideration of the written information that was provided (albeit it only one page), and given that participants did not get a copy of the information to read later, there are reasons to doubt the extent to which they could have been informed. Therefore, it can be suggested that genuinely informed consent in those specific cases was not obtained.

Usually when someone goes to the treating physician in a regular follow-up clinic, he or she assumes that, unless stated otherwise, everything that happens in the clinic will be geared toward clinical investigation, treatment, and/or their care. In some cases in this study, however, patients were not just asked to donate blood but seemed to have been allowed to think that the blood collection was necessary for their treatment. Most of the interviewees confirmed that they were not informed. In the case below, the treating physician, who was expected to introduce the study and get the patient's preliminary consent, did not tell the person anything. The patient was basically ignorant about the whole process of donating blood:

Res: How did you know that there was research...?

P3: He [the doctor] did not tell me anything.

Res: So, the doctor did not say that there is research or blood withdrawal or—.

P3: *Wallahi* [By Allah], he told me nothing about research.

Eventually the patient gave blood to the research team, but he claimed that he was not informed about the nature of his donation. In this specific interview, I

wanted to tease out what the donor's decision might have been if he had been given more information. In the following exchange, I was interested in exploring what his reaction might have been had he known that the benefits of this research would likely not accrue to him.

Res: If they had told you that this research is for a lot of people and you won't benefit from it personally, will you agree to donate? Or will you say let me think about it?

P3: *Wallahi*, I do not know, but I might say 'let me think about it'.

It is reasonable to assume that one of the principal pieces of information that research participants need to understand is what risks participation might entail. In the Saudi culture, there are specific adverse consequences for individual and families arising from the stigmatisation surrounding some genetic conditions. The potential impact – if this had been explained – is not something individuals are likely to have forgotten about in the few days between their donation experience and interview for this study. This is especially the case if they would themselves be stigmatised for taking part, or face stigma as a result of the findings of that specific MGE research project. I, therefore, tended to assume that if the interviewees did not mention that stigma was a risk when they were asked about the risks of their participation, the most likely explanation for this is that it was not brought to their attention during the informed consent process. Other suggestion could be that due to the nature of the stigma, participant may not have mentioned it for the fear that it would stigmatise them in my eyes. If this was the case, the nature of the answer would reflect that the participant was hiding something, or at least some of them. To the contrary, the response I had, was a very assuring, affirmative tone which, at least to my

interpretation and given my understanding of the Saudi culture and what I had learned from Phase One, did not indicate that they were hiding something.

Res: All right, have you been told about any specific risks and the measures they have to deal with those risks?

P7: No.

Res: In general, do you know about any risks related to your donating to MGE research?

P7: Never... They assured me, and I do not have any fears, I mean regarding blood donation for genetic research. They asked me and immediately I agreed.

This participant was confident that no more information was needed before deciding to donate. Some patients only wanted to be assured that the blood was taken into the custody of the hospital. They seem to trust that the hospital would not do anything wrong and that anything done would be in their benefit. This is definitely a point of difference between the usual assumptions of what patients should be told while in this context. The patients did not care because they trusted the hospital.

Res: Do you know where the blood [you gave] went?

P8: No.

Res: She did not tell you where?

P8: No.

Res: Do you want to know?

P8: ... This is a hospital. Of course it will be used for something to benefit me and not harm me, for sure.

Some of the interviewees said things that could be attributed to some level of uncertainty about the research activity in which they participated. I considered such uncertainty problematic for two reasons: 1) the information (e.g. where the blood is going to be used) I was looking for was not provided to them in the recruiting session, and 2) their responses would have been more focused on their knowledge about the donation if they had been given the proper information. As per the Saudi research ethics regulations as well as the international guidelines that were used as

references for the Saudi regulations, information about blood donation should have been given to participants before they decided to participate. Many participants seemed unaware of things as simple as the difference between his or her research participation and the clinical care that he or she came to receive.

Res: All right, do you have any idea about the difference between your regular medical intervention and your research contribution? Do you know the difference?

P10: No, I do not know.

Similarly, the participants did not have a clear idea of what genetics research is, even at a very basic level. This could be found in the majority of the interviews.

Res: Good! Do you know that it is a genetic study?

P2: What?

Res: A genetic study?

P2: [Hesitant and muttering.]

Res: Do you know what a genetic study means? Did your doctor tell you what it is?

P2: No.

‘There is no awareness... We are a developing country, we are still developing, and we might know about these things [research] but... the majority of people do not have an idea or they do not understand... I mean most of them do not know what is needed, exactly, from them or why it is needed...’ (P7)

In conclusion, one of the most important themes to emerge was the amount of ignorance around the topic of donating blood for research in general, and for MGE research specifically. This theme supports the observation results in Phase One. It is reasonable to assume that the participants did not have information to share because they had not been introduced to it during the recruiting process. This form of information deception varied between not telling a patient that he or she was going to

donate to research, to not giving information about the real risks of participation in MGE research.

**(b) Who asked**

Many of the participants suggested that the treating physicians asked them to donate blood for MGE research.

‘We went to the doctor during our clinic appointment, and she said that they will take blood samples, and we said, “No problem.”’ (F5/S)

The treating doctor seems to have provided sufficient information to one participant. She initially refused to participate, but she came back after one week and signed the informed consent form. She was the only one who reported this way of consenting. She was a registered nurse and worked in the same hospital in which she participated in the research.

‘And the doctor gave me the informed consent form and told me to read it and come back again after one week, so after one week I can be back to do it.’ (P7)

In conclusion, all of the participants were asked by their treating physicians to donate blood during their regular follow-up clinics. The physician-patient influence could be suggested by the sound of helplessness in the voices of the interviewed patients. Another factor that seemed to play a role in the interviewees in research was that the treating physicians had asked them to donate in the follow-up clinics. The context was that the patients had waited a long time for their appointments; they were desperate to be seen. They also were eager for subsequent follow-up appointments to be scheduled within a reasonable amount of time. In my own experience working with similar environments, if the physician asked the appointment clerk to give a patient an appointment at a specific time, it would be



done. However, if the patient was transferred to the appointment desk in the regular way, he or she would re-join a long waiting list with a minimum expectation of waiting from six months to more than a year. The desire for a quicker appointment may incline patients not to refuse any request the physician made. In the research at hand, I cannot confirm that this was the case because the arrangement of appointments was not included in the topic guide. The interviews uncovered one occasion in which a physician appeared to do everything correctly: he saw the donor in his clinic but gave her information and the option to think and come back later. This specific incident could be attributed to the fact that the donor was a registered nurse who worked at the hospital in which she had the follow-up appointment.

**(a) Rushing**

Most of the participants were ill and needed medical attention. However, the time allocated for them in their long-awaited appointments seemed to be insufficient even for their medical needs let alone for introducing the concept of MGE research blood donation.

Res: The period between the times they called you in until they took the blood sample: do you remember how long it was? Five, ten, fifteen minutes, an hour, in that range?

P9: Nothing more than half an hour.

The lack of time could be interpreted in two different ways: either this patient did not need more time to decide, or they were encouraged to decide more quickly than they wanted to. Although this particular patient did not use the word ‘rush’, the way “nothing more than...” was said reflected a level of dissatisfaction. Other patients were more frustrated and actually explained how they felt.

... we wished if she talked a little longer, to educate us ... she just quickly checked ... and did not chat much, we came from a long far away distance, she

did not even ask about the medication follow up. She quickly chatted; checked and sent us out ... Honestly she only said quick things. She was in a hurry and about to leave.’ (F5)

Due to the rushed nature of informed consent that was reported, it could be argued the participant did not consent in the way they should have (i.e. the patient should be given time to think with no stress or sense of time constraints). This added to my impressions based on the data from Phase One, that those research participants did not freely choose to participate.

### **6.3.3.2 Patient vulnerability**

In the interviews, some participants made statements that suggested feelings of vulnerability. Others seem to have felt sufficiently empowered to bargain with the research team for their participation in the research, and they asked the research team to do something for them in exchange for their participation.

#### **a. Vulnerability of patients recruited by their treating physicians**

Vulnerability in the context of blood donation could take many forms. An example of this can be seen from F1, who suggested an invitation to participate via a poster would be more appropriate than a personal request from the treating physician.

To put a poster giving short details about the research like that “If you want information about [the research], you can refer to [the clinic].” Then the patient will have the advantage of participation and will receive better care. It will be better for the patient to go personally, and he or she will be the priority for medical care. (F1)

In the Saudi culture, there is a tendency for patients to not want to disappoint their physicians, and the above quote can be taken as the patient’s polite way of asking to avoid confrontation with the research team. The importance of this quote

comes from the fact that the son seemed to want to regain the power to make decisions about donating without the influence of the research team. Though in general there were many signs of frustration that could be attributed to many factors, without trying to overanalyse this quote it seems these family members were not happy with the way they were recruited. It is also important to mention here that I used a poster to announce our research in the recruiting process for these interviews, and we displayed it where patients could see it and decide if they would like to contact us. As this was the first time a poster advertising research was used in either of the two institutes, it could be the case that the patient was influenced by the way he was recruited to this research when he made this suggestion.

‘Whenever I ask for a report or a request for air tickets [under the hospital policy], or a sitter, he always cooperates with me fully, whenever I request something.’ (P9)

In some cases, though, patients understood that what was asked of them was something extra, but they felt indebted to the kind, helpful behaviour of the treating physician, and therefore assumed the favour should be reciprocated by donating blood if the physician asked. It appears that this patient felt that he did not have any choice but to accept, based on the Saudi culture characteristics, as explained earlier in Section 1.

**b. Vulnerability of patients asking if they would lose treatment privileges**

Another suggestion of vulnerability emerged from the interviews in many places in the form of participants’ inquires if they would be losing treatment privileges and being concerned that their rights would be compromised if they

expressed their opinions. This was the question most commonly asked by participants during the rapport building and before the voice recording permission and the informed consent signing. Based on my assurances of privacy protection, the patient signed an informed consent and voice recording started.

F1: Will our opinion and comments affect our ability to receive medical care?

The importance of this question stemmed from the context of how Saudis express fear. Saudis usually like to be seen as proud and fearless, even if they are not (See Subsection 1.2 The Saudi Arabian Context). None of the interviewees said anything harsh or made serious complaints about the hospitals or the treating teams. In the above case, the person expressed, in an extremely polite way, his frustration with the service he received which he expressed in the interview (quoted in Subsection d- Vulnerability counterargument), the fact he was not treated in the way he expected as a donor, and the general lack of organisation at the hospital. Yet, he was not comfortable enough to complain. One way of interpreting F1's question is that in context, it reflected implicit feelings of fear that he might lose his treatment privilege, although this fear was not expressed explicitly.

**c. Vulnerability of Saudis wishing to appear to be devoted Muslims**

Patients were also vulnerable to the use of religion and suggestions that God rewards people who donate for altruistic reasons. Donation was presented as a charitable act:

Res: Why didn't you want your name mentioned in the blood donation informed consent?

F5 I just want the Godly reward.

Res: OK.

F5: If my name is known, my Godly reward is gone.

Res: How can the Godly reward go? What is the relationship between the name and the reward?

F5: Because it is charity and charity has to be secret.

Res: OK.

F5: It is then between you and your God only.

It is beyond the scope of this work to analyse the merits of charitable acts and their basis in religious belief. However, in the context of this research, it could be the case that religion and the notion of pleasing God rendered patients vulnerable in the sense that they felt unable to protect their interests because they would be unable to say even if they wished to, without risking be perceived as being impious. I believe the idea of charity was a result of how the researchers convince the patients to donate for two main reasons:

- In Phase One, I observed the research team using religious innuendos to make the connection between donation and '*Sadaqah Jariah*'. This Islamic concept signifies the highest level of charitable acts—continuously rewarding charity that will continue to reward a person even after his or her death.

- Once a suggestion is made that 'donating blood for research is a virtue', Saudis are less likely to refuse to do it. Saudis like to be perceived as religious people for cultural reasons, and the failure to perform a charitable act would be regarded as at worst a sin and at best the loss of the opportunity to portray oneself as a devoted Muslim. To engage the concept can therefore be to manipulate someone's behaviour in the direction of the designated charitable act.

It is fair to say that this point can be interpreted in a different way. For instance, it could be the case that what I witnessed in Phase One was not the norm. It

could be that patients in Phase Two were more oriented toward charitable actions and did not need the researchers to nudge them to donate.

**d. Vulnerability counterargument**

The argument for vulnerability was supported by many themes that emerged from the data. However, it is true that everyone is vulnerable to misinformation and deceit, but this produces a very wide and arguably meaningless understanding of vulnerability for it essentially means that everyone is vulnerable and that there is not special category of vulnerable person (Mackenzie et al, 2014). In this section I provide data to illustrate the point that despite the policy assumptions, patients are still vulnerable. This interpretation is viable if patients were unable to make adequate donation decisions for themselves. Some of the interviewed patients showed a degree of understanding and might have made their decisions based on anticipating the benefits of participation, which contradicting the claim of total vulnerability.

Some participants demonstrated very clearly that they had expected something more in exchange for their agreement to donate. This suggests that some patients did know about the value of their contributions, expected the research team to pay them back in some way and felt able to assert themselves in this respect.

‘Then the patient will have the advantage of participation and will receive better care. It will be better for the patient to go personally, and he or she will be the priority for medical care.’ (F1)

This suggests that the person had some sort of expectation based on the assumption that he would be privileged as a patient gain advantages greater than patients who did not donate blood. In this particular case, the person wanted to get priority medical treatment.

The theme of vulnerability was not straightforward and easy to draw conclusions from because some patients seemed helpless. Based on previous suggestion in Chapter One, one might ask whether any typical patient in the Kingdom feels empowered when it comes to making medical decisions given that they are accustomed not to questioning their doctors, which seemed to be underestimated by the policy. On the other hand, there were other contexts in which patients had an agenda regarding benefits (e.g., gift reciprocation or being the first to benefit from the research outcomes). Given the context of the Saudi culture and health care system, it seems that patients were vulnerable insofar as they did not have the opportunity to refuse fearlessly. On the other hand, even those who were afraid to refuse to participate did have some level of hope or assumed some sort of payback, whether religious benefits from pleasing God or some more tangible benefits.

#### **6.3.4 Summary**

To conclude this subsection, the Phase Two interviews were very important for giving an insight into the perspectives of the interviewed patients. Without the observation data from Phase One, it would have been very difficult to understand why patients seemed to have little to share in these interviews. The researcher teams in Phase One seemed to assume, according to the policies, that Saudi patients cannot decide individually in an autonomy-based manner. It seems that two sets of values were playing against each other in the field of donating blood for genetics research in Saudi Arabia. The researchers' world, as seen in Phase One, seemed to uphold research governance that assumes the values of autonomy, liberalism and principlism. On the other hand, the interviewed patients seemed to lean more toward

the values of trust, hope, piety, and, on some occasions, fear. The contrast of the two worlds seemed to encourage researchers to work pragmatically to satisfy both research governance by providing auditable documents, and the patients' culture by providing assurances and promises. This claim will be discussed in the next chapter.



## 6.4 Phase Three: Focus groups

Two focus groups were convened. The first group consisted of the researchers, research assistants, technicians and research nurses who actually collected blood from patients, either for their own research or on behalf of senior researchers who employed them. The second focus group comprised the policy-makers, ethics committee members and chairmen, national committee members and senior researchers.

### 6.4.1 Participant Characteristics

The characteristics of the participants in the first focus group are described in Table 6-3. Although the amount of recruitment experience they had varied, all held fairly junior posts.

TABLE 6-3: CHARACTERISTICS OF FIRST FOCUS GROUP PARTICIPANTS\*

Code	Gender	Number of patients recruited**
FG1/1	M	More than 50
FG1/2	M	More than 500
FG1/3	M	More than 80
FG1/4	F	More than 500
FG1/5	M	More than 500
FG1/6	F	More than 500
FG1/7	F	More than 100

\*Occupation and years of experience are not presented to protect participants' identity.

\*\*In this column, every participant who claimed to have recruited less than 500 was asked to estimate the number of recruited patients.

There were eight participants in the second focus group; only one of them was female. The original distribution of the invitations had sought a gender balance. Women are under-represented in higher position in Saudi Arabia, so the time of the

meeting was fixed mainly based on the availability of the women who accepted the invitation, only one of those who confirmed eventually attended.

TABLE 6-4: CHARACTERISTICS OF SECOND FOCUS GROUP PARTICIPANTS\*

<b>Code</b>	<b>Gender</b>	<b>Expertise</b>
FG2/01	M	Bioethics
FG2/02	M	Genetics
FG2/03	M	Bioethics
FG2/04	M	Genetics
FG2/05	M	Bioethics
FG2/06	M	Senior genetics researcher
FG2/07	F	Bioethics
FG2/08	M	Bioethics

\* The occupation and level of seniority are not reported to protect participant identities.

#### **6.4.2 Results of the first focus group**

In general, the findings from this phase (asking people general questions in the beginning and then asking them to reflect on the data from Phases One and Two complement those of the previous phases, and they provide further explanations for some of the behaviours noticed earlier. When the participants were asked to reflect on the Phases One and Two data their general response was to accept the results, and many actually expressed shame. No one seemed to question the findings. On the contrary, they shared more stories that matched the findings.

The group had a very thorough discussion about rushing patients' decisions and why some of the attendees did think it was the best course of action under the circumstances. There was a consensus about the lack of organisational support, and participants offered some suggestions for how to overcome that challenge. In addition, the researchers revealed their opinions about patients' vulnerability in light

of evidence about both patients who were totally ignorant and patients who had some knowledge and had tried to bargain with the research teams about giving blood.

#### **6.4.2.1 Coercive practices**

Coercion was a major theme that emerged from the data the participants provided. Several different strands could be found within this theme, including deception. Many participants agreed about the challenges that arose around organisational support. However, some of the participants felt strongly that current practices were the most pragmatic means of addressing the shortcomings of the health services in their hospitals.

##### **(c) Deception**

Some participants shared stories about researchers whom they thought knew the policies and how they had, according to the participants, deceived patient's by taking blood without consent.

FG1/6: They were drawing people's blood without even consent. Sometimes patients were in the ICU.

FG1/4: Or maybe because he was unconscious.

The participants thought that the deceptive nature of the actions (in this case, extracting blood for research and telling the patient's guardian that the extracted blood is for routine tests) deceiving the unconscious patient's guardian about the nature of blood extraction) was due not to ignorance about those guidelines but to the senior researchers' conflicts of interest, which motivated behaviour most of the group agreed was unethical and illegal.

In the participants' experience, deception was not limited to patients. Some of them witnessed researchers trying to deceive ethics committees into retroactively approving research by claiming they got their results accidentally.

FG1/2: They may say, 'We found this in our way [by coincidence]...'

FG1/6: Exactly.

FG1/2: Have they done a special test? ...

FG1/6: I think what they did is unethical. For me,[in my opinion] I do not know, but this is unethical. *Inshallah* [God's will] it will never happen to me, but I know what I will do...

FG1/2: This is just an example for the point raised—.

FG1/1: For me,[in my opinion] this is because informed consent is to protect organisations, not those 5,000 patients.

From the data provided in the group discussions, deception as a theme was further divided into several strands, including deception through misinforming and deception through not informing.

#### 1) **Misinformed**

I was more able to discuss interim findings and explore the focus group participants' understanding, explanations and justifications in some cases for most of the actions. From my analysis of data, deception through misinformation emerged as a subtheme of these discussions.

The collected data reveals that there was a general consensus among the group that researchers might provide inaccurate information for two main reasons:

- Lack of information: some of the participants seemed to think that there was a significant level of ignorance even among senior researchers themselves. The example they used to illustrate this point was the risks. Patients were not told about the risks of genetics research because, the group thought, the researchers themselves were not fully aware of them. Even if this could be true,

information about risk is not all that is being withheld, as presented in the previous phases.

- Some of the participants seemed to believe that a strong sense of authority existed among the physicians. These participants tried to portray the sense that it was not physicians' ignorance but their feelings of power or superiority that were significant—the physicians thought they knew better than the patients and everyone else including the research team members.

One participant related the following experience:

Well that time I was not the assistant of that researcher, but I said, “Do you know that you need a consent to take this blood?” He said, “No, I do not need consent. We draw blood from those patients every day for various reasons.” I replied, “Yeah but... this patient or his relatives... they need to know that you are not taking it for regular blood work.” Not to know that was, you know, Creatinine or whatever. He [the doctor] is doing it for a certain study. He eventually said, “No, no, no! ... We do not need that [informed consent]!” (FG1/6)

Another line of discussion in which the participants were in agreement was that prospective donors were told that they were going to receive the genetics test results as soon as they were ready. It was likely that researchers did not believe this was true.

I received a call earlier today. The blood was taken one year ago. The patient asked, “What happened to my blood? I keep calling you and you keep referring me to the doctor and to everywhere else. You keep saying call next week or next month. Now... tell me. Do you have any results for me?” So I had to refer him once again to my colleague who would have a better answer for him. (FG1/2)

## **2) Not informed**

The focus group participants agreed that patients were given highly selective information, or, as they said, patients were only told about ‘the white part of the

project'. By 'the white part', participants meant that the researchers provided only the positive information and deliberately omitted the information that might negatively affect donors' decisions or what they called it the 'black side' or 'black part' of the research.

But... doctors... or what happens now under research projects [is that] they are trying to get [to present], as [FG1/3] said, the white parts of the project. But they did not try to mention the other part...

He doesn't know the consequences. If he is giving his blood, what is the black part of it? He knows the white part of it but what's the black part he [does] not know, and we do not mention that to him. (PG1/01)

From the context, it seems that what this participant meant by the 'black part' is the information that might incline the donor against participation in the research. It is interesting that this participant referred to the omitted information as a 'black part'. From the context, what seems intended is that patients were given the versions of the story that would make them favourably disposed toward donating without letting them know about anything that might disincline participation.

There are many commentators in the literature who have questioned the level to which physicians should be truthful to patients and who note that full truthfulness in the field of providing medical services can sometimes be harmful to patients' interests (Blackhall et al, 1995; Higgs, 2007; Adlan & ten Have, 2012; Adlan, 2013). Even the Hippocratic Oath urges doctors to say only what patients can take, which might not be the full truth. "Perform [your duties] calmly and adroitly, concealing most things from the patient while you are attending to him ... turning his attention away from what is being done to him; ...revealing nothing to the patient's future or consent conditions", Hippocratic Oath as cited by Jackson (2013) p166.

In the context of this work, it seems that some of the researchers transferred the authoritative view from the field of medical practice to the field of medical research. It seems that the participants had witnessed enough from the physicians' and senior researchers' behaviours to agree with each other that most of those senior researchers patronised their patients, giving them minimal information in order to facilitate gaining their signatures.

Many physicians do not believe in the consent process for a surgical procedure. The same goes for how they think of research. Some even think that it is just a routine practice: "I do not even need to tell the patient." So... "I am the physician, and I know better than them. Why do I need them to sign this consent?" On the other side, still, there are some researchers who believe in patients' rights. (FG1/05)

The main difference was that in the case of recruiting for research, there were conflicts of interest between the physicians as treating doctors and their eagerness to research. The participants collectively believed that education was the best way to ensure patients were equipped to protect their interests. However, there was no specific reference to what they meant by education. The best explanation is that they were talking about improving patients' general education levels, since there were no discussions of out-of-curriculum education like conferences or media.

OK, they do not ask about the black part, but if he is educated he asks [about the black part]. Meaning if it [the research] doesn't have a direct benefit to me or if the effect is not OK, sometimes they refuse to participate if they are educated because he [the patients] talks about the other part. I agree with it—70% of subjects who are not educated would agree to participate without question. (FG1/3)

It was agreed that when it came to recruiting patients, because they belonged to the same culture, they knew what made people participate and what scared them away. Such knowledge was a double-edged sword, as it could have been used to help

patients make decisions with help from people who understood their fears and hopes. On the other hand, it could have been used as a recruiting tactic where the aim was to get the patients' blood regardless of other considerations. The participants seemed to agree that the latter was more widely practiced based on what they had seen in the field. The test case was using the word 'research' when inviting patients to donate blood, as the word has connotations that made patients afraid. Researchers knew, the participants suggested, that if the word was used, patients would lose interest in participating.

Because he will not come to the clinic with the name "research" on it. If you ask him to a clinic without the word "research", he will come. (FG1/3)

**(d) Who asked**

As in the previous subsections, another potential source of coercion was the effect physicians had on patients. This was the case when there was a power differential between the doctor as a PI and his or her patient. Such a power differential may lead to patients being less likely to refuse what their physicians asked of them. It would appear that there was group consensus about the fact that coercion of this type existed.

Many scholars have written about the patient–physician relationship and how the dynamic could easily be dictated by the hope factor in the sense that patient needs to be reassured by the treating physician (Williams, 2002; Higgs, 2007). As discussed in Chapter Two, most Saudis look at physicians as healers. Such an image appeals to patients' hopes of being healed under the guidance of their physicians. So when a physician asks for something, it is likely to be perceived as an order even if the physician does not intend it to be—the kind of order that will upset the healer or



prevent the patient from being healed if it is not followed. This sense of the relationship was confirmed by the participants:

Actually, they listen to us or to the doctor, and they feel it's part of the treatment even [if] it is for just a study. And they will not say "No". Even the feeling from the doctor when he asks them—[they think] that [this] means he will find for us a cure or treatment. There is another problem: if we explained anything to the patient, he might say "No", but if the doctor said anything, the patient would say "Yes". (FG1/3)

The data also seem to suggest that some of the participants felt they could not refuse the treating doctor's request. The participants also reported, however, that whilst they thought that patients appeared to agree with their clinician, they also felt that this may not reflect their actual feelings. They noted from their own experience that some patients, as soon as they were out of the examination rooms, changed their minds. For them this is a source of frustration as it puts them in unwanted confrontations with the physicians/PIs.

Some of the patients, they are first introduced to the study by my PI and they agree. Once we are shifted to another room, they disagree. Why did you agree in the first place? All of the sudden, they are busy... they have pharmacy... they have I don't know what. (FG1/4)

Some participants felt that the physicians they work with knowing they had influence over their patients, used it to persuade patients to reconsider their decisions not to participate, either by sweet-talking them or by overbearing questioning:

Sometimes they [the patients] say no to me, [but] the doctor really wants the patient. He asks me, the doctor, to follow it up, I said "No". He comes [to the patient] and said, "Why you do not want to participate?" He [the patient] says, "No... no, I will... I will [participate], no problems". (FG1/2)

When the doctor wants them to sign, he usually talks to them friendly to get them to sign. (FG1/3)

In contrast, it seems that participants were aware of the potential coercion and tried to resist it. The participants shared many examples in which they tried to educate patients and told them it was their right not to participate, and in some of those cases patients changed their minds about participating. This would be evidence of practice that does conform to the guidelines; however, they also suggested that this is not the usual practice. In addition to the above quote from (FG1/2), demonstrating how some doctors used their authority to change patients' minds about participating in research, another story that was shared indicates that patients changed their minds about participating after being told that they really did not have to participate.

It was also the consensus that this kind of power was not only in the hands of the treating physicians. The participants thought that the same effect could be replicated by others for instance by wearing a white coat or introducing him- or herself with the title 'doctor'.

Because he was approaching the patients with the words "I am doctor such and such [his name]", they believed in him more, and they consented, or they agreed to participate in the study more than with her [a person who did not introduce herself as doctor], even though she has better communication skills than he. (FG1/5)

FG1/3: ... we tell the patient that he can refuse [to consent], but we know that he [the patient] will never say no to the doctor.

FG1/1: Do you, usually, wear a lab coat when you approach patients?

RG1/3: No we do not.

FG1/1: May be this is [the] problem [i.e. the patients do not listen to you].

Res: Why did you ask about the lab coat?

FG1/1: Because, if the patients did not see a person wearing a lab coat, they would think that this person is not a physician.

In the last quote, there was a consensus among the group that attire plays a major role in patient decision to participate in research. This is because the lab coat,

according to the participants' consensus, makes the participant think that the person wearing it is a doctor.

**(e) Rushing**

The participants seemed to agree that rushing patients to consent is a strategy for securing participation. However, using rushing as a tool of coercion did not receive the same level of consensus as the other themes. Some of the participants seemed to argue that, in their experience, giving patients more time to think about things meant they would be less likely to come back and/or they would have more scope for questioning their participation.

If I allow them to go home, they will ask many questions when I call. If they are here, it is just a direct yes or no. (FG1/3)

Other participants argued that getting the consent on the same day is a pragmatic solution to the logistical problems that would inevitably accompany patients having to return to the clinic to participate. They thought that things like the lack of ready car parking and the absence of reliable public transportation in Saudi Arabia could work as deterrents to participation in research. This judgment chimes with the experience of one of the interviewees in Phase Two, who reported that she came from a very remote place and that her journey to the clinic took ten hours. For these kinds of reasons, the focus group participants thought it would not be right to call such patients back to the clinic to participate in research.

It is difficult to come back... parking is a disaster. (FG1/4)

Some patients... it is difficult for them to come to two appointments in one year. (FG1/3)

So whilst the focus group participants seemed to agree that patients were rushed to decide, they disagreed about whether rushing should be regarded as a coercive strategy. Some of the participants did argue that it was a coercive, while others tended to draw on the distinction between working under the pressure of time and rushing as a coercive practice. The latter thought that rushing in that context was a pragmatic measure to prevent people from suffering the hardship of visiting the hospital on additional occasions. However, regardless of the motive for the rushing, the Saudi regulations on research ethics stress the importance of giving patients enough time to think about their decisions. The definition of ‘enough time’ would raise the question of where the line should be drawn between rushing as a coercive tool and rushing as a necessity dictated by a pragmatic approach to conducting research. In the next chapter, I will discuss further whether such rushing may have contributed to the severe lack of comprehension that I witnessed in Phases One and Two.

#### **6.4.2.2 Obstacles, challenges and responses**

Members of the group were very clear about the challenges they had faced and the obstacles they had experienced recruiting research participants. They also suggested a few measures that would help them to be more efficient and recruit in the most sensible and ethical way.

##### **(a) Lack of support**

Organisational support seemed to be perceived as lacking in light of the participants’ statements. The participants thought it was their job to recruit patients in the way that made sure patients gave blood, as opposed to recruiting patients in

way that give them the opportunity to say no, as they had to please the PIs. Some of them seemed sympathetic to the pressure doctors were under in terms of the number of patients that they had to see in each clinic in addition to their research patients.

FG1/1: Also, we have to speed up the recruiting.

FG1/6: Yes... if the researcher wants that, then yes. I mean, if you have a PI who has 35 patients in his clinic.

FG1/4: This is only during the morning.

Such agreement from the participants that researchers' actions were excusable because of the amount of stress they were under suggests the question: 'Why didn't the institutions step in to help improve the quality of recruiting?' A possible explanation is that the health system as a whole is under the stress of huge waiting lists. Some might argue that such stress makes the research activity seem like an expensive luxury that can be supported but will not be prioritised.

There were other areas where participants reported a lack of support. Some participants acknowledged that their accommodation was inadequate and did not facilitate the protection of participant privacy during their recruiting sessions. Moreover, the clinical PIs were unwilling to help by offering one of their allocated clinic rooms when recruiting for their own research.

FG1/2: We do not have special rooms for research...

FG1/4: [Agreeing strongly] Once I asked a patient to consent in the corridor.

So when I start to take the pedigree, the physician asks to leave the room. He thinks it's OK because he has many patients. (FG1/2)

The lack of support was not limited to the availability and quality of the rooms. There were also no specific ancillary services or personnel devoted to the research, which meant that the research patients had to suffer the experience of sharing the

out- or in-patient clinics with other patients. This created extra stress for the FG participants.

Even when I start to use the conference room, we receive a complaint from the charge nurse. “This room is not for you or the patients,” she says. We also are asked to leave the room for a physician, or for whatever... I don't know what reason. It is a conference room! (FG1/4)

...if I have a patient who needs examinations, ultrasound, blood for genetics, there is no support from other department and there is no support if he has research questions. (FG1/2)

This suggested to me that it is not that the participants were not aware of how they ought to conduct recruitment but rather that they lacked the infrastructure and support to accord to the guidelines.

**(b) Distance, return trips and funding**

Among the challenges that researchers faced in the Saudi hospitals were that patients had to travel long distances, and the research centres did not have the financial means to reimburse their travel fees or even to provide logistical support like allocating parking spots for research participants. Three different issues within this theme were noted from the group discussions:

i. Seizing the opportunity for patient follow-up clinics

Patients who were needed for research often either came from remote places or were busy people. The fact that they were going to be in the hospital anyway seemed to encourage group discussions in favour of seizing the opportunity and inviting them for research.

We cannot do it that way. Some patients don't live in Riyadh. Even if they are in Riyadh, they won't be free [from other commitments]. For some research, they need to be seen before and examined. How we can bring them in again? My

opinion: take time now and read it. If you like it, then that is it. Why do I have to send him home? (FG1/2)

ii. Asking patients to return at their own expense

Several participants reported that patients were asked to come from remote places to participate in research without reimbursement for travel expenses.

FG1/2: We have a project, and we need to call patients to come to our hospitals. We bring them from remote places like Jizan [remote and to the south] or Tabouk [remote and to the north]. They paid for the tickets.

Res: Who paid for the tickets?

FG1/2: The patients did... We do not pay them any travel money reimbursements, but they are happy to come. *Wallahi*, they are very poor, yes... [It is true that] we have something; we call it a travel order for the patient, but we need the [whole] family, not just the one eligible patient.

...

FG1/1: We are [the researchers] abusing them [the patients].

This admission was strongly condemned by the group. Even the person who shared the story was not proud of what he thought he had to do.

FG1/2: Yes I call it abuse... we do not care... Even as a coordinator I am not comfortable with it.

iii. A potential conflict between what is regarded as the ideal situation and the reality

The following lines discuss what could be interpreted as articulating a conflict between the ideal situation that is regulated by the NCBE and the reality, given the context of those two organisations and their geographical location.

FG1/6: When I started to work as a CRC [clinical research coordinator], even before I attended the course, I was trained that every single patient has the right to take the consent and read it at home.

FG1/2: In our area it is very difficult. I cannot just tell the patient to go and then come back in 24 hours.

This exchange illustrates a very central point in this research about the difference between what ought to happen in an abstract domain as per the bioethics guidelines (in this particular case, the ICH-GCP) and the concrete reality, with its difficulties and obstacles. This suggests a bigger question about what trade-offs between the two norms should be appropriate—i.e., the international norms seem to be written for a context in which services are closer to patients and there are public means for reaching them, while local reality admit that it is unreasonable to ask someone to return to a hospital that is hundreds of miles away.

#### **6.4.2.3 Patient vulnerability**

In agreement with what was noticed and reported in the previous two phases, the next theme to emerge from the data was that of patient vulnerability. The participants came to agreement through discussion and shared different scenarios in which patients, according to their experience, could have been taken advantage of, although some patients showed some signs of understanding the process.

The participants seemed to believe that there was a level of vulnerability among patients, as they were eager to be seen and could not say no to their doctors. The participants suggested that patients were helpless in front of their treating physicians. They were very keen to be seen. Some of them had been waiting for appointments for a long time, so it is expected that, given the context of their opportunity to come to the hospital, they would not refuse. This finding overlaps with the view that research participants are confused about the difference between treatment and research. However, the argument for employing the concept of vulnerability here is supported by what the participants thought was a sense of



desperation that forced patients to participate in research in hopes that they would be seen.

This one of the difficult things I did. I explained that, OK... yes we [will] examine you, but you will be [in] the research. And as a patient who doesn't have [an] appointment for 6, 8 months, [he] just wanted to come. Especially with glaucoma, they want to see the [eye] pressure, they want to get the medication. (FG1/2)

She said that “on a monthly basis at my work”—she works in a private lab—“they take our blood for a study.” She even showed me the process and said, “I have a phobia now, and still I cannot say no.” (FG1/4)

**(a) Patient vulnerability counterargument**

The main assumption underlining the idea of vulnerability is that patients are helpless and feel pressured to participate or sometimes participate just to gain medical attention that they would normally have access to if it were not for the lack of health services. This assumption seemed to be undermined when some patients bargained to donate for MGE research, which suggested a sense of power rather than powerlessness. Members of the group tended to agree that from their experiences they had seen patients asking for favours in return for their participation in research. Other patients seemed to have information about the risk of stigmatization from MGE research, and the participants thought that they would tend to refuse to participate on the basis of that concern.

I once had a patient who said that he won't sign unless I go and get his medicine from the pharmacy. Because for me, I will stand in the queue of the employees and I might know one of the staff who might make it easier [laughs]... and we did bring him the medication. So I said, well, it is fair, I need something from you and you need something from me. (FG1/4)

Some of the patients afraid of stigmatise [are afraid of being stigmatised] with specific genetic disorders or diseases. (FG1/6)

#### **6.4.2.4 Responses to the presented data**

The themes reported to this point arose spontaneously from the conversation with minimal interaction from me as the focus group moderator. This following subsection is about how the focus group reacted to the summarised interim results of Phases One and Two. In general, the substance of the discussions they engaged in might imply that what was presented was not far from what was really going on. The group's first reaction when I had finished the presentation was one of long and total silence, and then participants started talking and discussing the issues raised. They seemed uncomfortable with the results, but they did not deny them, either. They admitted that they had personal experience of most of the themes.

##### **(a) Oversight regarding policies**

From the very beginning, participants were in agreement that what was reported was not the proper way to recruit patients for any kind of research, let alone MGE research. They attributed most of what they thought of as wrongdoing to the lack of authoritative, thorough inspection or oversight (they called it 'upper hand'). They saw the lack of oversight as the main problem to be dealt with.

The upper hand for imposing [enforcing] those guidelines and its rule is not fully activated. So, let's take the American example, they have the FDA. ... But here! We do not have that yet. We are not afraid that the Saudi FDA will come and inspect us. ... So until now, we do not have an upper hand in the country. Once we have that, I would say that following or adherence to the regulation will be much better. (FG1/5)

They also seemed to believe that there were differences in how strict each institution was when it came to compliance with guidelines.

I do not know, but I noticed that doctors prefer to establish their genetics research in our hospital rather than other hospitals. I do not know, but maybe the restrictions in our hospital are less than those for clinical research. (FG1/1)

Another point of agreement among the group was that they believed that there was a notable lack in adherence to guidelines.

Are we following them [the international guidelines]? This is the question? Are we following these guidelines 100%? (FG1/6)

Different speakers like FG1/5 and FG1/1 repeated the same question, ‘What are these international guidelines?’ which suggests in its face value that researchers do not know if there is an international code for MGE research or not.

**(b) The need to educate donors**

Educating donors about their rights emerged as a solution to most of the challenges that were mentioned.

I think it has to do with educating the community, let them know that you are trying to do genetics research... or study, you know, Saudi Arabians in some sort of a family or group. (FG1/6)

This call for patient education was supported by others in the focus group. However, the term ‘patient education’ was not fully explained—i.e., it was not clear what they actually meant by patient education. Patient education can range from the basic education provided through the education system to very specialised efforts for specific educations, such as those targeting vulnerable groups with specifically-tailored education activities (Branch et al., 2000). It could also take the form of conferences and meetings that provide educational materials (Marks, 2009). In the case of these participants, I think they meant about specifically educating patients about their potential participation even before the informed consent process was to take place.

We also need an education media to talk about research and what are patients' rights if someone becomes a subject of research. Even inside the hospital and the committee, to approve at least a brochure or any education for patients. (FG1/3)

FG1/5: I think this is lack of knowledge and lack of education.

Res: Which part?

FG1/5: It is the patient part.

### **(c) The need to educate the doctors**

On the other hand, the participants also suggested that it was just as important to educate the doctors. They compared RCTs regulation in GCP which is comprehensive and clear to MGE regulation. They thought that apart from a few lines in the national guidelines, there was nothing to it.

OK! Let us all agree then that the most important thing is to educate the researcher himself, the... the... principle investigator. (FG1/4)

Yes, what are the international regulations, if any? When it comes to clinical research I know the GCP. When it comes to genetics research, all what I know is few guidelines according to the NCBM. But strong, officially-imposed standards, I am not aware of them. (FG1/5)

Because there are new people in the research. Maybe he is a consultant in his specialty, but in research he is a beginner. He needs also education in there. They need at least three months of coursework, at least. (FG1/7)

It seems that there was unreserved agreement about the need to educate the researchers.

#### **6.4.2.5 Genetic material: Its importance in Saudi Arabia**

'Genetic material' seemed to mean any tissue that could have genetic material, or readily extracted genetic material. In very general terms, the presence of genetics research did not feature strongly in the discussion; most of what was said could be easily applied to any other kind of research, such as epidemiology, or even clinical

research. I tried to tease out what the group thought of genetic material in general, as an introduction to getting them talking about the genetics research specifically.

The participants seemed to have a strong feeling about the Saudi genetic material, as they believed it had strategic value. They thought it could be used as biological weapon against Saudis. One of them actually tried to imply that Corona virus seems very specific in attacking only Arabs of a certain age. In a similar explanation, it could be the case that the group shared the belief that Saudi genetic material, if it fell into the wrong hands, could be used to develop biological weapons (e.g. viruses) specifically designed for Saudis, which could be seen as a matter of national security.

...It may end up creating a biological weapon actually for a particular country or particular race inside that country. (FG1/5)

Just by agreeing to send blood abroad, you are risking the society, not only the individual. (FG1/1)

There is no specific touchable [concrete] reason right now, but you can see around us now that the Corona disease is now in the Eastern province. I do not know, but the disease attacks specific people. All of them are Arab, and all of them are either under or over a specific age, and... (FG1/1)

#### **6.4.2.6 Summary**

In conclusion, the focus group was in harmony with my interpretation of the data from the previous phases and gave narratives to support the findings. It also confirmed that the focus group had experienced what can be themed as coercive practices in the form of giving misleading information and omitting important information. Also, there was enough to suggest that participants also had witnessed similar patterns of what I have interpreted as rushing patients into making quick decisions. This was for many reasons, some of them to coerce the patients, but some

of them were due to the lack of organisational support. However, the experiences participants related suggest that some patients knew what they were giving and began bargaining with the research team as a result. In addition, it appears that the group believed that Saudi genetic material needed to be protected, as it was considered to have strategic value. The genetic material was considered to be a direct threat to national security because it could be taken as the basis for race-specific virus or biological weapon of mass destruction, as well as raising concerns for the privacy of the donors who had given those materials.

### **6.4.3 Results of the second focus group**

The second focus group was run in the same way as the first: the first part was general discussion managed with the minimum intervention from my side around questions following the common topic guide. The second part asked for reactions and reflection on my interim findings from Phases One and Two. The general findings of this part of Phase Three were in agreement with all previous findings. This focus group consisted of policymakers some of whom had signed the actual Saudi National Bioethics guidance document before the King signed it as an indication of enforcement and political support. They also tried to defend some of the observed practices, as I will try to illustrate, but, in general, they tried to suggest corrective measures. Another important finding was that they all agreed that the topic was very difficult to tackle in Saudi Arabia for many reasons, including the lack of education.

Among the differences I noticed between focus group 2 and the focus group 1 was that the former assumed corrective action was needed. They tended perceive the data as highlighting problems that needed to be solved, including by revisiting the current regulations. The latter, in contrast, accepted the findings as the best that could be done given the context.

#### **6.4.3.1 Coercive Practices**

Members of the group seemed to agree that Saudi donors experienced some level of coercion from physicians. FG2/5 shared a very interesting story from his experience, as follows:

I always quote a story about one of my patients. He has thrombosis... That patient happens to be a legal advisor, a legal consultant. So they were running

the genetics study for [advanced MGE research]. Of course they asked the IRB for approval and there was an eight page information sheet and informed consent. So the nurse... everybody who comes in they ask him to sign that and give his blood for the study. So the legal advisor looked at those eight pages and said, "Look, I will take it home, I will read it and then sign it, the proper way of doing it." So the nurse went to the physician who is running the research and he came very upset, he torn up the pages... [Shouting] "You do not want to participate?!", and he scared him. (FG2/5)

This story was told by one of the leading bioethics experts in Saudi Arabia. This suggests that even among such high level bioethics authorities in the country, there is knowledge of a history of coercive practice.

**(a) Deception**

The composition of the group - senior, authoritative figures - had an effect on how the questions were addressed. They seemed more oriented toward finding problems, blaming them on something or someone and then trying to take measures to solve them. This attitude seemed to influence some of the discussions. For instance, they did not spend much time discussing the theme of deception. Instead, they agreed that it was a problem and then tried to pinpoint who was responsible, as the first step toward rectifying the problem. FG2/6 thought that it was usually the senior researchers/PIs (i.e., the people at the top of the research-authority pyramid) who were to be blamed, because the research teams usually aspired to satisfy them. Thus, research teams would pay more attention to what the PI and the research funding body wanted rather than to the correct way of collecting blood.

The research centre administration or the PI are to blame in this because the coordinator or the research assistant want to satisfy the PI or researcher... (FG2/6)



It seems that, from the discussion, the participants assumed a power differential between the physician/PI and the research team. This differential influences the research team to defer to the physician/PI. This is in agreement with the themes that emerged from analysing data from the first focus group.

**(b) Who asked**

As in the previous subsection, it appeared that this group also accepted the premise that physicians have some kind of power over patients. The consensus among the participants was that they thought that the treating physicians were authority figures for their patients. The nature and the limits of this power or authority were not fully agreed upon, as there were some voices that suggested that they were not ultimate authorities while others suggested they were, insofar as patients interpreted physicians' requests as orders. It seems that regardless of the limits of this power, the participants were not in favour of physicians recruiting for their own research.

So it is sort of a power gradient. It is not absolute power; it is a power gradient. The patient is usually vulnerable and tries to be nice to whoever is taking care of him in terms of health care. This creates a power gradient they [physicians] can easily just say any words to them and they can get what they want. (FG2/01)

It is always known that the treating physician has some authority over the patient. (FG2/5)

This also is in agreement with what was reported in Phases Two and Three in relation to patients giving more weight to requests from treating physicians than anyone else.

The significance of their agreement that physicians had this kind of authority over patients is that the participants were senior researchers and decision-makers.

Participants in this focus group claimed to disapprove of doctors who exercised this kind of authority over patients.

**(c) Rushing**

This theme was not a prominent in the data from these participants. They seemed to take for granted as a prima facie principle that patients should be given time to comprehend the information and then decide. They did not think the time allocated to patient/doctor encounter could be stretched to include research recruiting as well. The group seemed to agree that rushing was a symptom of a more serious phenomenon: the overcrowding at clinics.

... and to give the participant enough time to study it and ask questions. Your 8 minutes or 10 minutes does not do it right. (FG/5)

**6.4.3.2 Obstacles, challenges and responses**

**(a) Lack of support**

The lack of organisational support was a very prominent theme in the discussion. The participants seemed to explain it as a function of the lack of manpower. A lack of manpower in the health care field meant that the few experts' clinics and services were overcrowded with researchers having the same problems as clinicians.

You know... one thing, Saraha [truly] it is difficult here in the clinics, the genetics clinics. Or the practices of our physicians here, they are overcrowded. (FG2/4)

The word education was mentioned again in the context of lack of manpower. There was a consensus about the need to educate patients, but the main problem as the participants saw it was a lack of counsellors and people with the right backgrounds to carry out that kind of education. It seems that by education they

meant short, public programs that target specific groups like adult education. They thought many of the research ethics challenges in Saudi Arabia would be resolved if more people were available to facilitate this education.

We do not have enough, let's say, genetics counsellors—I mean the hospital has only two to educate people or participants. There [are] no workshops in the community. (FG2/2)

#### **6.4.3.3 Patient vulnerability**

##### **– Suggestions of vulnerability**

At the outset of the focus group meeting, and before giving any data, it was clear that the issues of patient vulnerability and ignorance about the genetics research challenges were familiar to the members. Many voices shared the same concern that the nature of the Saudi people and their general level of education might prevent them from comprehending what their donations for research entailed.

I've had that for a long time... haunting me... our... people in our country, in our society might not realize the actual dimensions of donating blood, as to what the consequences might be or what the future might reveal or what information could be taken out of the sample they delivered. (FG2/01)

Participants suggested that the complex nature of MGE research did not lend itself to simplification for the average person and some level of a technical terminology may be necessary. The topic itself is new to the average person. Among the things that are not mentioned even in the education programs is the fact of our genetically homogenous society, wherein blood from one family or group of families can give information about a whole tribe. Thus, it seems that educating members of the public sensibly about MGE research, without scaring them, is not an easy task. This might be seen as an area in which patients are vulnerable because they are ignorant or perceived to be ignorant by PIs. This may undermine consent because

patients do not comprehend what they need to before making decisions about participation.

I do not think that they are not aware only about the consequences, but also they are not aware about the genetics research itself. They cannot understand... most of the people, see... with the education standards... even people who [have] university degrees, they cannot understand well what genetics research is. (FG2/08)

It seems also that there was agreement about the vulnerability of women to stigmatisation. As I tried to explain in the second chapter about the context of the Saudi culture, a stigma is more serious if the stigmatised person is female.

Regarding females... some of them feel [the discrimination], and if they became stigmatised they will become more discriminated [against]. (FG2/7)

– **Patient vulnerability counterargument**

In the previous subsection, a few researchers shared stories about patients who had bargained with them over participating. The theme was not as prominent in this group as in the previous group. However, a few voices shared stories that counter-balance evidence that patients are vulnerable. Some participants shared stories about patients who seemed knowledgeable. For instance, some patients refused to participate in MGE research because they feared stigmatisation. There was a sense that some of patients felt that participating in MGE research was some kind of a sacrifice that they are not willing to make for society.

[They would say], Why should I go to participate? Why? Do we want to put ourselves at risk to be stigmatised... in the future... just to benefit the society? (FG2/7)

This was rated as a counterargument as it exhibits the ability to question and reason with the physician.

– **Suggestion of the presence of some knowledge**

It was in this group of participants that data emerged to suggest that they thought that some patients do know about the potentially stigmatising effects of the results of MGE research. It was interesting to hear that, in their opinion, patients had appeared to act on this fear and refused to participate because of the stigma that might come with it. The experiences members shared about Saudi patients who had not wanted to know about their results may also reflect a similar fear, or so the participants seemed to think.

But you know, at the tribe level, we know [a] certain disease [is] common in this tribe. They would say, “Why do you say [that] about this tribe, why do you mention this tribe?” [It is] always like that. So it is difficult, really, to deal... or convince, you know, people to donate or go on this. It’s fact of our society, [they] do not want to know about their results. They enjoy the veil of ignorance... (FG2/4)

We have a [disease] carrier test that was conducted a few years back, and we noticed the pilot study taken from hospital staff, doctors, paramedics and pharmacists. And the majority of them, when we informed them that “You are a carrier,” [and that] “We should screen your husband or your wife if you are planning future for marriage.” They ignore it... they ignore it... they do not want to know the answer... Sometimes people do not want to know the future. [They say,] “Just let me live with peace of mind and when it happens, it happens.” (FG2/2)

At the same time, the participants shared experiences that they understood to indicate that knowledge was not always a deterrent to participation. The participants shared examples of patients who were fairly educated about the risks, including the stigma and how the tests give information about more than just the individuals who donate, but elected to donate anyway. The consensus within the group was that the main reason patients donated in these cases was that they had altruistic motives.

Some people, of course, they may have some sort of altruistic attitude that they want to benefit the society with this research. That one thing: they know what they are getting into; the stigmatisation was mentioned, and so on. (FG2/5)

The participants had an interesting round of discussion when they started to reflect on and beyond the scope of genetics data in controlled health domains. Providing information resulting from genetic testing on uncontrolled websites that had started to be available to people outside the scope of health care—for example, websites with family tree information and family genealogies—was condemned by all the participants. The problem, as the participants saw it, was that Saudis started to use those uncontrolled websites to prove blood purity and in some cases to gain some kind of tribal nobility, as explained in Chapter Two. With the focus group's awareness about this sort of challenge, participants shared stories about lay people trying to use genetics technology available through these sites to prove nobility. This discussion suggests that there is not *total* ignorance about genetics in the Saudi population. On some public websites, there are very sophisticated discussions amongst the visitors to those websites about how to make sense of the genetics results these sites provide. One of the policy makers made a joking remark about one of his own relatives who suggested sending a buccal cell to the website so that they could try to confirm a higher social status, following the leads of another family of remote relatives who are now claiming that they have scientific proof that they are related to the purest blood of all, *Al Ashraf*. This kind of action is unregulated, and, according to this group, regulating it would not be an easy task.

I have been approached many times by groups of people or individuals from my family. They want to send a sample to the United States or Germany to find the DNA tree. I mean, to confirm [that they are] from this family or this tribe. They

are sending it without any controls! They just take a blood spot, and they send it. (FG2/2)

We can tell you that... not only Onaizy or Harbi, no, we can tell that you [are from a specific] Harbi family... I had a guest, last week, from our village. He said, "Do you know x family from the other village?" I said "No," he said, "Now they have become Ashraf [descended from the Prophet Mohammad's blood]." (FG2/5)

#### **6.4.3.4 Responses to the interim analysis**

##### **– Overview of policies**

There were a few voices suggesting enforced anonymisation as a solution to the stigmatisation risk. Those who suggested anonymisation thought that it would address the stigmatisation risks as well as most of the problems related to donor identity, like the promise of giving results (if the patient's identity is anonymous, then the results cannot be promised by the PI or expected by the patient).

Can we avoid all of that by completely anonymising all the samples that we are taking, so there is no stigma related to an individual? (PG2/7)

Anonymisation might be able to deal with some of the risks around MGE research. In the literature it has been suggested that genetic material is not fully anonymizable (Gitschier, 2009; Boddington, 2012). The policy makers did not appear to have taken this aspect into account when proposing anonymity as a solution.

The discussion took an interesting turn when I asked about how the group felt about using religious terminology in the recruitment process. Participants started talking about the larger role of religion in the Saudi Arabian bioethics guidelines.

Religion, they felt, can inform the guidelines by providing a framework or principles for ethical research conduct. They seemed to believe that even the four

bioethics principles of Beauchamp and Childress (2009) and the CIOMS guidelines were compatible with Islamic teachings.

An Islamic scholar in an Islamic organisation of medical science ... studied these guidelines ... and they found it is compatible completely. (FG2/08)

They also thought that religion could improve both researchers' adherence to guidelines and patient participation rates:

Probably [religion] leads the way to better understanding and better cooperation by people if such factors could be involved or incorporated, somehow, into the regulation. (FG2/1)

They suggested that religion might also be important in any sort of decision including medical ones.

I think religion plays a major role in major decision[s] in life, especially [in] our country. (FG2/02)

If... if... I speak to someone as a physiologist or atheist, they would say... "OK... the *Shaik Aish yeqool* [what does the religion say]?" Even if somebody is a physician that would speak volumes, but then they will wait and in the end ask, "Is it acceptable, is it permissible?" It will be taken as a fact if, only if, it is permissible by the religion. (FG2/01)

Who should control or benefit from the genetic material and data formed part of the discussion. Participants explored ownership in Islam and applied this to genetics data. As per some Islamic secular understandings of ownership, both the genetics data and the genetic material can be seen as areas to be controlled, they thought. In the beginning, some members of the group thought that what mattered was the information that could be taken from the material, not the material itself. Eventually, there was an agreement within the group that both the material and the data can be controlled under Sharei' law.



It's not the material itself. It's not the sequence... it's not the material itself, it's the sequence, maybe, or the mutation therein, and how you can benefit from that. It's... it's a matter of knowledge rather than the material. (FG2/01)

[Genetic] material is sitting there, it doesn't have any benefit unless the researcher has invested time and effort and generated information. The information that is generated from that is... what is of a sellable value. (FG2/5)

So it could be worthy [of benefit] also to generate that material again. So I think both sides. (FG2/4)

– **The need for education**

The very first response to the interim data was a long pause followed by conversations among the group that they are disappointed.

This [The lack of adherence] is shocking... because these are procedures. Those procedures should have been carried out very easily without any detour to that what been emphasized in the regulations... so we are shocked that there is still been clumsily executed. (FG2/1)

Based on that, education to both researchers and patient was suggested as a way to overcome the failure in adherence to the Saudi regulations.

Unless you concentrate on [educating] people as much as you can... and on increasing the awareness through the... umm, ya'ni [I mean] media [or] things like that... I think people will accept things like that. (FG2/4)

There [are] no workshops... for the community, I mean, like... some advertisements. For example, King Saud University, they have a community service department. They announce if there are workshops in computer skills... in writing skills. There are no workshops or even sessions regarding research or regarding genetics. (FG2/04)

It is not clear from the discussion what sort of education they were suggesting. The closest attempt to giving an idea of what education was needed was the idea that it should be an official governmental effort supported by universities in the form of short courses or conferences and given to those selected to donate blood for MGE research.

Some voices agreed that educating patients is not an easy task, but suggested the alternative would be stopping the MGE research altogether, which was not considered a realistic solution.

It is a far-fetched target, if you want to increase their awareness in the population, if you want to be certain that you are avoiding those aspects, the ones you've raised. Probably the easiest thing is to say, "Do not start any genetics research until you are certain that no ethics is involved with that subject," but that is not realistic. Genetic research has to start at a certain point, but you have to minimize the impact of the negative aspects that you just mentioned. (FG2/01)

#### **6.4.3.5 The importance of DNA**

The group express their opinions on whether genetics research could pose a challenging ethical question due to the country's tribal culture and its peoples' shared DNA mutations. They were also in agreement that tribal stigmatisation is one of the main concerns, as the group discussed earlier. This was mainly because of the possibility of gaining too much information about large groups from blood taken from a few families. They added also that it could reveal unwanted information, like that patients are at risk of some serious diseases.

Some, they know, just to know from which area they come... and... in some areas in Saudi Arabia there is nasopharyngeal carcinoma... It is very common... They know in certain areas there that if people are coming from there, they have it... It is not an individual stigma; this is a group or tribal or societal stigma. (FG2/2)

It could also be looked at in a reverse way. If you've got a mutation, then you can tell which tribe that is. So, this is also sort of a sensitive issue that needs to be considered in the regulations. (FG2/01)

In the first focus group, there was virtual consensus that the Saudi genetic material has some tacit strategic value and ought to be protected from being sent abroad for research without very thorough regulations or active monitoring. This

group shared these concerns. It appeared that there was unanimous agreement that Saudi genetic material should be protected for national security reasons.

So this something that is very, very strongly at the heart of Al Amn Al Qaumi [national security]. There will be a time, I do not know when, but a time will come when people could decide that because of our genetic makeup they could send drugs that either could affect us positively or negatively. (FG2/01)

Some of the participants seemed concerned that this genetic material was already used by other organisations without official Saudi permission.

We had a visiting professor three months [ago]. She was giving us the opportunity to take quantities of genome results and to share it with us to have a legal umbrella...She said that “the problem is that I already collected some, but I need more.” Then I consulted [the research director]. He said it is not allowed according to the [Saudi] guidelines. (FG2/4)

It also very important to note that the participants suggested that there are fluid boundaries between diagnostic work and research in the genetics field. This meant, according to them, that if we accept the premise that DNA has strategic value, even the diagnostic work should be looked at critically. The discussion went on to reflect on the fact that sometimes physicians are confronted with difficult cases that they cannot diagnose; they may then ask an international laboratory for full exon analysis (i.e. similar to individual gene mapping). As a result, those international laboratories seem to ask for full rights over the given material. The data that will be gathered from such laboratory work will be similar to the data gathered by MGE researchers. They then started to express concerns that the material and the information will be retained by the international organisations with consent to do anything they want with it.

I mean, you send, for example, for the whole genome sequencing, for exon sequencing because you do not know what the patient [has]... Like you are fishing [laughter]. (FG2/2)

#### **6.4.4 Conclusion**

Taking the data from all three phases into account the overarching finding is that there appears to be a difference between the aspiration for practice found in the written regulations and actual practice.

#### **6.4.5 Section Two Summary:**

So far, in the first section, I provided a normative analysis of the international guidelines that were used to inform the Saudi NCBE regulations. I also assessed in Section One the tensions between the NCBE regulations and Saudi culture and values.

This second section was dedicated to answering the research questions concerning the extent to which the analysed guidelines in Section One are followed in practice. Also, I assessed what seemed to be the challenges of collecting blood from Saudi donors for MGE research, as perceived by the stakeholders. Then, I assessed the feedback of those charged with generating the Saudi guidelines and norms for research to the results of the investigation into current practice in relation to blood collected for genetics research.

I am now in position to bring the findings from this section to bear on the issues and ideas discussed in Section One.

### **Section Three: Discussion and recommendation**

## **7 Chapter Seven: Discussion**

### **7.1 Overview**

In this chapter, I will argue that, due to the absence of specific oriented MGE research ethical guidance that is written with the Saudi culture in mind, MGE research should be seen as posing many challenges to the current NCBE regulations and that we need to move to more culturally-appropriate guidelines. In order to argue for this conclusion I will consider two pieces of evidence. First will be how blood is considered in the Saudi context. This will be explored in light of the findings outlined in the previous section and additional further evidence from Saudi culture, along with my personal reflections.

Second will be an argument as to why some elements of the autonomy-based bioethics (i.e. specifically the part that suggests individual informed consent should be at the heart of research) is not the best framework to adopt when considering using donated blood for MGE research in Saudi Arabia. This will be in two parts; the first will establish the presence of the influence from western assumptions about ethics. This will be done by discussing the concept of consent as well as vulnerability and paternalism. The second will outline why an autonomy-based ethics approach, as understood by the Saudi policy makers, would be problematic in the context of MGE research in Saudi Arabia. According to the arguments presented in Section One and the data presented in Section Two, some elements of the autonomy-based ethics can be seen to be in conflict with what was presented as Saudi cultural characteristics. In this chapter trust-based ethics will be investigated more closely as one of the possible

alternatives to the autonomy-based ethics in the analysed context of Saudi Arabia. In addition to that, I recognise the potential to commit the is/ought fallacy (see Subsection 1.4.2 The is/ought fallacy) and to appear to take a particular side in the wider debate around cultural relativism. Therefore, I will start this section with an argument as to why this work should not be regarded as appealing to moral relativism.

Having provided the overall outline of this chapter, I will now discuss the issues in detail.

## **7.2 What the findings can be taken to imply**

In this subsection I will introduce the dilemma of how to understand the collected data. One interpretation of my results is that they point to a total failure to comply with the regulations for research in Saudi Arabia and that this is a major problem that needs to be corrected. Such a discourse of failure would call for stronger, and much firmer, guidelines in terms of education, encouragement and policing. Another interpretation is that the lack of adherence to the guidelines suggests that the guidelines themselves are not followed because they do not reflect important normative beliefs in Saudi culture, and this suggests that it is the guidance that needs to change and not the practice. Local guidelines, from this point of view, should reflect local cultural norms, rather than adopting wholesale the normative assumptions that drive the international guidelines.

### **7.2.1 The discourse of failure**

In Chapter Four, I introduced the notion of an autonomy-based approach to bioethics that is prominent in research guidelines and appears to have been the strongest influence on the Saudi guidelines (see Subsection 4.2 Autonomy-Based Bioethics). The findings presented in the previous section suggest that some researchers seem only to be complying with the formal requirements of gaining an informed consent: i.e. ensuring that there is a document called an ‘informed consent’ that has been signed by each participant recruited. The actual presence of what is called an ‘informed consent’ with a signature on it should not eclipse what informed consent is meant to represent (i.e. competence and voluntariness, and also an information element (see 1.1.1 Informed consent.) Themes from the collected data in Section Two of this thesis suggests that in some cases informed consent was not recorded in the way it was intended by the NCBE (See Subsection 3.2.4 Informed consent.) For example, in Phase One, the theme of deception could imply that some Saudi researchers are not complying with the enforced Saudi research guidelines. In Phase Three, the Saudi policymakers seem to respond to that implication with ‘shock’, suggesting that at least some of them accept the narrative of failure to comply with the NCBE regulations. Therefore, corrective action (i.e. more education, and then discipline) is needed.

Empirically, the discourse of failure could be regarded as a convenient narrative because it apparently captures the first reaction of many of the Saudi policymakers to the data presented in this thesis. However, such an interpretation suggests that the international guidelines capture the relevant universally accepted

norms (e.g. individual liberty) and should be adhered to by the Saudis when it comes to MGE research in Saudi Arabia. From this point of view, it seems that we have strong indications that most of those who participated in the empirical part of this thesis treated their research subjects in an unethical manner by focusing on gaining a signature in the document as if were all that is required for an ‘informed consent’. However, such a view suggests that the international regulations must be adhered to, with no excuses or exceptions. It assumes that such guidelines capture what is universally important and ought to be applied universally. However, it could be argued that such an approach misses the importance of the observed cultural reality and this is something that must be taken into account when we think about how to make our moral judgments (Dawson, 2013). Accepting the discourse of failure would, therefore, run “the risk of over-generalizing moral discussion by appealing to abstract and absolutist moral formulations” rather than responding to the particular case before us (Dawson, 2013 p.2).

A clear example as to why local context matters to our ethical evaluation can be seen when we consider the meaning of blood in a tribal culture such as Saudi Arabia (see Subsection 7.3 The importance of Blood in Saudi Arabia). Giving an ultimate right to individuals to share or not share their genomic material for research, as the international guidelines do, ignores the fact that any results may potentially cause harm to a whole tribe due to the genetically homogenous nature of the Saudi tribes (see Subsection 1.3 Challenges of MGE research in Saudi Arabia). The same can be said if the state believes that the blood of its citizens ought to be protected for



national security reasons; autonomy-based bioethics would also be problematic and more difficult to justify.

It is equally important, also, to note that the notion of blood purity and its link to identity is so central to Saudis that, by insisting on a set of guidelines that do not take those issues into account, we may threaten or potentially damage identity issues and community issues that are really important in that culture. Imposing autonomy-based guidelines and their concentration on individual informed consent, at the expense of potentially damaging what is important to a local culture, can be seen to be ethically problematic. So, one might consider that it is for the concerned tribal community to decide whether or not certain kinds of outcomes that are promised by a specific piece of research are worth having, given the risks to the individual and the collective. Even if individuals are asked to consent to participate, and sufficient individuals agree to do so, and we assume that they understand what they are agreeing to, it does not mean that the tribe or community as a whole has been asked to consider whether, on balance, it believes that the research is worth doing and/or meets its needs. Of course, just because a community, on balance, agrees that a specific MGE research might be useful does not therefore imply, necessarily, consent for each individual in that population to participate has thereby been gained.

Even if we choose to reject the discourse of failure, and accept the need to be sensitive to local context, it is important to see that this does not necessarily mean adopting moral relativism.

### **7.2.2 The discourse of moral relativism**

The discourse of moral relativism would suggest that the Western-ethics dominated international guidelines have shaped Saudi policy and that this is inappropriate. It is important to see that an acceptance of the importance of social context does not necessarily mean accepting moral relativism. Critiquing moral relativism would require a thesis in its own right, and space is limited. Nonetheless, it is important to recognise, at least schematically, its potential strengths and weaknesses.

Moral relativism, as described by Sheehan (2007, p93), is the view that any moral judgment must be made from within, or relative to, a culture or society. Thus, according to Sheehan (2007) there is an absence of universal moral truth that holds across all cultures and contexts. Thus, different cultures may have different answers, and each may be regarded as correct within a specific cultural context.

It could be attractive, in the context of this thesis, to adopt a position of moral relativism and argue that different ethical norms can reasonably be applied in the context of research ethics within Saudi culture as opposed to Western culture. Such a stand would call for totally rejecting the current Saudi research guidelines, given their Western origins, and the production of a new set of guidelines based on an informed and rigorous understanding of what is culturally acceptable to the Saudi population.

The main challenge of moral relativism is that it tends to state that there is no universal moral truth. In a way, this could lead to more tolerance towards other

cultures, but it also means that practices, such as female genital mutilation (FGM) in Africa (Macklin, 1999), should be accepted by those outside of Africa (at least within Africa) because it is acceptable to those who share this cultural practice. In the west, FGM is condemned ethically and legally, and rated as a human rights abuse (Cook et al, 2002). Similar kinds of cultural behaviours would be difficult to defend as morally acceptable practices unless moral relativism is embraced.

Some anthropologists/sociologists see the acceptance of such cultural behaviour as being a way to show tolerance to others and avoid imposing their (Western) cultural norms about what is right and what is wrong on other cultures (Macklin, 1999; Dawson, 2013). However, one potential challenge to moral relativism in this context is that the appeal to the value of tolerance itself seems inconsistent with the idea that values are only culturally-specific. One way out of this position is to see that moral relativists might be forced to accept that there is at least one universal value, namely, tolerance. The coherence of such a position can be challenged because, for example, if society A is intolerant of society B, then society B ought to accept this fact if they accept relativism, because A's societal views govern A's behaviour even if this is a problem for B. In the context of MGE research, if society A does not believe in the importance of informed consent by individuals, they can basically collect blood from anyone using any means. If relativism is embraced, society B should not reject research collaboration with society A on the grounds that they do not share similar consent processes and norms, even if society B detests the action of conducting research without what they consider to be the proper informed consent procedures.

As mentioned earlier, in the context of this thesis, it could be an attractive position to appeal to moral relativism in order to respect Saudi cultural diversity. According to such a position it could be argued that individual autonomy is not something that is appreciated in Saudi in the same way as in the West, Therefore, as a gesture of tolerance, we ought to accept that it is acceptable to receive donated blood for MGE research in Saudi Arabia without consent. However, the problem with this approach is that “such practices are [only] to be understood, but are not legitimately open to debate, not to be labelled as wrong, and presumably not to be the focus for change” (Dawson, 2013, p2.) If moral relativism is embraced in order to understand the presented data, then we cannot label moral claims as right or wrong (Macklin, 1999; Dawson, 2013). This is attractive because it does not require any effort to change the status quo. Any judgment about any ‘wrongdoing’ can be attributed to cross-cultural differences. However, it is problematic because even inside the same culture, smaller groups could have different way of doing things. For example, I reported in an earlier publication a case where a huge family (more than 40 persons) came in at the same time, driving from a remote place to a Saudi hospital to donate blood to a particular MGE research. The case was unusual and when investigated the research team found that the family elder (i.e. the one decide for the family) had been convinced by the physician/researcher that donating blood for this MGE research was a charitable act that would be rewarded generously in the hereafter (Adlan, 2013). In the data collected for this thesis a similar attitude towards recruitment was visible, namely convincing donors that donation was a charitable action and showed piety. Such action could be deemed as acceptable if we want to be consistent with the account of moral relativism, but in the view I am defending it can

be seen to be disturbing and could result in more difficult or rather impossible to justify actions. So, criticising autonomy-based guidelines in the context of Saudi Arabia does not mean accepting using genetic material without consent.

Now, having argued against both the narrative of failure and the narrative of relativism, I will discuss how I suggest the data should be considered.

### **7.2.3 Embracing the importance of social reality**

As I argued before, both the narratives of failure and of relativism are not the best way to look at the data in hand. The characteristics of an alternative plausible approach, I argue, must be both modest epistemically and modest ethically (Dawson, 2013):

- Epistemic modesty can be seen as a non-ideological pragmatism, as “accepting that we can be in error, proposing interpretations and proposals cautiously, open to discussion and the need for revisions in our view” (Dawson, 2013, p3). It reflects the importance of the empirical data and how they can be essential to understand the culture and its social context in order to provide the best ethics advice. This, however, should not be seen as moral relativism. In addition, such a view can be seen to assert the importance of the normative within bioethics. Epistemic modesty allows us to look at empirical data critically, allowing them be fully understood and analysed. Based on that, a normative moral judgment will be produced and we should not

be afraid to say that any practice is wrong if we believe it is so, and then use this judgment to produce further argument or policies.

- Commitment to epistemic modesty implies being modest ethically insofar as “our moral judgments must also be open to reflection, discussion and the capacity for change.” (Dawson, 2013, p3.)

To provide ethical answers within this understanding fits directly with the idea of encountering the Saudi MGE research experience that was explained earlier in justifying the choice of methodology (see Subsection 1.4 The Need for Empirical Data). Ives (2008) describes an encounter with experience as ‘[b]ringing philosophical ethical analysis to the ground, and rooting it in real people and in real problems’ (Ives, 2008). In the first section of this thesis I produced an understanding of the international guidance and used philosophy to determine and justify what reasonable guidelines should seek to achieve. I then attempted to find out what Saudi stakeholders, in the context of MGE research, thought. It is important to let the first section encounter the second and use reflective balancing to produce a ‘theory’ as to how the guidelines and future practice should look that both reflects the philosophy and the experience.

After deciding how we ought to look at the data in hand, we are in a position now to introduce the argument that the current regulations are not an appropriate way to regulate MGE research in a social context like the Saudi one. In order to do so I will introduce how blood is regarded in Saudi culture.

### **7.3 What is blood in the Saudi context?**

In the previous section, I reported how confusion may occur generated by using the words for ‘donation’ and ‘participation’ interchangeably, and how this confusion had normative overlay related to the way in which charity is perceived as a religious duty in Saudi Arabia. If MGE research in Saudi Arabia is to be regulated appropriately, this regulation will need to acknowledge and accommodate the cultural significance of ‘blood’ in Saudi Arabia, and how this might differ according to context.

#### **7.3.1 Blood in the Islamic literature:**

As I explained in the introduction, Islamic values are central to Saudi culture (see Subsection 1.2.1 The Social Context in Saudi Arabia). Religious commitment is taken as a given, and for this reason social guidance often comes from religious sources. For example, insulin dependent patients are advised strongly not to fast during the Holy month of Ramadan because it could lead to serious hypoglycaemia and risk death of the patient. When it became clear that some diabetic patients were not heeding this advice, the MOH appealed to the Saudi religious leaders to issue a Fatwa forbidding such people from fasting (Adlan, 2013). Therefore, understanding how Islam thinks about blood is essential to understanding blood donation for research in a Saudi context.

Blood is a frequent topic of discussion in Arabic and Islamic literature and is used in many ways with different meanings being attributed to it. One example of the word in Islamic literature equates it with life. In the Quran, many verses feature the word ‘blood’ with reference to ‘life’ in the sense that shedding blood means killing a

person: ‘And when we made a covenant with you: You shall not shed your blood...’ (Al Baqarah: versus 84). A similar notion is expressed in the Hadeeth (the prophet’s words), as narrated by Al Tirmidhi: ‘Everything belonging to a Muslim is inviolable for a Muslim; his honour, his blood and property. Piety is here (and he pointed to his chest thrice)’ (Hadeeth 234 An-Nawawi, 2014). These metaphors were common to ancient Arabic societies, where blood was a signifier of connection, life and honour.

### **7.3.2 Blood in the Saudi context:**

In the Saudi context, there are generally three different perceptions with regard to donating blood. Firstly, it is seen as an opportunity to act altruistically with only godly rewards expected in return. There are many reasons why this notion seems to be rooted most in patients’ minds:

1. The advertising campaigns in the media seeking blood donation for clinical blood banks.
2. As a result of those companies the media seems to equate donating blood to saving lives.
3. The act of saving a life is among the best rewarded actions in Islam; as the Quran says, ‘...and whoever keeps it [a man’s life], it is, as though he kept alive all mankind’.
4. The other Islamic notion of eternal charity is also a factor, as explained earlier.
5. For many years, the finalization of Saudi driver licence paperwork required the proof of a recent (less than two months old) blood donation. In



other words, a person needed to donate 500ml of his blood to a local blood bank and get a stamped and dated certificate to include it in the driver licence application. If someone was unable donate for a medical reason, a waiver certified by their hospital had to be produced instead. The King Faisal Specialised Hospital and Research Centre blood bank mobile clinic used to be parked outside the driver licensing offices in the main cities to withdraw blood from those seeking a driver licence and then provide the required certificate. Currently, it is not clear whether this is still an active obligation. The official site of the ministry of the interior (MOI, 2014) does not mention this obligation while *Okaz*, a daily newspaper, reports that despite the fact that the MOI does not mention it on its official website, blood donation is still a requirement and driver licence applicants are expected to present that certificate in the main cities (Okaz, 2010).

6. The governmental honor program known as the King Abdulaziz Medal is presented to those who donate blood more than 10 times. This incentive, someone might argue, undermines the notion of altruism insofar as people might donate blood for the medal and the opportunity to shake hands with the King or the King's delegate.

In the interviews, there were clear signs of confusion between three purposes for giving blood: donation to blood banks for use in the treatment of other patients, donating blood as part of a MGE research project, and providing a blood sample for clinical investigations as part of one's own on-going clinical care. I noticed people speak with pride when they mentioned that they have donated blood. One of the

participants mentioned that he would donate blood every month if his health would permit him to do so when I asked him about his experience in donating blood for MGE. Confusion persisted in my own research existed me taking care not to use the word *tabru* which is linked to donation for people in clinical need (See Subsection 6.4.3.2 C. Vulnerability of Saudis wishing to appear to be devoted Muslims).

All of the above helped reinforce the notion of blood in Saudi Arabia as something valuable. It saves life; it gets you a highly ranked honour medal given by the King's representatives; it is a pre-requisite for obtaining a driver's licence.

The cultural and tribal norms of honour, linked to tribes' generosity, represent an additional factor that endows blood donation with connotations of virtue. Consequently, abstaining from donating blood is given very negative connotations and is denounced and rejected by most Saudis. Indeed, refusing to donate blood for blood banks based on a hospital's request or the call of a friend requires strong justification. In fact, an act of bravery is required to challenge linking blood donation to godly rewards and tribal generosity (See Subsection 6.4.3.2 C. Vulnerability of Saudis wishing to appear to be devoted Muslims).

The second widely held notion of blood's status in the Saudi context concerns its value as a commodity, though not one with a literal monetary value. Some participants seem to describe donating blood for the purposes of research as a kind of transaction between the doctor and the patient. What they suggested was that patients offer blood and research teams offer in exchange a more compassionate service and, in some cases, special treatment. Hence there were reports of patients requesting specific favours in return for donating blood. This is exacerbated by the nature of

Saudi health care and the long waiting lists that sometimes deny patients care even when they need it urgently. Patients clearly feel that accommodating the research team will pay off for them in terms of accessing health care.

### **7.3.3 Blood as identity tool**

In this subsection I will draw attention to how information derived from blood is currently used among Saudis, and some non-Saudis as a tool for political gains such as entitlement to Saudi Nationality. I build upon the evidence that other nations reinforce identity through the use of genetics. I will also reflect on what was presented in Chapter Four (Subsection 4.6 Sending Saudi genetic materials outside Saudi Arabia) about how MGE research is being used as a tool to racially label Saudi tribes as either superior or inferior. This subsection draws attention to the serious repercussions of allowing MGE research to continue without specific regulation.

In the Saudi political system, nationality is not a birth right in the sense that not every person born and raised in Saudi Arabia is entitled to be Saudi. This status is mainly determined by the father's nationality, with some limited exceptions. For instance, offspring may obtain Saudi nationality if their mother belongs to the third generation of a Saudi family (i.e., if there is documentation proving that her paternal grandfather was originally Saudi).

Furthermore the tribal borders are different from, and older than, the contemporary Saudi political borders. This means that, for example, tribal members who are inside the Saudi borders are distinguished from members of the same tribe outside Saudi borders. As a result, a system has been put in place so that tribal

members who are outside the borders could be identified, so they can assert rights of reunion with their fellow tribe members inside the Saudi borders. Previously, it was the responsibility of the tribal elder to write to the state, notifying them that a person was a blood relative and a tribal member. Based on the elder's recommendation, a case would be opened and the state would study the case carefully prior to issuing a ruling on it.

In recent years, people have been advertising in newspapers such as *Al Sharq*, *Al Awsat*, *AL Jazeera*, *Al Watan* and *Okaz* to request that the available genetics technology be used to provide evidence of entitlement to the Saudi nationality on the basis of a blood relation to a Saudi tribe member (AlRiyadh, 2012). A similar notion of biological citizenship was reported among the indigenous tribes in North America and the Native Americans, who sought entitlement to a list of benefits aimed at native Americans. In Vermont in the USA, for example, a bill was proposed in the General Assembly of the State of Vermont to establish standards and procedures for DNA testing in order to provide evidence of race identification (TallBear, 2013).

For centuries, essential factors such as sharing blood, culture, geography, history, and loyalty, combined to determine Saudi tribal identities. Most people are proud to be linked by blood to their tribe, which gives them access to many privileges that would not otherwise be available to them. For example, marriage to a tribal woman is a guarantee of financial, legal, cultural and other types of support by the tribe's political structures. Before 'disembodied' genetic information, tribal systems were like clubs with only a birth right membership entitlement. With the presence of DNA technology, people began to question each other's blood purity and

in some cases, demanded that individuals ‘clear’ their names by volunteering to test their ancestry. A similar trend was reported by TallBear (2013) in her work on the genetic identity of Native American tribes; she thinks people seek these expensive tests for two main reasons: 1) to establish a lineage link in order to get access to benefits, and 2) for genetic anthropology reasons (TallBear, 2013). In contrast, while some scientific efforts in Saudi Arabia are dedicated to understanding Saudi genetic anthropology (Abu-Amro et al., 2009), the main consumer interests are to validate their claims to a certain status/membership.

MGE research has the potential to promote blood purity by providing a new means of identity verification based on genetic traits. In the subsection on normative challenges, I described how blood purity could be seen as a racist tool with dangerous consequences (see Subsection 4.6 Sending Saudi Genetics Material Outside Saudi Arabia). Some tribes start to aspire to claim nobility based on genetic traits, and this notion becomes dangerous when groups use this to downgrade another tribe using genetic testing, claiming that members of that other tribe are not of pure blood.

According to the website of the Texas-based genetic testing company [www.FamilyTreeDNA.com](http://www.FamilyTreeDNA.com) their ‘...long term goal is to link written Arabian genealogies (tribal kinships) with DNA science in order to find genetic signatures of tribes, interrelationship between Arabian tribes and their common groups’. Arabs have one of the most detailed and intertwined subsection on their website. According to the members of both focus groups in my research, such genetic signatures are exactly what the Saudi policymakers and some of the senior researchers are trying to

protect society from with their activities in the field or when attempting to articulate related articles in the guidelines. The problem is that, the access to this service is not regulated.

Websites such as [www.familytree.com](http://www.familytree.com) seem to introduce a new approach to social ranks among the Saudi tribes. The joking remarks from one of the focus group members about his cousin's invitation to send blood to one of those website to prove noble blood, gave an indication that such websites and their use may be raising awareness of the potential problems of an emerging new genetic identity.

Members of the second focus group were very sceptical about the service provided by those websites. They thought that such activity was gaining momentum among Saudis and should be looked at carefully. The main challenge is that the current policy fails to provide guidance about these website practices.

#### **7.3.4 DNA ownership**

In this subsection I will discuss ownership of DNA material as mentioned in the Saudi guidelines. The importance of this point stemmed from the fact that the NCBE regulations tried to solve the above mentioned challenges by asserting what the policymakers perceive as a strict level of control over the Saudi National genetic material. I will discuss in this subsection the importance of clarity and the importance of drawing a clear line between different actors like the donor, the researcher, the research centre and the NCBE.

In Saudi Arabia, biomedical practice has not responded to the problematic business behaviours resulting from genetics research like monopoly ownership of

gene mutations, diagnostic tests and excessive patenting. However, it is not realistic to assume that the current policy is equipped to deal with those challenges without addressing those issues openly and firmly by the Saudi policymakers. In MGE research in Saudi Arabia, the stakes are potentially high in terms of what genetic information implies for the indigenous people of Saudi Arabia. The fact that the state represented by the NCBE has the right to control DNA material is interesting insofar as it may be seen as contradicting the more democratic values the Saudi bioethics guidelines appeared to be embracing, as discussed previously in Chapters Two and Three. If Saudi's genetic material is owned by the state, theoretically the state can reverse someone's decision to donate which appears to go against the autonomy-based norms supported by the NCBE. In theory, the absence of clear boundaries between individual and state rights to genetic material risks a potential clash between different perceptions regarding how the rights over genetic material will be interpreted. The findings presented in Chapter Six suggest that some of the interviewed research participants tended not to care about who controlled their donations, albeit most of the interviewees lacked knowledge concerning their donation in general. If such lack of interest is present, it could be attributed to the many hypothetical reasons that actually were reported among some of the interviewees, like those listed below:

1. They could be patronised by the treating doctor.
2. They could be merely concerned with the notion of godly rewards.
3. They could be interested, but only in the aspect of exchanging something for an immediate tangible benefit.

4. They trust the health care system to the extent that they entrust control of their health to it.
5. They do not understand what they are doing in terms of donating or trading information. For example they know they have something the research wants but do not really know/understand what this is (and perhaps they do not care to know either?)

I will discuss the trust factor in further detail later. The four remaining points assume some level of consciousness about control in the context of the ability to trade. The notion of having something to ‘trade’ whatever the context (e.g. favours from researchers or Godly rewards) has some elements of ownership. However, generally in Saudi Arabia, absolute ownership of any kind of tissue (i.e. such as body organs or blood) does not have the same concept of absolute ownership in the sense of the private property rights (i.e. private property rights in the sense of absolute ownership in the sense of commodification of material (Jeremy, 2012)). This is mainly because in Islam people do not have the right of property over their bodies (Aramesh, 2009). The Saudi Guidelines clarified that the Islamic values ‘shall be observed’ (NCBE, 2010, p87).

In Phase Two, the question ‘who owns [controls] the donated genetic material right now’ was considered strange by the participants, who felt that either the material was no longer controlled by them, or that it was now for the doctor or the hospital to decide about those donated material. This was the case to the extent that the majority of them were not concerned about what happened to the blood; that is, whether it was analysed locally, sent to an international collaborator, or reused by the



research team or any other researcher without specific donor consent. Perhaps it is not a real problem to Saudis (specifically those interviewed in the context of this research) who donated blood for MGE research because they were concentrating on other more important issues like the concept of reciprocation in a gift-like transaction (see Subsection 6.3.3.2 a. Vulnerability counterargument.) This is one interpretation of the data gathered in my study, although this cannot be generalised due to the nature of the chosen design.

The view that the state owns Saudi genetic material seems to be an over simplification, that might easily be challenged by the fact that there is no clear guideline regarding how and when the state should practise its right of ownership or even control against donors, against doctors and researchers, against Saudi research centres and against international research centre collaboration. Western ethics, however, might well emphasise individual control (even ownership) over genetic material.

In Western legal literature, there is no consistent view on the specifics of who owns what, when and why when it comes to tissue ownership (Lipworth et al, 2011; Flaman, 2014). For example, the boundaries relating to biological matter when it is still inside the body and when it is outside the body and controlled by someone else are not clear (Boggio, 2013). Rao (2007) studied the legal trends in terms of how the body is perceived and as a result, provided three different paradigms for the body, body parts, blood and tissues. In his view, it is either protected by property, defined by a contract or under private protection (Rao, 2007; Allen et al, 2010; Boggio, 2013). In the context of blood and tissues, it seems that these paradigms ‘exemplify

body as property' (Rao, 2007, p376), which is problematic in the MGE research in the Saudi context for two main reasons: a) religious reasons as explained earlier, and b) the genetic nature of the Saudi tribes DNA, which indicates that all the tribe's members, including those who have not yet been conceived, ought to be partners in this ownership model, or ought to protect their interests/have their interests protected.

The main challenge of the Saudi NCBE guidelines is that they might not fit the reality of MGE research in Saudi Arabia for they lack the essential differentiation between biosamples and the data derived from them. Even if it is accepted that the biosamples are owned by the State, this fails to protect the State's right over the data because the nature of data ownership is different from the nature of the genetic material, and therefore fails to protect research participants from potentially being harmed through the distribution of such data because non-maleficence should be articulated in this specific context to avoid ambiguity.

The ownership issue was discussed between members of the second focus group when they were asked about ownership of the genetic material. They seemed to be in agreement that the donor and the researchers shared responsibility to control the genetic material based on the premise that they both needed each other to achieve the final results. However, there was extensive discussion about the actual value of the genetic material or the data harvested from it, and the response to this question will provide a better understanding of how ownership should be decided.

### **7.3.5 The absence of specific regulations for blood donation to MGE research in SA**

As I explained in Chapters Three & Four, there is no regulation in Saudi Arabia that is specifically oriented to regulate donating blood for MGE. The Saudi NCBE bylaws and their guidelines are the active tools currently regulating all kind of research using human participation, including MGE research (see Chapter Three).

As analysed in Chapter Three, the Saudi NCBE regulations are general enough to cover some of the issues concerning donating blood for MGE research in the Saudi cultural context. There are articles therein which try to tackle some of the important issues such as controlling the Saudi National genetic material, and the call for establishing Saudi National biobanks. However, due to the specific way blood is conceived culturally and religiously, it can be fair to say that the current regulations are in tension with the local norms of the Saudi culture when it comes to activating those guidelines in practice for the following reasons:

- a) As I concluded earlier in Chapter Three, the national regulations were inspired by the western normative assumptions about ethics in the international regulations that were used as a reference for the Saudi ones.
- b) Some of the challenges concerning MGE research in Saudi culture are not specifically addressed in those guidelines (see Chapter Four).
- c) The weight that is given to informed consent in the regulations seemed to follow the western individualistic autonomy-based bioethics in prioritizing individual preferences above other values.

The above points, as well as the empirical data from this thesis, albeit that qualitative research is not meant to be generalizable, could be taken as an indication of tension between the Saudi NCBE regulations and the Saudi culture in the context of donating blood for MGE research.

The end of this subsection concludes the first argument. Blood and its derivatives, specifically genetic material, are highly rated among Saudis for different reasons, such as it being equated with saving lives, or a means of presenting a new way of gaining racial superiority. An autonomy-based approach - in the sense that informed consent documentation should be prioritised - risks neglecting those challenges, which is ethically problematic. Therefore its utilisation in MGE research inside the health services providers (like a research centre) or outside them (like websites promising genetic lineage detection) ought to be considered in a way that addresses these challenges. The lack of such regulations could be seen as the reasons for most of the noticed mismatch.

#### **7.4 Consent in the Saudi context**

In this subsection I will discuss my second argument in this thesis which concerns the Saudi trust culture that is manifested in the patient-physician relationships. I will take consent in the Saudi context for MGE research as an example to illustrate how a western understanding of consent in the domain of health related research is dominant. I will then contrast this with how more of a trust culture is prioritised in the lives of Saudis.

The reported data revealed more serious concerns about whether or not those participants in MGE research can be regarded as consenting, and whether or not informed consent was gained in the prescribed way; in other words was there any coercion, was he or she given enough information to decide for him/herself whether or not to participate, and to what extent vulnerability should be considered in MGE research in Saudi Arabia (See Subsection 6.5.3.3 Patient Vulnerability)? These questions will be addressed later in this chapter. Both international and Saudi guidelines emphasise participant consent in many ways, but a key issue is the process of informed consent. A powerful assumption can be seen in the emphasis given to the individualistic value of a person, whereby that person is best placed to decide what is best for him or her as a free-choice (Gillon, 2003, Beauchamp and Childress, 2009). However, against this understanding the reported findings suggest some of the patients did not choose according to this understanding of free choice. According to the reported data, patients were asked to sign a document but told this document is nothing but ‘paper work’. Each patient did, however, sign what was called an ‘informed consent’ document. This suggests that a request to sign the informed consent document may be something that is done to satisfy the regulations. So, in effect, this appears to be an interaction where the patient gives something, the researcher takes something and the interaction is underpinned by documentation that satisfies the regulations. This document does not, necessarily, reflect the true nature of the interaction; however, it has a legally authenticated signature. Because of the authenticated signature of the patient, it is very difficult to suggest that the process is illegal or unethical if an audit is carried out in the manner advocated by the ICH-GCP. This suggests that the informed consent, in this specific context, was used to

justify the research or to tick a very essential box in the process required for conducting research. It is important to consider why Saudi researchers included in my study were inclined to manage that interaction the way they did. Understanding the reasons will help us explore the existent norms and values underpinning those transactions in the context of MGE research in Saudi Arabia.

In general, the nature of this interaction gives rise to an even deeper question, regarding the place occupied by 'consent' itself in the Saudi context. According to Beauchamp and Childress (2009) consent can be implied (when patients hold out their arm willingly to have blood withdrawn) or explicit (when specific information is given to a patient who then decides between at least two options), in the context of medical ethics the latter is usually documented and is generally seen as a means of respecting autonomy. The Saudi regulations inherited the assumption of how we ought to regulate and document consent from the Western ones used as reference documents (See the 4.3 Informed consent in the Saudi context).

In the Western context, consent is generally assumed to be more of an individual practice than a family decision (Tan-Alora and Lumitao, 2001; Beauchamp and Childress, 2009; Adlan, 2013) except in the case of genetics, where the notion of family consent is discussed and the weakness of an individualized way of looking at consent is more readily accepted/discussed (Tallbear, 2013; Boddington, 2012). In the Saudi context, on the other hand, the family has a more important role and a wider definition. As illustrated in Chapter Three, Saudi families are not just the next of kin but also include a much wider circle of relatives, and all family members come under the protection of the family as a whole. The oldest male

member of the family is of central significance to the extent that his opinions are regarded as orders rather than suggestions. This is reflected in the practice observed in Phase One of this study of approaches being made to families and not individuals. The consent given in cases like this is not necessarily for the good of the individual, but for the good of the wider family. In contrast, in Western literature relating to medical ethics, family consent is considered in a very limited context, for example, in the case of organ donation (Burroughs et al., 1998; Gortmaker et al., 1998; Siminoff et al., 2001) or critical care (Hackler and Hiller, 1990; Akabayashi et al., 1999; McNamara and Monti, 1995). Even in those limited contexts, in critical care for example, the family is supposed to decide what is in the best interests of the individual patient, but if caregivers are not convinced that the right decision (the right decision here is referenced against their perception of the individual's best interest) is being made, they have the right to intervene to reverse the next of kin's decisions (Lindemann, 1995).

#### **7.4.1 Claim of 'white coat' effect**

The 'white coat' effect in English refers to the ways in which individual results can be affected by the fact that the patient is being tested – e.g. blood pressure and heart rate can be raised by the stress of being tested (Pickering et al., 1988). In this thesis, however, I propose to use it in different way to describe how patients may sometimes feel submissive towards a person wearing white coat on the assumption that anyone wearing a white coat is a medical doctor.

The data collected for this thesis suggests that a patient's decision, at least in the context of this work, does not seem to be an individual choice. It reflected the

idea that valid individual consent was undermined by lack of information and practices that might be coercive. It could be argued that the regulations seek to outline an ideal practice, but they may not seem to represent what is genuinely important to Saudis. In addition to this, the logistic support given to researchers does not help them to achieve what the regulations highlight as important (i.e. individual consent). For example, the consenting venue, such as the long-awaited regular clinic, and the person requesting the donation (often in my study the doctor himself was the first to get patient approval) all play a major role in convincing patients to donate. Members in the first focus group in particular seemed convinced that the most decisive factor influencing patients' willingness to donate was that they trusted the doctor, more so than they trusted other caregivers or researchers. Moreover, participants in the focus group felt that patients assumed that anyone wearing a physician-style white coat was a doctor and in this sense it was the white coat that swayed their decision-making. Research led by Landry (Landry et al., 2013) reported that surveys at three locations in the Ochsner Health System (hospital clinic, satellite clinic, and inpatient ward), New Orleans in 2013 indicated a higher level of confidence in physicians who wore white coats, despite the patients' knowledge of the theoretical risk of infection transmission from the physician's attire. The reason for respecting the doctor's attire may be different in the UK, since it seems that the white coat helps patients to identify physicians in busy clinics (Douse et al., 2004, Gooden et al., 2001, Landry et al., 2013). In addition, according to Goodern (2001), patients felt they could communicate better with physicians wearing white coats (Gooden et al., 2001). Whether patients regard white coats per se as a symbol deserving respect has not been studied in depth. However, it could relate to some



level of patient vulnerability or to being non-verbally influenced by the physician (Bommier et al., 2013). This is mainly for two reasons. The first is the assumption that anyone who wears a white coat is perceived to be a medical doctor. According to both focus groups, the members seemed to think confirmed that this assumption is made. The second point is that, to some extent, patients are influenced by this assumption in a way that renders them vulnerable. There was a consensus among the focus group members that the non-verbal influence was a real concern between the Saudi physicians and their patients. This is in agreement with earlier works that established the link between patients-physician and how it reflects on the quality of informed consent (Abolfotouh & Adlan, 2011; Adlan, 2013). Both of the above factors have emerged as themes among Saudi researchers and I have included them in this study with one major difference, namely, that I studied the context of Saudi MGE research participants and potential participants, while Douse et al., (2004), Gooden et al. (2001), Landry et al. (2013), and Bommier et al. (2013) studied patients in their regular clinics and not as research participants or prospective research participants.

Patient vulnerability as a concept was present in all of the guidelines analysed, including the Saudi guidelines. However, with the exception of the Saudi national bioethics guidelines and the UNESCO principles, protecting vulnerability was a principle generally targeting special groups of people like children, pregnant women, prisoners and mental capacity impaired patients. Nevertheless, in 2013, the UNESCO report concerning the principle of protecting human vulnerability and personal integrity tried to explain its theory of the two types of human vulnerability

that could provide an explanation to how we might think of vulnerability in a Saudi context. The two types are specifically, 'a) special (temporary or permanent) disabilities, disease and limitations imposed by the stages of human life; b) social, political and environmental determinants: for example culture, economy, relations of power, and natural disasters' (UNESCO, 2013). Point b) requires further elaboration regarding patients in a clinical care context, where, for instance, patients' pain or the higher status of knowledge represented by the treating physician give rise to some level of vulnerability between patient and physician (UNESCO, 2013).

The Saudi National Bioethics Committee has a strict guideline stating that if the treating physician is a PI in a project, he or she should never ask the patient to participate. This is not related to the white coats issue per se; it more likely reflects the need to control, or eliminate, a perceived need to please the physician – which seems to be the underpinning reason why the white coat was highly regarded. The Saudi guideline was the only guideline - among the ones analysed in this thesis to take such a declaration. The ICH-GCP says “Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.” (GCP, 1996, p15). This can be taken as a call for a neutral party to be the person who records consent, it does not specifically declare that a patient's physician should not be involved in their recruitment to research. As explained in the Chapter Three, the NCBE guidelines seemed to anticipate the potentially coercive effect of the physician's involvement, by preventing the treating physician from recruiting for his own research. This notion is problematic if autonomy-based bioethics is the choice for the Saudi NCBE, because the research

team (i.e. the one actually consenting for MGE research) is recruited by the physician PI. Thus, the barrier between the patient and his/her physician in terms of recruitment can be very fragile; perhaps not sufficiently robust to protect the potential participant from the kinds of undue influence the guidelines seek to prevent. The PI appraises the research team performance. The first focus group discussed the relationship between themselves and a treating physician who is also a PI, noting that: a) the physician expresses frustration when they sometimes allow the patient to express the right to say no, b) they felt that it is their job to satisfy the doctor by recruiting patients, c) in their experience it is sometimes the doctors themselves who are violating the recruiting rules and refuse to listen to them when they try to provide advice (Results Subsection 5.4.3.1: Deception). The regulations suggest that the research team should work independently of the physician. However, in reality, the physician has the full potential to exercise influence on the patient through the research team.

The way I analysed the data does not lend itself to an exploration of the narrative of failure (see Subsection 7.2 What the finding can be taken to imply). Instead, I will look at the opportunity to learn from the context. It seems that there is enough evidence that, in this study, stakeholders believed that the physicians' attire has an effect on the patients' decision. They attributed that effect to a level of vulnerability. I, however, think that it is not the only reason. According to the Saudi cultural, religious and political contexts it would not be alien to attribute such an effect to the trust bestowed on the physicians as authoritative figures (see 1.2 The Saudi Arabian Context). I think that any effort aiming to regulate research ethics

cannot afford to ignore such a deep-rooted value. In such a culturally rich context both patient and physician have some cultural expectations that dictate the nature of the relationship. Therefore, and for similar reasons, informed consent process should not be taken as the only measure to justify research in such culturally rich contexts. This issue will be further discussed later in this section.

The other possibility is the assumption that the Saudi physicians are always going to exercise their superior knowledge to act in the best interests/advantage of their patients, or at the very least not use it to harm them. From the data collected in this project, a similar theme emerged when some patients reported that they were told to donate without any explanation, in addition to stories told by both focus groups showing how the physician's action could be seen as a restriction of the patients' freedom. This could be construed as patient vulnerability towards the treating physician that undermines respect for a patient's autonomy. The main challenge to this argument is that it assumes a tension between the patient and his physician. The connotation of the word 'vulnerability' suggests that an action to undo that vulnerability is needed. However, it is not necessarily the case that vulnerability is a negative property that needs to be addressed in all occurrences. Instead vulnerability could be seen as being value neutral. For instance in marriage, vulnerability is obvious as spouses make themselves vulnerable to each other's love and needs in a mutually trusting and healthy environment. This way of looking at vulnerability could be relevant to the Saudi health domain, where vulnerability might arise from trust and evoke trustworthiness in return. Thus, understanding how trust works is far more effective than regulating for autonomy.

#### **7.4.2 Trust in the organisation of health provision**

The two previous claims in the context of consent have paved the way to make the following argument about trust. According to the themes which emerged in my research, trust is central in the patient–physician relationship. Despite the risks of vulnerability, coercion or paternalism, trust can provide a contrasting explanation of the actors’ actions, which is no less credible than the other explanations.

Trust as described by Clayton (2013) is bestowed on the trustworthy. In this definition there is an important difference between trust as an attitude or sometimes a choice, and the trustworthiness as a characteristic. My findings would suggest that the culture, religion, politics and tribal values have contributed to the patients’ attitude to trust that the physician will act according to the patients’ best interests. However, trustworthiness as a characteristic is more important in the context of Saudi Arabia because it, arguably, provides a more tangible and easy way to measure characteristics (e.g. knowledge and experience). I think that working with trustworthiness, in terms of providing clear measures for the laypersons to be able assess it, is a more sensible route in Saudi Arabia than fighting trust as a cultural value and asking patients to be sceptical and suspicious that physicians are serving an agenda that uses the patient rather than serving them. Therefore, trust, as suggested by Davies (1999), is more applicable to the Saudi policy making context. Davies (1999) indicates that trust reflects “expectations by the public that healthcare providers will demonstrate knowledge, skill and competence; further expectations too that they will behave as true agents (that is, in the patient’s best interest) and with

beneficence, fairness and integrity. It is these collective expectations that form the basis of trust” (cited by Canlan & Sanford, 2004, p7).

My findings suggest that many participants have a genuine trust that the physician will only do what is appropriate. This could be explained by the physician’s social role as a person with knowledge (expert), as a healer, and as the one that will protect the patient’s best interests. In previous work, I documented my personal experience in a similar situation when my father was undergoing surgery. As the elder son, I was asked to make a decision during the operation. The physician indicated that “plan A” was not working, and they wanted me to choose between two alternatives. Despite all my education and what I stood for as a researcher, I genuinely wanted the physician to make the decision based on my father’s best interests. I thus asked the physician what he would choose for his own father in my place, and then just told him to do what he thought best (Adlan, 2013). At the time, informed consent in the contemporary sense of the term seemed to be unobtainable, as I was not equipped to take that decision with such grave consequences at stake. Although this experience relates to a treatment decision, it is likely that the same can be said about research in the health care setting. This experience is probably not unique. In general, the habitual trusting reference to doctors was such that people did not consider / develop the habit of questioning their judgments especially in Saudi culture (Abolfotouh & Adlan, 2011; Jamjoom et al, 2011; Al-Jumah and Abolfotouh, 2011; Adlan, 2013; Khedhiri et al., 2013). This is in contrast to the Western countries, where trust in the health care providers seems to have declined because the main focus has shifted towards autonomy, and the patient must decide for him/her

self (Canlan & Sanford, 2004; O'Neil 2002). This, in fact, does not necessarily mean that European and North American patients distrust their physicians, it may rather mean that for the decision to be legally sound it should be taken based on enlightened decisions with explicit information in the way advised by autonomy-based bioethics rather than by blind trust.

My data suggest that among the sampled stakeholders there was awareness about the importance of trust as a value in the Saudi health context. Based on that, we can assume that the reason for the absence of the trust as a value in the Saudi research guidelines could be that it is not the most applauded value in the international regulations used as reference for the Saudi ones (O'Neill, 2002; Manson, 2007; Manson and O'Neill, 2007) This seems inconsistent with how people deal with trust in general even in the Western culture. For example, someone buying a brand new car would trust that the tyres would not be bald and cause a life-threatening situation while driving. This of course may still be the case, but will not arise as a reasonable doubt if the car manufacturers and vendors are trusted for their professionalism. Trust-based bioethics does not necessarily mean giving in to paternalism and accepting any decision taken by the health care giver. On the contrary it could play a role in countering paternalism by suggesting when trust should be given and when it should be withheld. Trusting blindly might not be the wise thing to do. The appropriate call is to trust the trustworthy and not trust the untrustworthy. In this domain trust is an active decision rather than surrender to another's will. The challenge is that it is not very well understood or discussed in western autonomy-based bioethics, which as I introduced, could be the reason why

trust is absent from the Saudi policies. The importance of such a suggestion is that it would be a starting point to address the issue of trust in the Saudi policies. The start could come through a critical analysis of the informed consent process and how the Saudi policy can use the applauded value of trust to improve the process of consent for MGE research.

In this thesis I have presented some findings described as deceitful in the process of informed consent, which could instead be described differently through the trust narrative. It seemed to be the consensus in the focus groups that patients trust physicians when it comes to participation in health related research. The claim of deception in the findings was based on the failure to take essential steps such as providing information in the way specified in the regulations, and to let the patients decide freely after being thoroughly informed. It could be argued that some of those patients have given up their right to decide in preference to allowing the physician to make the right decision for them. This could mean that they trust the health service system to protect their best interests. In a way this could be an argument against deception, because we would not normally find those who set out to deceive us to be trustworthy. As I argued earlier, the informed consent doctrine has proved problematic in the context of Saudi Arabia for cultural, education, and logistical reasons. Trusting the treating physician, not only for health related issues but also in research participation, may be part of Saudi culture. The culture of trust would remedy the challenges of the contemporary understanding of consent in health care environments which is a claim that I will discuss further.



Adopting the international regulations committed the Saudi stakeholders to a specific way of how they ought to look at informed consent: that the patient should decide on his/her own interest based on an informed choice. To the contrary, my data would suggest the tendency to trust the physician. Thus, it is important to look for ways to use the value of trust and to translate it into a policy or part of a policy. It is not, however, in the interest of this thesis to go as far as suggesting a Saudi trust framework, but it is essential to indicate that the finding, if it would be shared by others, would act like a compass pointing towards the value of trust. It is also important to balance the call for introducing the value of trust between accepting it at face value in a moral relativist attitude -which I rejected in an earlier stage of this section- and totally ignoring the cultural reality by adopting the narrative of failure, which has also been rejected. This means that it is important to accept that even in the Saudi research context, it is important that people consent voluntarily to research. The call for introducing the value of trust should not mean that patient's consent is not important any more. Trust, I think, should be used as a tool to enhance the culture of research participation as well as the consent process. Ignoring the value of trust, however, is as wrong as over applauding the value of individual autonomy.

One way of looking at a trust-based bioethics is to start with Davies's (1999) definition that cast light on the characteristics of trustworthiness. The stakeholders might be able to do that if they introduced to a transparent system to measure trustworthiness and if it was to be made available to the patient or the research subject. A system in which the accountability of researcher is announced and the choice is given to the patient or the research subject to trust that person would be of

help as an investment in the trust value and of use as a tool for the patient and research subject.

As I argued earlier (see Subsection 4.2 Autonomy-Based bioethics), the level of information needed to fully inform the layperson is not realistic. “Trust-consent” may be a realistic additive to the fully informed consent. In the research domain, intelligent trust as advocated by Manson & O’Neill could be introduced as another element of professional ethics. Their argument is that to reach that level, it is important to shift the focus from patient consent to the patient–researcher relationship, and how the research organisation can introduce sufficient safeguards to prevent exploitation of the patient (Manson & O’Neill, 2007). The shift from consent-based participation to trust-based participation is not an easy one.

With the discussion of the trust and its challenges in the context of health related research in Saudi Arabia it is important to say that when it comes to MGE research there are other challenges such as the genetically homogenous nature of the Saudi tribes. In addition to investing in the trust culture to protect the individual interest, another measure should be considered to protect the tribal interest. In the next subsection I will discuss how research committees can fill this vacuum.

### **7.5 Ethics committees and protecting tribal interests:**

Almost two-thirds of the research ethics committee’s policy document is taken up by management regulations. The similarities between ICH-GCP and the Saudi bioethics research committee regulations are very noticeable, as explained in Chapter Two. In general, ICH-GCP looks at the role of an ethics committee as a review

board, with enough diversity to discuss if research proposals provide a justified balance between risks and benefits. However, risks in clinical research have a different meaning than risks in MGE research, as shown by two examples. Firstly, in the ICH-GCP, “risk” means any activity that subjects a person to more than regular day-to-day risk. This seems to have been the main reason that most of the stakeholders in this project reduced research risks to direct medical risks, such as the venepuncture in MGE research. Secondly, some might say that the use of identifiable genetic material in a proposal might be seen as a minimal risk to the donor. However, this disregards the wider understanding of risk in and around using identifiable material in MGE research in the Saudi context (see 2.3.3 Risk and 4.4 Stigma in tribal context).

It is fair to say that research committees are a very new phenomenon in Saudi Arabia. This is reflected by the amount of space dedicated to committee management in the Saudi guidelines. So there is little documentation to study the discrepancies between how the research committees actually operate versus how they are supposed to operate. The policy attempts to hold research committees liable for their decisions to approve research projects, and then to monitor them in the field in order to protect the research participants. In other words they are responsible both for assessing, and monitoring adherence to protocols.

According to the focus groups, research recruitment had to take place during regular clinic times due to a lack of resources. If this is the case, it is difficult to see how the research committees can do what is expected of them, especially if it has to recruit an expert or non-medical representatives. In my own experience, current

practice is that research committee members are not paid for this extra work that is expected of them. Payment, however, is not the only challenge, as the level of knowledge of the research ethics committee members may not be specialised enough to tease out the actual risks of MGE and deal with them. On the other hand, the problematic assumption that a detailed explicit informed consent will be the solution to any problem could also be conceived as part of the problem. I do not have enough data to state with confidence which of these explanations is more likely to affect the overall productivity of the Saudi research committees, nor indeed whether both might be factors.

In regard to MGE risks, as I argued earlier, there are three levels of genetic research awareness. Firstly, concerning patients: the majority of those who were seen or interviewed were not fully aware of the MGE risks, and the only risk they were able to recall being told about related to the venepuncture. Secondly, the awareness of the researchers is demonstrated by the first focus group. For the majority, if not all, of the participating research assistants, research nurses, and junior researchers, it took them a long time to reach the level of discussing serious risks like stigmatisation. They, initially, only discussed the venepuncture, which provides some explanation of the limited level of patient awareness. Thirdly, concerning the policymakers, it seems that they are aware of the many other risks in addition to the venepuncture, like the risk of stigmatisation and the risk around the notion of the national security aspect of genetics information.

I think, these different levels of awareness are reflected in the work of the research committee. Not all of the committee members are senior researchers. It is

important to provide some understanding of what kind of education of research committees in Saudi Arabia is most likely to prepare them for reviewing MGE research. This will be discussed in the following section.

### **7.5.1 The call for research committee education**

Another challenge is that, the education available to the human ethics committee members is based on what the national and international regulations say should happen in the operation of research. This is problematic for two reasons. The first is that these guidelines are very general and not equipped to deal with challenges concerning MGE research in Saudi Arabia. Second, there are no specific guidelines oriented to regulating MGE research. Therefore any education based on those guidelines will fall short of addressing the real problem of MGE research in Saudi. In order to protect participants they have to look at issues from the perspective of participants. The fact that the Saudi research committees have to approve MGE research in a genetically homogenous tribal context is making the committees' job more challenging. Tribes have the right to be protected from the MGE risks such as stigmatisation. I believe that Saudi research committees are not very well equipped to deal with these issues. The policymakers in Saudi Arabia should look at this problem and provide prospective solutions and prevent harm, rather than wait until it is too late and then try to react afterwards. In theory, the person who should be educated enough to raise these issues should be the lay committee member (i.e. the non-affiliated member according to article 10.1 (NCBE, 2010 p32-33). However, this is practically problematic. This layperson will be from one tribe specifically and so may be, if he is educated enough, able to raise concerns regarding research either

within his geographical tribal frontiers or on diseases known to be common in his tribe. However, not all the Saudi tribes will have a voice on this specific committee, which could be problematic if we assume that representation from each tribe is necessary to protect the interests of all tribes. I do not think that this problem can be solved with the current authority bestowed on the local committee in terms of education and awareness of the problem that needs to be addressed. I think that such a task is better to be taken on at a higher and more serious level by the national committee. It could be suggested that the national committee invites representatives, highly educated in genetics, from all the tribes. These representatives should then be educated about those challenges, and then asked to give general guidelines that local committees can follow. The local committees could then forward research proposals to these representatives, if their input would be deemed important by the committees. This should go hand in hand with educating the research committees.

In Saudi Arabia, as I explain earlier, we do not have philosophy education for committee members (see 1.4 The need for empirical data) and so they might lack the normative background that enables them to see and evaluate the differences in moral claims. This could be the reason for why the doctrine of informed consent is still highly regarded despite the complicated challenges around it. This is very troubling because in the NCBE regulations, as I explained in Chapter Three, the local ethics committees are legally responsible for the ethical conduct of the researchers in their organisations. To the best of my knowledge, there are no current assessments of the awareness of the risks of health related research in the Saudi context, among the members serving on research committees. Also, from personal experience, there is a

gap in the knowledge between what the research ethics members are expected to do and what they are currently doing. Therefore, it is crucial to work on an education program that is specifically tailored to research committee members in order to bridge the gap in the knowledge about the MGE research challenges in the Saudi context. There is also a crucial need to develop a specialised education in bioethics, including the moral theories to equip Saudi policymakers with better normative and analytic skills.

## **7.6 Conclusion**

The two main lines of argument presented in this discussion were as follows: the fact that there are no specific regulations related to MGE research in a Saudi context, means that the existing regulations are in tension with Saudi culture. I also argued that trust is an important value to Saudi culture and it should be looked at more openly with reflection on the importance of having a transparent system to measure trustworthiness.

Blood donation in the Saudi context is associated with positive values such as saving lives, generosity, and honour. In the Saudi tribal culture of consanguinity that has existed for hundreds of years information gained from genetic material can be very harmful to a larger population; the risks extend therefore beyond a consideration of the interests of the few who donate the blood that makes this research possible.

The Saudi guidelines seem to anticipate the problems and the potential harm to patients that may arise from genetic information, including a threat to national security. One way that the NCBE tried to activate a system of protection for this

national security (i.e. genetic information) was to announce that the State owns the Saudi genetic material.

The system by which genetic material is collected currently is based on autonomy-based bioethics, which posed many challenges as it assumed a specific level of education the absence of power differential between patient and physician. Physicians/researchers are also the ones who are expected to take measures to satisfy those guidelines that could be considered coercive or have a paternalistic nature. I have argued that introducing the value of trust could be the remedy to those challenges as it accords with the medical service in Saudi Arabia.

Promoting trust-oriented bioethics is not an easy task. It requires work and dedication and whilst its success cannot be guaranteed, it provides the best platform for success in Saudi Arabia given the cultural challenges.



## **8 Chapter Eight: Recommendations**

### **8.1 Introduction**

In this final chapter, I will illustrate my thesis' contribution to original research, limitations, and considerations for future work. Also, as this project used qualitative methods, it is important to be reflexive, which I will do towards the end of this section.

The aim of this thesis was to explore the particular ethical challenges associated with using donated blood for MGE research in the context of Saudi Arabia, as a preliminary step to enabling policymakers to generate culturally sensitive bioethics guidelines for collecting and using blood for MGE research in Saudi Arabia. I decided that the best methodology to fulfil this aim successfully was to use normative policy- or practice-oriented bioethics (NPOB) (see General Introduction: Section One). To meet this aim through the chosen methodology, I normatively analysed the international guidelines that were used as reference documents for the Saudi National Bioethics Guidelines (NCBE) in order to investigate how those guidelines can regulate the collection and storage of blood samples taken from adults for research purposes (see Chapter One). Subsequently, I did the same with the NCBE guidelines with specific elaboration on the Saudi context (see Chapter Two), which paved the way for testing how those guidelines can be applied to the Saudi MGE research normative challenges (see Chapter Three). This work was then combined to produce a general picture as to what the dominant ethical expectations are, based on the analysed guidelines, and what could be the

challenges based upon reflection on how the Saudi context might pose a challenge to the requirements of these guidelines.

The second stage was to see how the stakeholders of Saudi MGE research operate under the guidelines' assumptions and context outlined in the first section. The empirical project was completed in three phases. The first phase was an observation phase focussed on how Saudi MGE research is managed in current practice (Subsection: 4.2.1.1). The observation generated questions that I addressed by asking patients who had recently been offered the opportunity to participate as potential donors to reflect on this experience, which was done in Phase Two through in-depth semi-structured interviews (see Subsection 4.2.1.2). To close the circle, the experiences, perspectives and reflections on MGE research in Saudi Arabia of researchers and policymakers were gained in two separate focus groups. Participants were also asked to reflect on an interim analysis of the data collected in Phases One and Two (see Subsection 4.2.1.3.)

The last stages of this thesis provided the opportunity to reflect on the normative assumptions shaping the regulations and compare them to practice, and then listen to what the policymakers made of that current practice (see Chapter Seven). In Chapter Seven I was able to provide a suggestion as to why there are challenges and I concluded:

- Introducing the cultural value of trust may remedy the challenges which come with the autonomy-based bioethics.

- The current regulations do not deal with the issue of MGE research's effect on the tribes and how it could introduce irreversible damages like stigma.

- The crucial need for specialised education in bioethics, including the moral theories to equip Saudi policymakers with better normative and analytic skills.

## **8.2 Research Gap and Contribution**

In the early stages of this study, it was clear that Saudi Arabia with a tribal context poses a challenge to the straightforward adoption of the internationally accepted research norms, particularly in relation to MGE research. Many researchers study the application of international guidelines in places different from where those regulations were initiated. However, no one has looked at MGE research in a context like the Saudi one. The importance of this investigation is that it provides a contrasting view to the context that generated the guidelines in question. Based on the fact that tribal cultures are not unique to SA, the findings of this study may be applicable to any culture that shares a similar tribal culture.

The need for a specifically tailored education program for the research committee's members was a very important finding in order to introduce the changes in Saudi bioethics practice by allowing normative analysis focused on moral and philosophical reasoning as a step to better bioethics practice. This was communicated to the funding body for this thesis and has already been adopted into two education activities: the first was 5 days at the University of King Saud bin Abdulaziz for Health Science, King Abdullah International Medical Research Centre from 7th July

– 11th July 2013. The second one was 3 days at Kind Saud University, King Khaled Hospital from 10th Feb -12th Feb 2014 (Resalat Al Jameah, 2014) .

The Saudi NCBE showed interest in this study's finding. This may lead them to apply some changes to the current regulations. It will also lead to engagement with King Abdullah International Medical Research Centre (the funding body) in education and consultation projects to study the suggested improvements to the regulations.

I am, however, aware that my work did not give specific solutions to remedy the revealed challenges. It is, conversely, crucial to start with analysing the challenges in a rigorous way, as a first step towards dealing with them. One of the major findings is that I could not really interview participants because they knew so little – I wanted in depth interviews and barely managed to get people to speak for more than a few minutes. This actually calls for future work to understand this phenomenon and try to cast light on the actual reasons behind such lack of knowledge if we want to explore and expose hidden incompatibilities between the inherited assumptions of two studied contexts (the normative assumption about ethics in the regulations and the cultural values.)

### **8.3 Study limitation**

Every research has its limitations, and this study was not an exception. I also faced some problems and dealt with them in the most professional way, given the available time and funds. It is important to acknowledge that this study did not aspire to give a specific set of solutions in a form of a checklist to be followed or avoided,

and it was not expected to provide one. It, rather, set out to question the status quo in the practice of MGE research regulations, and this it has achieved.

The interviews were a total surprise insofar as they were much shorter than anticipated and were therefore not very informative. For example, one of the interviews was only 7 minutes, although it was expected to be 60 minutes. The lack of knowledge affected the way questions were asked. I had to use rather closed questions after the open-ended questions failed to get any responses. Even those closed questions were not understood, so I had to resort to more closed questions and the suggestion of possible options to get any responses at all. I concluded that this could be attributed to the fact that the participants had been given so little information by the researchers and apparently lacked much understanding as to what was going on in the research. On the other hand, the two focus groups were very successful and yielded rich data. It is unfortunate, however, that I had funds for only two focus groups. Perhaps in hindsight and with more money, more would have been better and it would also allow further follow up interviews to address the paucity of data.

The translation issue was one of the problems that took a long time to solve due to a lack of qualitative research experience among the translators in Saudi Arabia. For the greater detail of how this was remedied, see subsection (5.2.3.4). I am satisfied that the final English translation was an accurate verbatim representation of the Arabic original texts.

## 8.4 Reflexivity

It is important to see that this study used a qualitative method, and that as argued by Koch and Harrington (2002), it is essential for the researcher to engage in self-critique and self-appraisal, and to explain how his own experiences have, or have not, influenced the way he/she looks at the qualitative data. Reflexivity is regarded as a crucial contribution to the trustworthiness of any qualitative research, as it declares 'up-front' the values and processes that have guided the research stages. These include choosing the design, collecting the data, identifying the research informants, analysing the data, and writing the discussion (Lincoln and Guba, 1985; Sandelowski, 1986; Cutcliffe and McKenna, 1999; Meyer et al., 2001; Spencer et al., 2003). I will start with reflexivity to help the reader to understand my perspective.

I am a middle-aged, middle-class, research bioethics advocate in the Kingdom of Saudi Arabia. I originally trained as biochemist and worked in molecular biology for a few years and then moved to health related research and became a certified clinical research professional. In my 15 years of experience in research, both genetic and clinical, I have been confronted with myriad bioethical dilemmas stemming from either the unsuitability of international research ethics guidelines to a country like Saudi Arabia, or the lack of understanding of, and adherence to, those guidelines. Early on I had conflicts with many stakeholders (including Western expatriates working in Saudi Arabia) who saw the Western ethical guidelines as a new imperialistic attempt to control research progress or a hurdle to complicate research rather than to help it, so they decided to ignore them. At one point I was in charge of

a clinical research unit that oversaw patient recruitment and I had to take decisions that, in some way, conflicted with those of my colleagues who did not see the importance of the bioethics guidelines. Sometimes those decisions put me in awkward situations and (with the help of supporters) forced me to question the status quo, in order to educate researchers to carry out more ethical research.

The extent of how this could impact the process of the current research is uncertain, but it may have had an influence. I have no explicit agenda besides my declared aims and objectives. With this in mind, and with the support of my supervisors, I have maintained a high level of self-criticism and self-appraisal regarding the influence of my own preconceptions and beliefs on my research. This is a necessary step to minimise the impact of those perceptions and beliefs and allow my analysis to be driven by the data.

## **8.5 Future work**

As I explained in this chapter I ended up with more questions than I started with. I rate this as a healthy outcome as it calls for more work, more understanding to provide the most accurate solutions or frameworks. Among the future work that can extend and continue the work of this thesis, is the need to understand what role Islamic bioethics might play in this field.

Another area that has caught my interest as promising material for future work was the level of genetic information that patients need to have to empower him/her to decide for him/herself in the autonomy-based model of bioethics or to act as foundations for trust in the trust-based model of bioethics.

In the end, the research for this thesis was a learning process in which I came to understand how to think as a researcher in analysing and exploring my research questions, and ultimately provided the most suitable solution to the problems that can be solved, or accept it as limitation if it is cannot, in an academic open-minded spirit.



## **Appendix 1: Phase One, the observation phase, case 1 field note**

### First Observation:

The location is a very small screening room. Family of two females was interviewed. They refused to be separated for the consent process. Blood for MGE research was only requested of the mother, who is almost 70 years old, and she was the patient.

The consent duration was 9 minutes from the time the coordinator started talking up to the signature.

The coordinator was talking very quickly; he asked if the patient knows why she is here. 'No, I do not know,' the patient replied. He started asking what the doctor has told her, then she replied that the doctor "just asked her to give blood".

After that, the coordinator told the patient that this is research, and it is not a compulsory test; at this stage the patient started to be confused. The patient wanted to know what is needed exactly. What is the needed sample? The coordinator explained to her that it is 'only a blood test' with no risk whatsoever.

The coordinator told the patient that the research will be oriented towards the greater good and will help other patients, and if any good thing came out of the research that she will be given the priority to be treated with it. Also, the coordinator mentioned that consenting to give blood is something that she will be rewarded by God for.

After that, the patient signed the informed consent, which is one page, without reading it. The blood extraction took place and patient was dismissed.

### Observations:

- The location was very small for 5 people. The door was open, and the voices were very loud in a busy clinic.
- The patient was not given a copy of the informed consent form
- She was not given any time to think about it
- The physician told her that it was just a blood test
- The patient did not know what genetics research is
- She signed without reading
- The coordinator's attitude was to get the blood
- The only risk was discussed was the venepuncture risk

## **Appendix 2: Clinic Poster Phase One, for researchers**

### **Donating blood for Genetics Research in Saudi Arabia**

**Are you expecting to recruit blood donors for genetics or molecular epidemiology research in the coming few weeks? If so, you may be able to help with our research.**

Abdallah Adlan is a PhD student in the University of Birmingham. The purpose of his research study is to help policy makers in Saudi Arabia provide culturally sensitive bioethics guidelines on donating blood for Saudi genetic and molecular epidemiology research.

#### **He would like to observe your consent interviews**

- ❖ This is not an assessment of your work.
- ❖ You will not be identified in his results
- ❖ You do not have to agree to let him observe you, but we would be grateful if you would.

If you are willing to be observed:

- ❖ Please make sure that your interviewees have seen our poster in the patients' waiting area, understood it and does not object to the observer's presence at the start of the interview.
- ❖ You can request that the observer leaves the consent interview at any point.
  
- ❖ Do not try to engage the observer in any way during the recruiting session
- ❖ After the interview he will ask your participant if he or she is willing to be interviewed separately for a different phase of his research.

This study has been approved by the University of Birmingham Science, Technology, Mathematics and Engineering Ethical Review Committee. (Reference ERN\_12\_1394 06/02/2013) and the local ethics Committee of KKESH: RP 1319-P, Date of Approval: 10/03/2013, and of NGHA: RC12/090/R, Date of Approval: 26/03/2013.

### Appendix 3: Clinic Poster Phase One, for patients the Arabic Version

#### إعلان للمشاركة ببحث

في دراسة للدكتوراه حول التبرع بالدم للبحوث الوراثية في المملكة العربية السعودية

هل متوقع أن تقوم بالاشتراك كمتبرع بالدم لبحث جيني أو متعلق بال DNA خلال الأسابيع القادمة؟

هل عمرك فوق ال ١٨ عاماً؟

إذا أجبت بنعم، هذا الملصق موجه لك.

عبدالله عدلان طالب دكتوراه في جامعة برمنغهام يدرس ظاهرة التبرع بالدم لبحوث علم الأوبئة الوراثية والجزيئية في المملكة العربية السعودية. والغرض من هذا البحث هو لنصح واضعي الأنظمة في المملكة العربية السعودية بمعرفة السمات الثقافية للمجتمع بشأن أخلاقيات علم الأحياء لتبرع بالدم لبحوث ال DNA السعودية.

يرغب الباحث بالحضور معك في الجلسة الأولى لتبرعك و توقيعك لوثيقة القبول المتبصر. لك الحق بأن تقبل أو ترفض هذه الدعوة كما أن لك الحق في تغيير رأيك و ذلك بأن تطلب من الباحث عبدالله عدلان مغادرة الإجتماع في لحظة دون إبداء الأسباب.

وقد تمت الموافقة على هذه الدراسة من قبل لجنة المراجعة الأخلاقية لكليات العلوم و التكنولوجيا و الهندسة و الرياضيات بجامعة برمنجهام البريطانيه ( ERN-12-1394 dated on 12 Feb 2013 ) واللجنة المحلية الأخلاق لمستشفى العيون ومستشفى الحرس تباعاً RP

10/03/2013 ، 1319-P

RC12/090/R, 26/03/2013

**Appendix 4: Verbal Consent Confirmation - Phase One**

Donating Blood for Molecular and Genetics Epidemiology Research in Saudi Arabia

Researcher: Abdallah Adlan, PhD student, University of Birmingham  
Supervisors: Professor Heather Draper and Professor Angus Dawson, University of Birmingham

Please  
initial box

1. I confirm that I have seen the poster for staff about the above study and spoken to Dr Adlan about this research. I have had the opportunity ask questions and have had these answered satisfactorily. I have agreed to allow him to observe me gaining the consent of a patient to donate blood to research. I understand that my participation is voluntary and that I am free to withdraw at any time up to 48 hours after the consent interview has taken place without giving any reason by ringing Dr Adlan on the number on the poster.

2. I confirm that I have spoken to my patient, that my patient has either read (or had explained to him/ her) the patient poster about this research and that s/he understands and agrees that his/her consent interview will be observed as part of Dr Adlan's research. S/he knows that Dr Adlan can be asked to leave at any point by either of us.

Name of researcher-  
participant.....  
.....

Signature: ..... Date:  
.....

Name of patient whose consent will be observed: .....

## Appendix 5: Clinic Poster Phase Two, for patients the Arabic Version

### إعلان للمشاركة ببحث

في دراسة للدكتوراه حول التبرع بالدم للبحوث الوراثية في المملكة العربية السعودية

هل تم توجيه الدعوة لك بالاشتراك كمتبرع بالدم لبحث جيني أو متعلق بال DNA خلال  
الأسابيع القادمة؟  
هل عمرك فوق ال ١٨ عاماً؟

إذا أجبت بنعم، هذا الملصق موجه لك.

عبدالله عدلان طالب دكتوراه في جامعة برمنغهام يدرس ظاهرة التبرع بالدم لبحوث علم الأوبئة الوراثية والجزيئية في المملكة العربية السعودية. والغرض من هذا البحث هو لنصح واضعي الأنظمة في المملكة العربية السعودية بمعرفة السمات الثقافية للمجتمع بشأن أخلاقيات علم الأحياء لتبرع بالدم لبحوث ال DNA السعودية.

يرغب الباحث بتوجيه بعض الإستفسارات عن تلك تجربتك. لك الحق بأن تقبل أو ترفض هذه الدعوة كما أن لك الحق في تغيير رأيك و ذلك بأن تطلب من الباحث عبدالله عدلان مغادرة الإجتماع في لحظة دون إبداء الأسباب.

وقد تمت الموافقة على هذه الدراسة من قبل لجنة المراجعة الأخلاقية لكليات العلوم و التكنولوجيا و الهندسة و الرياضيات بجامعة برمنجهام البريطانيه ( ERN-12-1394 dated on 12 Feb 2013 ) واللجنة المحلية الأخلاق لمستشفى العيون ومستشفى الحرس تباعاً RP

10/03/2013 ، 1319-P

RC12/090/R, 26/03/2013

## **Appendix 6: Information sheet (Phase Two) the English version**

### Donating Blood for Molecular and Genetics Epidemiology Research in Saudi Arabia

Researcher: Abdallah Adlan, PhD student, University of Birmingham  
Supervisors: Professor Heather Draper. Professor Angus Dawson

## **Participant Information Sheet**

### **Invitation to participate**

Thank you for thinking about taking part in my research project. Please read the following information. It explains the purpose of this research and what taking part will involve. You can discuss this information with others if you wish. If you would like further information, please contact me. I will be in touch with you in a couple of days to see whether you are still interested in taking part, and if you are, we agree a date and time for your interview.

### **Purpose of the research**

This research will try to help the policy makers in Saudi Arabia to improve the policies that rules donating blood for genetics research. To do that, I will analyse both the current Saudi and international policies that rules donating blood for genetics research. This will make me able to compare between those guidelines and the actual practices like the one you attended.

I would like to interview you about your recent experience of consenting to give blood for research.

### **Why have I been selected?**

You have been selected because you have recently agreed to donate blood for research.

### **Do I have to participate?**

No, it is up to you to decide whether or not you want to take part. If you do decide to take part and then change your mind, that's fine. Just let me know. You can also stop the interview at any point. If you change your mind after the interview, you will need to tell me within 48 hours. You can do this by ringing me on [REDACTED]. If this email is being read to you, the researcher will give you this number on a piece of paper so you can keep it safe in case you want to withdraw. After this time the information you have given me will be combined with the information from other people, and because this is done without names, I will not know what information is yours to take it out again.

**What will happen to me if I participate?**

If you decide to participate, I will arrange a convenient time and place to interview you. The interview is expected to last for approximately one hour. During the interview I will ask you about your experience of donating blood for research. This interview will be audio-recorded. Your contact details will be destroyed once the interview has taken place, unless you want to receive a copy of the research summary. In this case once I have sent you the summary I will destroy your contact information.

**What are the possible benefits of taking part?**

There is no direct benefit to you.

We hope that the development of better guidelines for donating blood for research will benefit everyone in Saudi Arabia.

**What will happen to the results of the research?**

We will write a report of the results of all of the interviews. These will be part of my PhD thesis. We also hope to publish the result in academic journals. I quote some of the things that you said in your interview in these results. I will not use your name and I will be careful not to identify you in others ways.

**Are there any risks involved?**

You will not be placed at risk in this study.

**Will my participation be confidential?**

Yes. All your personal information will be securely stored. Your name off will not be used and nor will that of anyone you talk about. After the audio- recording has been typed up word for word, only my academic supervisors and I will have access to anything with your name on it. The people doing the typing will have signed a confidentiality contract.

We have to keep the audio-recordings for ten years to prove our research was real. This will be the responsibility of my supervisor Professor Heather Draper, who will ensure that they are kept safely and destroyed after ten years.

**How is this research organised, approved and funded?**

This research is a part my doctoral research at the University of Birmingham, where my supervisors are based. It is funded by a scholarship from the National Guard Health affair, Riyadh, Saudi Arabia

The research has been favourably reviewed by the University of Birmingham Science, Technology, Mathematics and Engineering Ethical Review Committee, ERN\_12-1394, Date of Approval: 06/02/2013, and by and the local ethics Committee of KKESH: RP 1319-P, Date of Approval: 10/03/2013, and of NGHA: RC12/090/R, Date of Approval: 26/03/2013 in Saudi Arabia.

**My Contact details**

If you want more information, please contact me:



If you wish to make a complaint you can contact: (if this sheet is being read to you, you will be given this information on a piece of paper to keep safe in case you need to complain)



**Thank you for taking the time to read this information.**



## Appendix 7: Information sheet (Phase Two) Arabic Translation

### دعوة للمشاركة

المفترض أن توضح لك الغرض من هذه الدراسة و ماذا يتوقع من المشارك. لك أن تناقش مع من شئت. في حالة رغبت بالمزيد من المعلومات تستطيع الاتصال بي. سأعود الاتصال بك خلال الأيام القادمة للتحقق من رغبتك بالمشاركة و تحديد التاريخ و الوقت المناسب لك لكي تتم المقابلة.

الغرض من هذه الدراسة:

هذا البحث يهدف لتقديم النصح لواقعي الأنظمة في المملكة العربية السعودية بمعرفة السمات الثقافية للمجتمع بشأن نظام أخلاقيات التبرع بالدم لبحوث الـDNA السعودية. للقيام بذلك سأحاول تحليل و دراسة الأنظمة السعودية و العالميه المتعلقة بالتبرع بالدم للبحوث الوراثية مما يمكنني من المقارنة بين تلك الأنظمة و الممارسة الفعلية لها في الواقع بحضور الجلسات مثل تلك التي حضرتها.

لماذا تم إختياري؟

لقد تم إختيارك لأنك مؤخرًا قبلت التبرع بالدم لبحوث جينية وراثية.

هل يجب علي المشاركة بهذه الدراسة؟

لك أن تشارك أو ترفض المشاركة كما يحق لك تغيير رأيك في أي وقت تشاء أثناء المقابلة أو خلال ٤٨ ساعة من انهاء المقابلة بمجرد الاتصال علي علي الرقم ٠٥٠٥٢١٨٧٩١ -سيتم اعطاء الرقم لك لذلك الغرض. بعد الـ٤٨ ساعة المشار إليها بسبب أن المعلومات من هذه المقابلة سيتم دمجها مع المقابلات الأخرى بصورة يصعب معها التعرف علي المصادر.

مالذي سيحدث لو قررت المشاركة؟

لو قررت المشاركة سأنسق الوقت و المكان المناسب لكي أجلس معك في مقابلة لمدة حوالي الساعة. أثناء هذه المقابلة سنتحدث عن مشاركتك و تبرعك بالدم. سيتم تسجيل هذه المقابلة صوتيا كما سيتم طمس جميع معلوماتك مباشرة بعد الانتهاء من المقابلة مالم تطلب مننا الحصول علي نسخة من النتائج النهائية. في هذه الحالة سيتم تأجيل طمس المعلومات لحين ارسال المعلومات لك بحسب طلبك.

ماذا سأستفيد من مشاركتي؟

لا نعد بفائدة شخصية مباشرة

غير أننا نأمل بتطوير الأنظمة الخاصة بالتبرع بالدم للبحوث الجينية و الوراثية مما يعود

بنفعه للمجتمع بصورة عامة.

كيف سيتم التعامل مع نتائج هذا البحث؟

سنقوم بكتابة التقرير الخاص بتحليل المعلومات التي حصلنا عليه من المقابلات الشخصية كجزء من بحث الدكتوراه الخاص بي. كما سنتطرح بنشر النتائج للمهتمين في الدوريات العلمية الأكاديمية. بحسب طبيعة هذه الأبحاث قد يحتوي التقرير علي مقتطعات من المقابلة دون الإشارة بأي حال من الأحوال لشخصك بأي صورة من الصور.

هل توجد أية مخاطر مترتبة علي مشاركتي؟

لن يتم تعريفك لأي نوع من أنواع المخاطر في هذه الدراسة.

هل سوف تكون معلوماتي الشخصية سرية في هذه المشاركة؟

نعم. جميع معلوماتك الشخصية سيتم التعامل معها بحرص و لن يتم ذكر اسمك أو اسم اي شخص ستتحدث عنه. بعد أن يتم تفريغ محتوى المقابلة الصوتي لن يطلع أحد علي التسجيلات سوى المشرف الأكاديمي. في حالة الرستعانه بأي شخص خارجي لعملية الطباعة سيتم توقيعه علي تعهد بالسرية.

بحسب الأنظمة سنحتاج للاحتفاظ بالتسجيلات لمدة عشر سنوات لكي نبرهن علي حدوث المقابلة و ستكون هذه من مهام البرفسورة المشرفة هيذر دراير و التي تتأكد شخصيا من الحفاظ علي مستوي عالي من السرية و اعدام التسجيلات حين ينتهي الغرض منها.

كيف تتم ادارة هذا البحث وممن تمت الموافقة عليه و دعمه؟

هذا البحث هو جزء من بحث الدكتوراه الخاص بي و المسجلة في جامعه برمنجهام البريطانيه. وهي دراسة تم دعمها من قبل إدارة الابتعاث بالشئون الصحية للحرس الوطني، الرياض.

وقد تمت الموافقة على هذه الدراسة من قبل لجنة المراجعة الأخلاقية لكليات العلوم و التكنولوجيا و الهندسة و الرياضيات بجامعة برمنجهام البريطانيه (ERN-12-1394 dated on 12 Feb 2013) واللجنة المحلية الأخلاق لمستشفى العيون ومستشفى الحرس تباعاً RP 1319-P، 10/03/2013 و RC12/090/R، 26/03/2013

معلومات الاتصال الخاصة بي:

د. عبدالله عدلان

٠٥٠٥٢١٨٧٩١

صندوق بريد ١٧٧٨٧

الرياض ١١٤٩٤

[Redacted]  
[Redacted]  
[Redacted]  
[Redacted]

إذا رغبت بالتقدم بالشكوي يمكنك الاتصال علي (إذا تمت قرأت هذه الورقة سيتم اعطائك هذه العناوين مكتوبه):

بروفسور هنر دراير  
تلفون +٤٤١٢١٤١٤٦٩٤١



شكرا لقرائتك هذه المعلومات



## Appendix 9: Arabic Informed consent Phase Two

بحث التبرع بالدم للأبحاث الجينية في المملكة العربية السعودية

الباحث: د. عبدالله عدلان، طالب بجامعة برمنجهام  
المشرف: بروفيسور. هيذر دراير و بروفيسر أنجوس داوسن جامعة برمنجهام

أمل التأشير  
في المربع

١. بهذا أؤكد بأني قد قرأت أو قرأت لي صحيفة معلومات الدراسة المؤرخة بتاريخ ٢١-١-٢٠١٣ ميلادي و الإصدار رقم ١-١ و المتعلق بالدراسة المعنونه بعاليه و انه قد اتاحت لي الفرصة لفهم المحتوي و توجيه الأسئلة التي تمت الاجابة عنها بصورة مرضية.

٢- أعلم بأن مشاركتي في البحث تطوعيه كما يمكنني الانسحاب من الدراسة في أي وقت أشاد أثناء المقابلة أو خلال ٤٨ ساعة من المقابلة دون ابداء اي أسباب و ذلك عن طريق الاتصال بال د. عدلان في رقمه الموضح في صحيفة المعلومات.

٣. أعلم بأن المقابلة سيتم تسجيلها صوتيا.

٤. أمل الحصول علي ملخص النتائج عن طريق الاتصال ب:

أشر علي رغبتك	بالبريد	بالبريد الالكتروني	لا أرغب بالملخص

٥. لا أمانع من اتصال فريق البحث بي اذا رغبوا بأخذ رأيي في نتائج البحث

٦. أوافق علي المشاركة في البحث الموضح أسمه عاليه

اسم المشارك:.....

التوقيع:.....

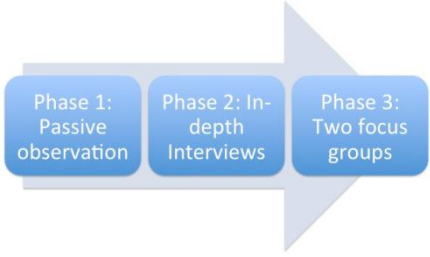
التاريخ:.....

اسم آخذ الموافقة:.....

التوقيع:.....

التاريخ:.....

## Appendix 10: Focus Groups –Phase Three - Power Point Slides

<p>The Biomedical Ethics of Donating Blood for Genetics and Epidemiology Research in Saudi Arabia</p> <p>The results of the the 1<sup>st</sup> and 2<sup>nd</sup> phases of the Project By Abdallah Adlan</p>	<p><b>Aim</b></p> <p>To help policy makers in Saudi Arabia to fashion culturally sensitive Saudi bioethics guidelines for donating blood for molecular and genetics epidemiology research (MGE)</p>
<p><b>Objectives</b></p> <ul style="list-style-type: none"> <li>• The MG research challenges in SA</li> <li>• The presumption of the international guidelines</li> <li>• The presumption of the Saudi guidelines</li> <li>• Empirical attempt to investigate the field</li> </ul>	<p><b>What is Your rule today</b></p>
<p><b>This research phases</b></p> 	<p><b>Phase 1</b> Observation results</p>
<p><b>Phase 1- Results</b></p> <ul style="list-style-type: none"> <li>• Total of 11 attempts to attend the consent interviews;</li> <li>• Verbally consent obtained to observe 6 consent interviews;</li> <li>• Of the other 5, only 2 of patients agreed to donated blood (I was later informed);</li> <li>• The interviews lasted between 8 minutes (when only blood was needed) to 17 minutes (when extra information was needed); the average time was 11 minutes;</li> </ul>	<p><b>Observation Descriptions</b></p> <ul style="list-style-type: none"> <li>• The researcher was a passive observer and did not interfere with any aspect of the sessions.</li> <li>• 6 interviews were observed: 4 different researchers and 4 different projects at 2 different sites</li> <li>• The sessions took an average of 10 mins (with the shortest being 7 mins and the longest 12 mins)</li> </ul>

<p><b>Observations Rooms descriptions</b></p> <ul style="list-style-type: none"> <li>• 5 of the 6 observed interviews were in small regular clinic rooms.</li> <li>• Those 5 rooms were designed as cubical with no individual sealing (any conversation can be heard clearly from other rooms).</li> <li>• 3 out of those five interviews were conducted in hearing distance of other patients.</li> <li>• The patients in all 6 interviews were asked to sit down, the recruiting researcher sat in front of them.</li> </ul>	<ul style="list-style-type: none"> <li>• The average number of people in one room was 5 (the observer, a researcher, a technician, the patient; and a patient's relative)</li> <li>• The minimum number of people was 3 (the observer, a researcher, and the patient)</li> <li>• The maximum number was 7 (a researcher, the observer, a technician, the patient; a patient's relative, and two children)</li> </ul>
<p><b>Privacy of the interviews</b></p> <ul style="list-style-type: none"> <li>• 3 of the 6 interviews were done with a door semi closed</li> <li>• 2 of the 6 interviews the door was fully open</li> <li>• 1 interview a sliding door was fully closed</li> <li>• 4 of the 6 interviews were interrupted by nurses or an assistant to collect various things from the rooms</li> </ul>	<p><b>Observations Results</b></p> <ul style="list-style-type: none"> <li>• No patients/family members were given a copy of the IC or the PIS</li> <li>• No time was given to think or reflect</li> <li>• Very little information was provided (about the nature of genetic research, where the blood goes, what happens to the access, withdrawal rights and its limitations etc.).</li> <li>• Confusion between clinical (tests) and research was not rectified</li> <li>• 5 out of the 6 recruiters showed 'Salesman' tendencies (i.e. giving information in the way that persuaded patients to donate).</li> <li>• All of the observed patients signed without reading.</li> <li>• The only highlighted risks was risk related to actual venepuncture.</li> </ul>
<p><b>Phase 2 Interviews results</b></p>	<p><b>General Topic Guide</b></p> <ul style="list-style-type: none"> <li>• What patients recalled of the initial invitations</li> <li>• Why patients participated</li> <li>• How do they recall the informed consent process</li> <li>• What patients know about genetics research</li> <li>• What are the risks as they understand them</li> <li>• If they would encourage relatives to donate (as a measure of their confidence)</li> </ul>
<p><b>Sample size</b></p> <ul style="list-style-type: none"> <li>• The original plan was to interview 20 donors of blood for genetics research;</li> <li>• Saturation was reached after 10 interviews;</li> <li>• Further 2 interviews were done to confirm saturation.</li> </ul>	<p><b>Interviews descriptions</b></p> <ul style="list-style-type: none"> <li>• Donations were made to 8 different research projects;</li> <li>• Participants had given consent to 10 different researchers from 2 organizations;</li> <li>• 2 interviews were with families: <ul style="list-style-type: none"> <li>– A person and his parents (2 of them donated);</li> <li>– A son and his elder father (both donated);</li> </ul> </li> <li>• 10 interviews were with individuals who donated blood for MGE research.</li> </ul>

<p style="text-align: center;"><b>Interviews Durations</b></p> <ul style="list-style-type: none"> <li>• The average time of the interviews were 13 minutes;</li> <li>• The shortest interview was 7 minutes;</li> <li>• The longest interview was 17 minutes.</li> </ul>	<p style="text-align: center;"><b>Organizational Issues</b></p> <ul style="list-style-type: none"> <li>• Person making the approach: the physician or the researchers. <ul style="list-style-type: none"> <li>– All the participants were asked to participate by the treating physician in their regular clinical appointments</li> </ul> </li> <li>• Whether blood taken there and then or elsewhere <ul style="list-style-type: none"> <li>– Participants dissatisfied with organisation e.g. waiting times or having to move from place to place.</li> <li>– Convenience vs no time to consider, and pressures created by long waiting time for treatment.</li> </ul> </li> </ul>
<p style="text-align: center;"><b>General findings</b></p> <ul style="list-style-type: none"> <li>• Ambiguity concerning what is the nature of the relation between the researcher and the patients from the patients' perceptions.</li> <li>• Assumption that the only risk is the amount of donated blood.</li> <li>• Underestimate their participation in genetics research, thinking that it is just a blood sample.</li> </ul>	<p style="text-align: center;"><b>Reasons for participation</b></p> <ul style="list-style-type: none"> <li>• How approached: the attitude of person asking was influential.</li> <li>• How persuasive the research coordinator was</li> <li>• Tangible personal gain: <ul style="list-style-type: none"> <li>– Some wanted benefits (e.g. priority treatment)</li> <li>– Some wanted treatment: <ul style="list-style-type: none"> <li>• Some has a misconception that they were being offered treatment</li> <li>• Some where hoping that there will be a treatment eventually</li> </ul> </li> <li>– Some wanted more information about their illness</li> </ul> </li> </ul>
<p style="text-align: center;"><b>Reasons for participation (con't)</b></p> <ul style="list-style-type: none"> <li>• The personal satisfaction of helping others (reasons differed);</li> <li>• Hoping for God's rewards;</li> <li>• Willing to help others and help self, assuming no harms to self.</li> </ul>	<p style="text-align: center;"><b>Lack of essential information</b></p> <ul style="list-style-type: none"> <li>• Misunderstandings about purpose for which blood given</li> <li>• Lack of knowledge about what genetics research is and its risks for individual and societies</li> <li>• Majority were not given an information sheet nor a copy of the signed informed consent form.</li> <li>• Majority was not sure if they were told about what will happen to the blood</li> <li>• Majority was not sure who owns the donated materials</li> </ul>



### **Appendix 11: Focus Group – Phase Three - Topic guide**

*For researcher and policy makers:*

- How do you think the regulation of bioethics in the field of genetics is appropriate to Saudis?
- What are the challenges in recruiting for MGE research in Saudi Arabia
- How do stigma play role in disseminating the research results
- How can you protect your patients
- What did you wish to see in the Saudi research guidelines and you did not find it?
- How do you compare the SA research guidelines with the international ones?
- How do you see the future of the new Saudi research guidelines?
- Can you recall any case where the research ethics guidelines were hindering your ability to do research?
- How do you recruit patients for your research?
- What are the first things that happen when you see an interesting case for your research?
- Can you walk me through the recruiting steps in details so I can imagine the process with you?
- Why do think Saudi patients donate blood for research?
- Who do you think own the donated material? Why?
- Can you recall a patient discussing any sensitive issues like privacy, stigmatization, share patents rights, or any other concerns?
- If your team was successful in patent a test based on donated material, what do you think should happen?
- Have you been asked by a patient to withdraw the researched material? If the answer is “yes”, then what did you do? Otherwise, how to deal with such request?
- Have you been asked by a patient to withdraw the collected data? If the answer is “yes”, then what did you do? Otherwise, how to deal with such request?
- What are the patients’ main fears? And how do you deal with them?

## **Appendix 12: Information sheet Phase Three –The first Group**

### Donating Blood for Molecular and Genetics Epidemiology Research in Saudi Arabia

Researcher: Abdallah Adlan, PhD student, University of Birmingham

Supervisor: Professor Heather Draper & Professor Angus Dawson, University of Birmingham

### **Participant Information Sheet**

Thank you for being willing to consider taking part in my doctoral research. The following will give you more information about the research and what taking part will involve. If you would like further information, please contact me. I will be in touch with you in a couple of days to see whether you are still interested in taking part, and if you are, begin the process of setting a date for the focus group.

#### **Purpose of the research**

The aim of this research is to help policy makers in Saudi Arabia develop culturally sensitive bioethics guidelines for donating blood for molecular and genetics epidemiology (MGE) research in Saudi Arabia. It will analyse the current Saudi policies for MGE research and all the international policies that were used as reference points for these. I will then compare and contrast existing policies with current practice to assess how they address the emerging ethical issues. The results will be discussed in two focus groups, one with leading thinkers in Saudi bioethics and the other with more junior researchers. I will facilitate these focus groups.

#### **Why have I been selected?**

You have been selected because you one of the leading thinkers in the field of bioethics in the kingdom of Saudi Arabia.

#### **Do I have to participate?**

No, it is up to you to decide whether or not you want to take part. If you decide to participate in the focus group and then change your mind, please let me know. Once the focus group has started you can leave at any point without giving a reason. It will not, however, be possible to withdraw from the research anything you have said up to this point as the focus group is interactive and depends upon the input of all concerned, so it would be impossible to withdraw your data without impacting on the participation of others.

#### **What will happen to me if I participate?**

You will take part in a focus group that will discuss the results of my research to date. The discussion will audio-recorded. There are no follow-up meetings. Your contact details will be destroyed once the meeting has taken place, unless you elected to receive a copy of the research summary. In this case once I have sent you the summary I will destroy your contact information.

### **What are the possible benefits of taking part?**

There is no direct benefit to you of taking part.

We hope that the development of revised guidelines for donating blood for research will benefit everyone in Saudi Arabia.

### **What will happen to the results of the research study?**

The results will form part of my PhD thesis. We also hope to publish the results in academic journals. I may quote some of the things that you said in the focus group. I will not use your name and I will be careful not to identify you in others ways. It is possible, however, that those who know your views well may recognise you if you are quoted.

### **Are there any risks involved?**

This is a low risk study.

As there are a limited number of leading Saudi bioethics thinkers and their opinions are likely to be recognisable to other colleagues. To mitigate this risk, we will not be specific about your background (e.g. lawyer, religious scholar, researcher) when quoting you.

We will also ask all of those attending the group not to discuss with others anything that was said during the meeting.

### **Will my participation be confidential?**

All personal data will be securely stored and will only be available to me and my academic supervisors.

Any identifying information will be removed during transcription and I will ensure this has been done properly when checking the accuracy of the transcriptions. The audio recording will be downloaded at the earliest available opportunity to local computer and the file will be backed-up on a firewall-protected University of Birmingham server. The recordings will then be deleted from the audio recorder device.

Contact details will be destroyed after the meeting. Audio recordings, transcripts and consent forms will be kept for ten years before being destroyed, in line with University of Birmingham research policy. Professor Heather Draper will serve as data custodian.

### **Research organisation, funding and ethics approvals**

This research is a part my doctoral research at the University of Birmingham, where my supervisors are based. It is funded by a scholarship from the National Guard Health affair, Riyadh, Saudi Arabia

The research has been favourably reviewed by the University of Birmingham Science, Technology, Mathematics and Engineering Ethical Review Committee,

ERN\_12-1394, Date of Approval: 06/02/2013, and by and the local ethics Committee of KKESH: RP 1319-P, Date of Approval: 10/03/2013, and of NGHA: RC12/090/R, Date of Approval: 26/03/2013 in Saudi Arabia.

**Contact for further information**

Should you need more information you can contact me:



If you wish to make a complaint, please contact:



**Thank you for taking the time to read this information.**

### **Appendix 13: Invitation Email - Phase Three - The Second Group**

Dear \_\_\_\_\_,

Re Donating Blood for Molecular and Genetics Epidemiology Research in Saudi Arabia

Researcher: Abdallah Adlan, PhD student, University of Birmingham

Supervisors: Professor Heather Draper and Professor Angus Dawson, University of Birmingham

Thank you for expressing on interest in my doctoral research.

As we discussed earlier, I am inviting you to participate in a focus group meeting that will consist of six to nine policy makers in the field of bioethics in Saudi Arabia.

Attached you will find an information sheet with more information about the project, the focus groups and what will be requested of you if you agree to participate..

Yours faithfully

Abdallah A. Adlan



## **Appendix 14: Information sheet Phase Three –The Second Group**

### Donating Blood for Molecular and Genetics Epidemiology Research in Saudi Arabia

Researcher: Abdallah Adlan, PhD student, University of Birmingham

Supervisors: Professor Heather Draper & Professor Angus Dawson, University of Birmingham

### **Participant Information Sheet**

Thank you for being willing to consider taking part in my doctoral research. The following will give you more information about the research and what taking part will involve. If you would like further information, please contact me. I will be in touch with you in a couple of days to see whether you are still interested in taking part, and if you are, begin the process of setting a date for the focus group.

#### **Purpose of the research**

The aim of this research is to help policy makers in Saudi Arabia develop culturally sensitive bioethics guidelines for donating blood for molecular and genetics epidemiology (MGE) research in Saudi Arabia. It will analyse the current Saudi policies for MGE research and all the international policies that were used as reference points for these. I will then compare and contrast existing policies with current practice to assess how they address the emerging ethical issues. The results will be discussed in two focus groups, one with leading thinkers in Saudi bioethics and the other with more junior researchers. I will facilitate these focus groups.

#### **Why have I been selected?**

You have been selected because you are a more junior researcher who has recruited blood donors for MGE research in Saudi Arabia.

#### **Do I have to participate?**

No, it is up to you to decide whether or not you want to take part. If you decide to participate in the focus group and then change your mind, please let me know. Once the focus group has started you can leave at any point without giving a reason. It will not, however, be possible to withdraw from the research anything you have said up to this point as the focus group is interactive and depends upon the input of all concerned, so it would be impossible to withdraw your data without impacting on the participation of others.

#### **What will happen to me if I participate?**

You will take part in a focus group that will discuss the results of my research to date. The discussion will be audio-recorded. There are no follow-up meetings. Your contact details will be destroyed once the meeting has taken place, unless you elected

to receive a copy of the research summary. In this case once I have sent you the summary I will destroy your contact information.

**What are the possible benefits of taking part?**

There is no direct benefit to you of taking.

We hope that the development of revised guidelines for donating blood for research will benefit everyone in Saudi Arabia

**What will happen to the results of the research study?**

The results will form part of my PhD thesis. We also hope to publish the results in academic journals. I may quote some of the things that you said in the focus group. I will not use your name and I will be careful not to identify you in others ways.

**Are there any risks involved?**

This is a low risk study.

**Will my participation be confidential?**

Due to the nature of focus group (participants deliberating face to face in a meeting), it is difficult to promise full confidentiality. We will ask all of those attending the group not to discuss with others anything that was said during the meeting.

Any identifying information will be removed during transcription and I will ensure this has been done properly when checking the accuracy of the transcriptions. The audio recording will be downloaded at the earliest available opportunity to local computer and the file will be backed-up on a firewall-protected University of Birmingham server. The recordings will then be deleted from the audio recorder device.

Contact details will be destroyed after the meeting. Audio recordings, transcripts and consent forms will be kept for ten years before being destroyed, in line with University of Birmingham research policy. Professor Heather Draper will serve as data custodian.

**Research organisation, funding and ethics approvals**

This research is a part my doctoral research at the University of Birmingham, where my supervisors are based. It is funded by a scholarship from the National Guard Health affair, Riyadh, Saudi Arabia

The research has been favourably reviewed by the University of Birmingham Science, Technology, Mathematics and Engineering Ethical Review Committee, ERN\_12-1394, Date of Approval: 06/02/2013, and by and the local ethics Committee of KKESH: RP 1319-P, Date of Approval: 10/03/2013, and of NGHA: RC12/090/R, Date of Approval: 26/03/2013 in Saudi Arabia.

**Contact for further information**

Should you need more information you can contact me:



**Thank you for taking the time to read this information.**



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