

# GENETIC TESTING AND GENETIC RESEARCH

A REPORT BY  
THE BIOETHICS ADVISORY COMMITTEE  
SINGAPORE

November 2005

## **FOREWORD**

Recent scientific advances in human genetics have greatly increased our understanding of genes and their role in maintaining health and causing disease. The application of this knowledge has led to the development of new and better techniques of diagnosing and treating diseases. Presently, a wide range of genetic tests is available clinically and research into developing novel tests for various diseases is taking place worldwide.

Owing to the sensitive and predictive nature of genetic information derived from genetic testing and the impact it can have on the individual and the family, it is important that such testing be conducted responsibly and ethically. As genetic testing is often an integral part of human genetic research, the BAC has considered the issues from both clinical and research perspectives.

The Human Genetics Subcommittee started considering ethical, legal and social issues of genetic testing and genetic research about two years ago. The recommendations in this Report were made after examining policies and guidelines from various international and national ethics and professional bodies, and after considering the views of international and local experts, as well as those of professional, religious and civic groups and members of the public. The BAC is much indebted to the various parties and individuals who participated in the three-month long public consultation process, which began in early April this year, as well as to the international and local experts who have contributed their views and comments.

It is hoped that these recommendations, which have been accepted by the Life Sciences Steering Committee, would not only provide ethical guidance to clinicians and researchers when carrying out genetic testing and genetic research, but also a useful reference for ethics committees reviewing such research.

I would like to thank members of the Human Genetics Subcommittee, chaired by Associate Professor Terry Kaan, for their dedication and commitment in the preparation of this Report.

Professor Lim Pin  
Chairman  
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### **About the Bioethics Advisory Committee**

*The Bioethics Advisory Committee (BAC) was established by the Singapore Cabinet in December 2000. The BAC was directed to “examine the legal, ethical and social issues arising from research on human biology and behaviour and its applications” and to “develop and recommend policies ... on legal, ethical and social issues, with the aim to protect the rights and welfare of individuals, while allowing the Life Sciences to develop and realise their full potential for the benefit of mankind.”*

*The BAC reports to the Life Sciences Steering Committee (formerly Life Sciences Ministerial Committee).*

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## LIST OF ABBREVIATIONS

AHEC	Australian Health Ethics Committee
ALRC	Australian Law Reform Commission
BAC	Bioethics Advisory Committee (Singapore)
CAP	College of American Pathologists
DNA	Deoxyribonucleic acid
ESHG	European Society of Human Genetics
ESHRE	European Society of Human Reproduction and Embryology
HFEA	Human Fertilisation and Embryology Authority (UK)
HGC	Human Genetics Commission (UK)
HGS	Human Genetics Subcommittee (BAC)
HGSA	Human Genetics Society of Australasia
IRB	Institutional Review Board
IVF	<i>In vitro</i> fertilisation
MOH	Ministry of Health (Singapore)
NHMRC	National Health and Medical Research Council (Australia)
NMEC	National Medical Ethics Committee (Singapore)
PGD	Preimplantation genetic diagnosis
PGS	Preimplantation genetic screening
PNGD	Prenatal genetic diagnosis
PTT	Preimplantation tissue typing
RNA	Ribonucleic acid
SAC	Singapore Accreditation Council
SINGLAS	Singapore Laboratory Accreditation Scheme
WHO	World Health Organisation

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# GENETIC TESTING AND GENETIC RESEARCH

## EXECUTIVE SUMMARY

### **Introduction**

1. As part of its remit to examine and recommend on issues arising from research in biomedical sciences in Singapore, the Bioethics Advisory Committee (BAC) has prepared this report on genetic testing and genetic research.
2. Genetic testing is often an integral part of human genetic research. Our intention is to provide a broad treatment of the subject, taking into account the current status of genetic testing and ethical principles observed in major jurisdictions.
3. Issues of confidentiality of test results, counselling and the conduct of research arise in consequence. Accordingly, this report considers:
  - (a) genetic testing for the detection of specific heritable genetic conditions or susceptibilities;
  - (b) the genetic information thereby derived; and
  - (c) human genetic research.
4. Issues relating to third party use of genetic information, such as by insurers or from linked medical registries, are far reaching and important. They will be addressed in more detail in a future report. We have also not considered genetic

- testing for forensic purposes or solely as a means to ascertain parentage or kinship, and research that involves only history taking such as in the construction of family trees where direct genetic testing is not performed.
5. Issues of consent for research have already been mentioned in our IRB Guidelines Report.<sup>1</sup> In the present report, these issues are elaborated as they apply to human genetic research.
  6. Genetic tests are a valuable aid to diagnosis and prevention of genetic disorders, but the conduct of such tests and the use of the information they yield are of concern. Test results may affect aspects of life, such as the job or marriage prospects of the individual tested, may have repercussions for family members who are genetically related, and may also impact family members, such as spouses, who are not genetically related.
  7. In preparing the report, the BAC examined policies and guidelines from various international and national ethics and professional bodies. The views of the National Medical Ethics Committee (NMEC) were sought, and considered. Views and comments from the public and 30 professional, religious and civic groups were also considered, in addition to the views of our international advisors. The BAC is grateful for all these inputs.
  8. Part I introduces the report. Parts II and III are concerned with definitions of genetic testing and genetic information respectively. Part IV, the main part of the report, considers general and specific ethical issues in genetic testing. Part V considers the direct supply of genetic tests to the public. Part VI deals with human genetic research.

### **Genetic Testing**

9. Genetic testing is the analysis of human DNA, RNA, genes and/or chromosomes, or the analysis of human proteins or certain metabolites, with the primary purpose of detecting a heritable genotype, mutation, phenotype or karyotype.
10. Genetic testing can be for research or for clinical purposes. Research genetic testing is done when the primary aim is to generate new information or test a research hypothesis. There are over 800 laboratory-based genetic tests already available for clinical use.
11. Clinical genetic testing subsumes the following:
  - (a) Confirmatory diagnosis for specific genetic disorders;
  - (b) Carrier testing for recessive disorders;

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<sup>1</sup> BAC, *Research Involving Human Subjects: Guidelines for IRBs* (November 2004).

- (c) Preimplantation genetic testing on embryos created by *in vitro* fertilisation (IVF), for the purpose of selecting or excluding embryos for implantation into the uterus;
  - (d) Prenatal genetic diagnosis (PNGD) to identify a specific genetic disorder in a foetus;
  - (e) Predictive testing of asymptomatic individuals; and
  - (f) Genetic screening of healthy individuals.
12. This report highlights concerns that can arise from the predictive and sensitive nature of genetic information deliberately obtained from genetic testing. Genetic information may be uncovered in the course of standard clinical tests for diagnosis or treatment and the conduct of such clinical tests should be in accordance with accepted medical guidelines. In the clinical context, our recommendations relating to consent and counselling for genetic testing do not apply, except when analysis of human DNA, RNA, genes and/or chromosomes is involved.

### **Genetic Information**

13. The nature of genetic information, as determined in the major jurisdictions, is reviewed. The most distinctive feature of genetic information is its predictive power for individuals and for their close relatives. It has to be interpreted with care as it is generally probabilistic in nature. In consequence, clinical genetic testing has been done in Singapore through registered physicians, who bear ultimate responsibility with regard to the use of tests and the interpretation of their results.

### **General Ethical Considerations in Genetic Testing**

14. When conducting genetic testing, it is important to observe the welfare, safety, religious and cultural perspectives and traditions of individuals.
15. The principle of informed consent should apply to genetic testing as with other medical procedures. For consent to be informed, the individual will need to be given appropriate counselling.
16. It is possible to conduct genetic testing on tissue samples obtained through deception or taken without the consent of the individual, and the resulting information could be used in ways that are not in the interests of the person tested. We are of the view that the non-consensual or deceitful taking of human tissues for the purpose of genetic testing should be prohibited.

17. Vulnerable persons require special safeguards. We consider three categories of vulnerable person:
  - (a) children and adolescents;
  - (b) the mentally impaired; and
  - (c) other persons in dependent relationships.
18. In the case of children and adolescents, legal issues regarding consent and the management of their best interests arise. Subject to limitations in law, we are of the view that if a child or adolescent is capable of understanding the purpose and implication of genetic testing, they may be regarded as mature enough to give the necessary consent.
19. We are of the view that carrier testing of children should generally be deferred till the child is sufficiently mature, or until he or she has to make reproductive decisions. We recognise exceptions in certain cases where it may benefit family members, or may reflect public policy in the eradication of diseases. We do not encourage predictive testing on children unless there are preventive measures available in childhood.
20. Additional safeguards are appropriate for persons lacking the mental competence to decide on genetic testing. In clinical testing, the best interest of the person tested is the important consideration, qualified only by the possibility that an imperative need may exist for the confirmatory diagnosis of genetic disease in related family members. The legal guardian in such cases is the appropriate person to give consent.
21. For persons in dependent situations (such as prisoners or students) it is especially important to ensure that consent is given freely, and in particular, that no benefits currently provided or in prospect would be jeopardised by a refusal.
22. Healthcare professionals and researchers have an obligation to protect the confidentiality of genetic information. Genetic test results should therefore not be released without consent to third parties.
23. In the event that nondisclosure of the test result may endanger the life of a third party, however, we concur with the NMEC's position that a physician's duty of confidentiality may be overridden if certain conditions are met.
24. Generally, individuals would want to know the results of genetic tests taken by them or their genetic relatives. However, there may be cases where the individual does not wish to know if he or she is at risk of a genetic disorder or to share this information with family members. Notwithstanding this, the individual's wish should be respected, but with appropriate counselling.

### **Specific Ethical Considerations in Genetic Testing**

25. The report reviews ethical concerns arising from the use of specific types of genetic testing.
26. Preimplantation genetic diagnosis (PGD) is of value in allowing an option for some couples to conceive a child without certain genetic diseases, because candidate embryos obtained by IVF can be tested and only unaffected embryos implanted. However, it is ethically debatable.
27. The ethical issues raised by preimplantation genetic testing include religious concerns about the sanctity of life and assisted reproductive technologies generally. There are also wider concerns about whether such testing could in principle be used to select favourable traits, rather than just the exclusion of genetic diseases. In addition, it is an expensive and therefore restricted technology. This raises equity issues of public concern.
28. As the experience of other jurisdictions suggests that effective regulation is possible, preimplantation genetic testing should be allowed to prevent the transmission of a serious disease in genetically at-risk couples to the next generation. We are further of the view that a provision for conscientious objection should be included in the regulatory framework.
29. We do not think preimplantation genetic testing should be allowed for purposes of eugenic enhancement, even if feasible, nor to accommodate individual parents who might actually prefer an affected embryo (for example, to have a deaf child) for reasons of family compatibility. It seems to us that children should not be born having to meet expectations derived from decisions made by parents about desired genetic makeup.
30. We are of the view that sex selection for non-medical reasons is generally unacceptable, as it may promote or reinforce gender stereotyping and discrimination. It may also promote gender imbalance in the population structure, which in turn may have undesirable social implications.
31. Preimplantation tissue typing (PTT) can be used in combination with PGD to allow couples to have a healthy child who is also immunogenetically compatible, as a potential stem cell donor, to a sick sibling. While this does raise an ethical issue of whether a child should to this extent be created as a means to an end, we give some weight to the argument that parents willing to go to such lengths are unlikely to deny equal affection to a child conceived by way of PTT. We therefore think that with appropriate regulation, such cases may be allowed.
32. Germline genetic modification is a type of gene technology, currently still in experimental stage, which involves the alteration of a person's genetic makeup in a manner that is permanent and can be transmitted to his or her offspring. As

- such, its effects in future are incalculable, and we do not think it should be allowed in clinical practice at this time.
33. Routine prenatal care may include PNGD. Couples can be counselled on the basis of results and helped to make a decision as to whether or not to continue the pregnancy, if appropriate.
  34. For reasons as given in paragraphs 29 and 30, we do not think that PNGD should be employed for trait or gender selection without medical justification.
  35. Predictive genetic testing identifies healthy individuals who have inherited a gene or genes for a late-onset disease, that is, a disease that normally becomes symptomatic only in adulthood.
  36. The predictive information may be almost certain, as in late-onset dominant diseases such as Huntington's disease; more commonly it may reflect an increased risk but not a certainty, as in cases where there are interactions of multiple genes and environmental factors. Alzheimer's disease, diabetes, and certain cancers and heart diseases fall into this latter category.
  37. Predictive genetic information can be burdensome or traumatic, given the uncertainties of the risk, and this reinforces the need for voluntary informed consent and counselling pre- and post-test.
  38. Genetic screening involves tests offered to healthy individuals with an increased risk of developing a particular genetic condition. It aims to prevent a disease or minimise morbidity and mortality through early diagnosis and treatment. In genetic screening programmes, a confirmatory diagnostic test should be performed as soon as possible after a positive screening test, so as to minimise unnecessary anxiety or to enable measures for the prevention or treatment of the condition to be instituted without delay.

### **Quality Control Issues in Clinical Genetic Testing**

39. The welfare of tested individuals depends on the integrity of the diagnostic process and the test methodology. These aspects should be carefully monitored, keeping in mind the increasing tendency for direct approaches to be made by clients to laboratories, or for tests to be available directly to the public, bypassing medical practitioners, as in internet-based services.

### **Genetic Counselling**

40. Genetic counselling is needed to achieve two objectives:
  - (a) to provide sufficient and unbiased information to enable full and informed choices to be exercised; and

- (b) to provide appropriate support to the patient and his or her family members.
- 41. Counselling should be provided in a timely manner by appropriately qualified healthcare professionals. It should be done in a manner appropriate to the needs and comprehension of the patient, in a face-to-face meeting wherever possible. Counselling requires an empathic manner and should generally be non-directive in character, though with regard to possible legitimate third-party interest in the patient's genetic information.
- 42. It may not be practicable for genetic counselling to be restricted to physicians. Others such as medical geneticists or nurses may be involved, even though the clinical responsibility for a case rests ultimately with the physician in charge.

### **Direct Supply of Genetic Tests to the Public**

- 43. The commercialisation of genetic testing kits and services direct to the public increases access to genetic tests without a medical consultation. This situation is causing concern in a number of countries. This concern is mainly focussed on the twin problems of potential misinformation and risk of testing without consent. We share this concern and recommend steps, as far as practicable, to ensure that genetic testing is done by qualified healthcare professionals, and to limit the availability of tests that provide predictive health information directly to the public.

### **Ethical Considerations in Human Genetic Research**

- 44. A general ethical framework for human biomedical research has been set out in our previous reports, and the comments here respect this framework.
- 45. All research participation must be voluntary and informed, and researchers must obtain consent from potential research participants, with suitable allowance in the case of vulnerable or dependent populations. The information given to potential participants must include the nature of any risks, whether or not any genetic information derived from the study will be disclosed to them if requested, and the procedures for protection, anonymisation, or disposal of information or biological materials on withdrawal from or completion of the research.
- 46. Human genetic research is not conducted with the aim of providing research participants with specific information about their genetic status or health. However, if there is a possibility that the research may yield individual data of clinical significance, the research participant should be informed of this possibility and whether he or she would receive such information if so desired, prior to participation in the research.

47. Researchers have an obligation to protect the privacy of research participants and their family members, and to ensure confidentiality of all genetic information derived from the research, including information about the participant's relatives, who may not be part of the research project.
48. Research considerations should not compromise or prejudice the clinical purpose of genetic testing where such testing is also providing information for research.
48. All human genetic research requires the approval of a research ethics committee or an institutional review board and in addition, if the research involves human embryos for reproductive purposes, written approval from the Ministry of Health.

## LIST OF RECOMMENDATIONS

### *Genetic Information*

#### **Recommendation 1:**

Genetic information derived from clinical genetic testing should be regarded as medical information and the usual standards in medical ethics apply in its derivation, management and use.

### *General Ethical Considerations*

#### **Recommendation 2:**

Genetic testing should be conducted in a manner that is respectful of the welfare, safety, religious and cultural perspectives and traditions of individuals.

#### **Recommendation 3:**

Genetic testing should be voluntary. The individual should be given sufficient time and information to ensure informed consent before testing. Consent should also be obtained for the future use of tissue specimens.

#### **Recommendation 4:**

The non-consensual or deceitful taking of human tissues for the purpose of genetic testing should be prohibited.

### *Genetic Testing of Vulnerable Persons*

#### **Recommendation 5:**

We do not recommend the broad use of genetic testing on children and adolescents. Confirmatory testing and predictive testing for genetic conditions where preventive intervention or treatment is available and beneficial in childhood are recommended. Carrier testing should generally be deferred until the child is mature or when required to make reproductive decisions, but where compelling interests of other family members or public health interests exist, the physician should be able to decide, together with the parents, whether or not to determine the carrier status of the child. Predictive testing where there is no preventive intervention or treatment, or where intervention or treatment is only available and beneficial during adulthood, should be discouraged.

#### **Recommendation 6:**

Clinical genetic testing involving vulnerable persons should only be conducted if it is medically beneficial to the vulnerable persons and after informed consent has been obtained. In the case of persons in dependent relationships, extra care should be taken to ensure that such persons clearly understand that refusal to consent will not prejudice any current or prospective benefit.

### *Confidentiality and Privacy*

#### **Recommendation 7:**

Results from clinical genetic testing should only be used to advantage or empower an individual or family and for the management or prevention of disease. Such information should not be disclosed to third parties without the informed consent of the individual unless in exceptional circumstances when the information is required to avert serious harm.

#### **Recommendation 8:**

An individual should be informed of the result of a clinical genetic test without undue delay unless he or she has clearly indicated a wish not to know.

### *Preimplantation Genetic Testing*

#### **Recommendation 9:**

Preimplantation genetic screening and diagnosis are permissible, subject to licensing and monitoring by a relevant authority and should be limited to preventing serious genetic conditions. Provision should also be made so that no one shall be under any duty to be involved in preimplantation genetic testing to which he or she has a conscientious objection.

#### **Recommendation 10:**

The use of preimplantation genetic testing for the selection of desired traits or gender for non-medical reasons should not be allowed.

#### **Recommendation 11:**

Preimplantation tissue typing, whether as the sole objective or in conjunction with preimplantation genetic diagnosis to avoid a serious genetic disorder, is permissible but should be licensed and evaluated on a case-by-case basis.

### *Germline Genetic Modification*

#### **Recommendation 12:**

The clinical practice of germline genetic modification should not be allowed at this time.

### *Prenatal Genetic Diagnosis*

#### **Recommendation 13:**

Prenatal genetic diagnosis should be limited to serious medical disorders. The use of prenatal genetic diagnosis for the selection of desired traits or gender for non-medical reasons should not be allowed.

### *Predictive Testing*

#### **Recommendation 14:**

Presymptomatic testing should be available for adults at risk who request it, even in the absence of treatment, after proper counselling and informed consent.

#### **Recommendation 15:**

Susceptibility testing should not be applied clinically unless there is significant empirical evidence of validity and utility.

### *Genetic Screening*

#### **Recommendation 16:**

In genetic screening programmes, a confirmatory diagnostic test should be performed as soon as possible after a positive screening test, so as to minimise unnecessary anxiety or to enable measures for the prevention or treatment of the condition to be instituted without delay.

### *Standards of Genetic Test Providers*

#### **Recommendation 17:**

All laboratories conducting clinical genetic tests should be accredited by a body designated by the relevant authority, based on standards it considers appropriate.

### *Results Interpretation*

#### **Recommendation 18:**

Interpretation of clinical genetic test results should only be performed by healthcare professionals who are appropriately qualified or have sufficient experience. As far as is practicable, genetic counselling should immediately follow the disclosure of the test result, particularly if the test result is not favourable.

### *Genetic Counselling*

#### **Recommendation 19:**

Genetic counselling should be offered to all individuals before and after they undergo clinical genetic testing.

#### **Recommendation 20:**

Genetic counselling should generally be conducted in a non-directive manner and should provide sufficient information and appropriate support to the individual and his or her family members.

*Professional Diversification and Development*

**Recommendation 21:**

The relevant authority should provide professional training and accreditation in medical genetics and counselling to healthcare professionals.

*Direct Supply of Genetic Tests to the Public*

**Recommendation 22:**

Genetic testing should generally be conducted through a qualified healthcare professional. Tests that provide predictive health information should not be offered directly to the public. The advertising of direct genetic tests to the public should be strongly discouraged. The relevant authority should develop an oversight framework for the supply of genetic tests, services and information direct to the public.

## GENETIC TESTING AND GENETIC RESEARCH

### I. Introduction

- 1.1 Human welfare can be elevated through the responsible development and application of biomedical science. One such application arises from advances in mapping the human genome. Such mapping has contributed to a better understanding of the role of genetics in many common diseases such as cancer, heart diseases and diabetes. This has in turn fuelled the hope that new and more effective means of diagnosis and treatment of diseases may be developed through the increasing application of gene technology in medicine. Currently, this principally entails the development and use of genetic tests. New treatments and gene therapy may become more prominent in future.
- 1.2 Genetic tests can help in the diagnosis, prevention and treatment of serious genetic disorders but they also present ethical, legal and social concerns to individuals and society. These issues are varied and complex, with long-term ramifications. Many countries and international organisations are beginning to attend to these issues, some of which may have imminent ethical, legal or social impact.
- 1.3 The demand for genetic information in the healthcare and health-related sectors of many scientifically advanced countries has been rising steadily and has in turn fuelled the application of genetic testing for a diverse range of diseases. Consequently, more than 800 different genetic tests may now be conducted by clinical and research laboratories.
- 1.4 Genetic information derived from genetic testing may disclose far greater details about an individual's health than medical information derived from a doctor's medical examination and interview alone. It provides information that has broader implications extending to genetically related family members, spouses, and future generations. Occasionally, unexpected or potentially sensitive information may be revealed, for instance, information about parentage or about the likelihood that an apparently healthy individual may develop a serious genetic condition later in life. The result of a genetic test, especially one that is positive for a serious genetic disorder for which there is no treatment, may have significant psychological impact on an individual and possibly on his or her family.<sup>2</sup> Due to the shared nature of genes and the predictive nature of genetic information, family members and third parties such

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<sup>2</sup> For the purposes of this report, the terms "family" or "family members" can refer not only to persons who are genetically related to the individual concerned but also to those whom the individual regards as family members in the broader sense of the family as a social unit. The context will make clear when genetic relatedness is the relevant concern.

as insurers and employers may have an interest in a person's genetic information, and there is a need to ensure that genetic testing is conducted with due consideration and protection of the individual's interests and rights.

## Objectives

- 1.5 This report is prepared with the following objectives:
- (a) to consider the ethical, legal and social issues arising from the conduct of genetic testing and research; and
  - (b) to provide guidance for the ethical conduct of genetic testing and research.

## Scope

- 1.6 In this report, we focus on three main aspects of human genetics:
- (a) genetic testing for the detection of specific heritable genetic conditions and susceptibilities;
  - (b) the quality of genetic information thereby derived; and
  - (c) research in human genetics.
- 1.7 The use of genetic testing and genetic information can have social and economic implications. As genetic information may be misinterpreted or misused, it carries the potential of causing harm if suitable measures of information control are lacking. In this report, we provide broad ethical guidelines for the derivation and use of genetic information derived from genetic tests.
- 1.8 This report does not cover in detail the ethical, legal and social issues relating to third party access of personal genetic information, such as access by insurers or employers and similar issues relating to the use of genetic information from linked medical registries and genetic databases for research purposes. Such issues are manifold and likely to have long-term implications for all levels of society. We intend to address these issues in a future report.
- 1.9 Ethical issues arising from genetic testing in Singapore were considered by the National Medical Ethics Committee (NMEC)<sup>3</sup> in its *Ethical Guidelines for Gene Technology* (NMEC Gene Technology Guidelines) published in February 2001. The Guidelines defined "gene technology" as "the use of techniques for

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<sup>3</sup> The NMEC was established in January 1994 to assist the Ministry of Health (MOH) in addressing ethical issues in medical practice and to ensure a high standard of ethical practice in Singapore.

the analysis and/or manipulation of DNA (deoxyribonucleic acid), RNA (ribonucleic acid) and/or chromosomes”<sup>4</sup> and focussed on gene technology in the context of medical practice and doctor-patient relationship.

- 1.10 In this report, we build on some of the NMEC Gene Technology Guidelines, and provide specific recommendations relating to the ethical conduct of genetic testing, the quality of clinical genetic tests and the interpretation of test results. We have placed particular emphasis on the importance of sound and effective counselling, which we regard as indispensable to the ethical conduct of clinical genetic testing. Genetic testing is often an integral part of human genetic research, for which we also set out the ethical considerations.
- 1.11 The recommendations in this report were made after examination of the policies and guidelines from various international and national ethics and professional bodies, and consideration of views from our international advisors and local experts and public feedback on a Consultation Paper entitled *Ethical, Legal and Social Issues in Genetic Testing and Genetics Research*. Position papers written by these local experts are at Annex C and the Consultation Paper prepared by the Human Genetics Subcommittee, is at Annex D. The Consultation Paper was publicly released on 5 April 2005 and 107 healthcare and governmental institutions, including the NMEC, and professional, religious and patient support organisations, were invited to provide comments. A list of these organisations is provided in Annex E. Thirty-one written responses were received and are set out in Annex F. In addition, the BAC held dialogue sessions with religious representatives and healthcare professionals to gain in-depth understanding of any concerns related to the issues discussed and the recommendations made in the Consultation Paper. To facilitate further discussion and to obtain views from members of the general public, 14 focus group discussions were conducted over the period of 14 May to 9 July 2005. Reports on the dialogue sessions and focus group discussions are provided in Annex G.

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<sup>4</sup> NMEC, *Ethical Guidelines for Gene Technology* (2001), Section 1.1.

## II. Genetic Testing

- 2.1 Genetic testing is the analysis of human DNA, RNA, genes and/or chromosomes, or the analysis of human proteins or certain metabolites, with the primary purpose of detecting a heritable genotype, mutation, phenotype or karyotype.
- 2.2 In the clinical context of patient care, our recommendations for counselling and consent are intended only for genetic tests entailing the analysis of DNA, RNA, genes and/or chromosomes. In this context where genetic tests entail the analysis of human proteins and metabolites, only the requirements of established medical ethics apply. We discuss issues related to counselling and consent in greater detail in Part IV.
- 2.3 Though many human diseases have a genetic basis in the sense that they are caused by mutations (alterations) in genes, most such mutations or alterations are not capable of being passed on to the next generation, and so affect only the patient. Such mutations are known as somatic mutations. In contrast, other mutations can be transmitted to the next and subsequent generations, so that a child may inherit a mutation from a parent. This kind of heritable mutation is known as a germline mutation.<sup>5</sup> We therefore restrict our definition to those tests involving germline mutations that define heritable conditions. Tests for somatic mutations that carry no implication of heritability are excluded.
- 2.4 Clinical genetic testing is the use of validated genetic tests for purposes which may include but are not limited to the following:
- (a) *Confirmatory diagnosis* performed to confirm the diagnosis of a specific genetic disorder in an individual who already has signs or symptoms of that disorder. A positive test result identifies the genetic basis of the disorder;
  - (b) *Carrier testing* for recessive disorders conducted to identify individuals with a genetic or chromosomal abnormality that generally does not

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<sup>5</sup> Many human diseases involve alterations in genes. If these genes only affect somatic cells, they are called somatic mutations and they are not heritable. Somatic DNA/tissue analysis from tumor specimens examines the genetic changes in the tumor that occur during the conversion to cancer. Amplification of HER-2/neu in breast cancers and the BCR-ABL gene translocation, also in breast cancers, are examples of somatic genetic alterations profoundly affecting the behaviour of the tumor, and which are used in standard diagnostics, but which are not inherited. This information does not have implications for heredity and therefore is limited to the patient and his/her condition. By contrast, mutations that affect the sperm and eggs of individuals can be passed on to subsequent generations and are called germline mutations, for example, in Huntington's disease, thalassaemia, or haemophilia. Mutations in BRCA1 associated with susceptibility to breast and ovarian cancers are further examples of germline aberrations. Germline DNA analysis has potential impact not only in predicting the future health of the individual, but also that of his or her relatives.

affect the person's health but puts him or her at higher risk of having a child with a specific genetic disorder;

- (c) *Preimplantation genetic testing* conducted on early embryos created by *in vitro* fertilisation (IVF), to determine the presence or absence of one or more genetic conditions, or a certain immunogenetic make-up, before selecting a suitable embryo for implantation into the uterus;
- (d) *Prenatal genetic diagnosis (PNGD)* conducted on a foetus or a pregnant woman so as to identify a specific genetic disorder;
- (e) *Predictive testing* conducted on asymptomatic individuals to determine if they are at risk of developing a genetic disorder in the future; and
- (f) *Genetic screening* conducted on healthy individuals to determine their status with regards to a specific genetic disorder.

2.5 Genetic testing can also be done for other purposes such as:

- (a) Identity testing or forensic testing, e.g. to exclude or identify a suspect in a crime, to search for missing persons or to identify deceased persons; and
- (b) Parentage or kinship testing, e.g. to determine if two persons are biologically related to each other.

The use of genetic testing for these two purposes will not be covered in this report.

2.6 Research genetic testing is the use of genetic tests with the primary aim of generating new information or to test a research hypothesis. It is a clearly circumscribed activity which should take place within a framework for the regulation of research involving human subjects. This would include scrutiny of the ethical aspects of the proposed research by an institutional review board (IRB) and monitoring of approved projects for compliance with ethical requirements. Information from genetic testing in research is research data, which although subject to strict rules of confidentiality, should not be included as part of the subject's medical record. An earlier BAC report entitled *Research Involving Human Subjects*<sup>6</sup> covers the fundamentals of ethical requirements for all biomedical research; their application to genetic research is discussed in Part VI of this report.

2.7 In the case of clinical genetic testing, the situation is less clear cut. Patients or members of the public may consult a physician for a specific medical complaint. In the course of the consultation, diagnostic investigations which do not entail

<sup>6</sup> BAC, *Research Involving Human Subjects: Guidelines for IRBs* (November 2004).

the analysis of the patients' DNA, RNA, genes or chromosomes, may nonetheless detect disorders which have a genetic basis. The biochemical investigation of anaemia, for example, could lead to a diagnosis of thalassaemia, a genetically inherited disorder. In such situations, we are of the view that the biochemical testing is covered by the standard and usual medical consent procedures for diagnostic tests assuming the patient has sought a consultation. But if, for example, the physician decides to further include a genetic test to determine a particular mutation for thalassaemia, specific consent would be required. Physicians and healthcare institutions are bound by medical confidentiality, and the disclosure of such information to third parties not involved in the patient's healthcare, would generally require the patient's consent.

- 2.8 In routine public health screening procedures, such as for neonates or other defined populations, the relevant public institutions have given consideration to the societal impact of early detection of such genetic disorders. However, the usual confidentiality obligations will apply to the genetic information thereby derived.
- 2.9 We emphasise that there are situations, even within the patient-physician relationship, where specific informed consent for clinical genetic testing would be essential. These situations include:
- (a) the analysis of patients' DNA, RNA, genes or chromosomes to detect a specific heritable disease or condition, particularly if the disease is likely to be serious and without effective medical treatment, e.g. Huntington's disease; or
  - (b) genetic testing to follow up findings uncovered in the course of standard clinical procedures for diagnosis or treatment.
- 2.10 In any event, there are legitimate concerns when managing genetic information from genetic tests, because of its perceived sensitivity. Clinical tests (other than genetic tests, and whether or not directed at somatic genetic mutations) may also reveal sensitive genetic information about the patient, such as information about paternity or about the presence of a heritable genetic condition. Physicians and researchers should be aware of these perceived or actual sensitivities in managing such information.
- 2.11 In sum, the intention of this report is to highlight concerns that can arise from the peculiar predictive nature of heritable personal genetic information obtained from genetic testing. These concerns arise when the acquisition of genetic information is the primary purpose, whether in research or in clinical practice, and should be taken into account in the management of research participants or patients. Genetic information may be uncovered in the course of standard clinical tests for diagnosis or treatment and the conduct of such clinical tests

should be in accordance with accepted medical guidelines. In the clinical context, our recommendations relating to consent and counselling for genetic testing are not intended to apply, except when analysis of human DNA, RNA, genes and/or chromosomes is involved.

### III. Genetic Information

- 3.1 Genetic information broadly refers to any information about the genetic makeup of an individual. It can be derived from genetic testing as defined in paragraph 2.1 in either clinical or research settings or from any other sources, including details of an individual's family history of genetic diseases. This report is concerned with information about heritable conditions obtained by genetic tests, whether it is for clinical purposes or for research.
- 3.2 The practice of genetic testing in Singapore has largely addressed medical concerns. Hence, genetic testing is generally conducted through a physician and in the context of a physician-patient relationship. Genetic test results, or the genetic information that is derived from such clinical genetic testing, are thus filed together with the medical record of the patient. Generally, the law and medical ethics require that medical records be treated as strictly confidential. Information provided or derived during the course of patient management should only be used for the treatment of the patient concerned unless important public interest (such as an immediate or imminent danger to the life of a third party) requires its disclosure regardless of the consent of the patient. As such, genetic information from clinical genetic tests is treated as a part of the patient's medical record and enjoys corresponding confidentiality.
- 3.3 The ethical and legal status of genetic information relative to other medical information is perceived differently by various authorities and ethics bodies. On the one hand, the US Task Force on Genetic Testing<sup>7</sup> and the European Commission's Expert Group on the ethical, legal and social implications of genetic testing have argued that both genetic information and other medical information should be accorded the highest level of ethical and legal safeguards.<sup>8</sup> On the other hand, certain characteristics of genetic information require that it be set apart from medical information in some circumstances. Some of these distinctive features have been articulated by the UK Human Genetics Commission (HGC) and the joint proposal of the Australian Law Reform Commission (ALRC) and the Australian Health Ethics Committee (AHEC) of the Australian National Health and Medical Research Council (NHMRC).
- 3.4 In its report *Inside Information: Balancing interests in the use of personal genetic data* (2002), the HGC identifies four overlapping categories of personal genetic information. These are observable genetic information (such as eye colour), private (or non-observable) genetic information (such as carrier status

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<sup>7</sup> US Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States* (1997). The Task Force was established by the National Institutes of Health-Department of Energy Joint Working Group on the Ethical, Legal and Social Implications of Human Genome Research.

<sup>8</sup> European Commission Expert Group, *Ethical, legal and social aspects of genetic testing: research, development and clinical applications* (May 2004), pages 46-47.

for a genetic condition, for example thalassaemia), sensitive genetic information and non-sensitive genetic information. The HGC observed that it is the predictive feature and significance for individuals and their family members, future reproductive choices and subsequent generations that render genetic information sensitive in the healthcare context. It further sets out the following features of personal genetic information that distinguish it from other forms of information:

- (a) It is almost uniquely identifying and capable of confirming, denying or revealing family relationships;
- (b) It may be obtained from a very small amount of material, possibly without consent of the person;
- (c) It has predictive power, predicting heritable disorders that develop later in life;
- (d) It may be used for purposes other than those for which it was originally collected;
- (e) It may be of interest to others, including relatives who may be affected, insurers and employers;
- (f) It may be important for establishing both susceptibility to rare inherited disease and the likely effectiveness of some treatments; and
- (g) It can be derived from DNA recovered from stored specimens or even archaeological material after many years.

3.5 The ALRC and the AHEC adopted a similar analysis and crystallised these features of genetic information into essentially three unique characteristics in their report *Essentially Yours: The Protection of Human Genetic Information in Australia* (2003):

- (a) It is ubiquitous in its availability from tissues (such as hair or fingernail) usable for genetic testing by sundry parties;
- (b) It is important not only to the individual but also to the individual's family due to the possible hereditary implications; and
- (c) It is predictive of the individual's future health.

While the ALRC and the AHEC stopped short of categorising genetic information as distinct from medical information, they did propose that a commensurate level of legal protection may be required where there is a likelihood of special threat to privacy or discrimination. On this subject, both

the Council of Europe<sup>9</sup> and the Bioethics Committee of Japan's Council for Science and Technology<sup>10</sup> have stated similar positions.

- 3.6 The most distinctive feature of genetic information is perhaps its predictive power. We note that other information such as a smoking habit, which is related to the carcinogenic effect of tobacco and exposure to certain toxic substances, also provides predictive health information. Nevertheless, potential difficulty in the use of genetic information may arise if the limitations on the certainty of prediction are not recognised and accurately conveyed to the recipient. Some conditions, such as Huntington's disease, are virtually certain to occur within the normal average lifetime if the disease gene is present. For many other diseases, however, genetic mutations only confer an increased likelihood of developing the condition. Even when it is virtually certain that a disease will occur, the age of onset and the severity of the condition is unpredictable. Unless the limits of certainty are carefully explained and understood, the burden of uncertainty of the economic and social implications that may be imposed on the carrier or the carrier's family may be unnecessarily heavy.
- 3.7 The current practice of clinical genetic testing in Singapore is through physicians qualified to practise under the Medical Registration Act. Such a "physician-based" system is also found in many leading jurisdictions. Under such a system, it is incumbent on physicians and other healthcare professionals working with or under the supervision of physicians to ensure that the conduct of genetic testing is in line with the ethics of clinical practice. In any case, the physician in charge of the patient has ultimate responsibility with regard to the use of a test and the interpretation of the test result.
- 3.8 Given the current practice of clinical genetic testing in Singapore, and the current use of genetic information derived from it, we are of the view that genetic information should not be treated differently from medical information. In saying this, we refer to genetic information as accessed and managed by or under a physician for a healthcare or health-related purpose.

**Recommendation 1: Genetic information derived from clinical genetic testing should be regarded as medical information and the usual standards in medical ethics apply in its derivation, management and use.**

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<sup>9</sup> Council of Europe, *Recommendation No. R(92)3 on Genetic Testing and Screening for Health Care Purposes* (1992), Part III.

<sup>10</sup> Bioethics Committee, Council for Science and Technology (Japan), *Fundamental Principles of Research on the Human Genome* (2000), Principle 11.

## IV. Ethical Considerations in Genetic Testing

### Section A: General Ethical Considerations

- 4.1 As with many other types of technology, genetic testing not only presents healthcare benefits, but also possible harms if misused. In the conduct of genetic testing, the following ethical principles articulated in our earlier reports should continue to apply:
- (a) respect for the welfare, safety, religious and cultural perspectives and traditions of individuals;
  - (b) informed consent;
  - (c) respect for vulnerable persons; and
  - (d) privacy and confidentiality.

#### *Respect for Welfare, Safety, Religious and Cultural Perspectives and Traditions*

- 4.2 In a multi-cultural and multi-religious society, researchers and healthcare professionals must be sensitive to the religious and cultural perspectives and traditions of individuals. For instance, certain cultures may be particularly sensitive to the presence of a hereditary disorder in a member of the family. Any communication of this nature, in the context of genetic counselling or disclosure of genetic test results, should be carefully managed. Similarly, in selecting a group to be screened, it is important to avoid stigmatisation of the entire group.
- 4.3 In both clinical and research settings, the health, welfare and safety of individuals undergoing genetic testing should be of paramount consideration. When genetic testing is conducted primarily for a clinical purpose, research considerations should not compromise or prejudice this purpose.

**Recommendation 2: Genetic testing should be conducted in a manner that is respectful of the welfare, safety, religious and cultural perspectives and traditions of individuals.**

#### *Informed Consent*

- 4.4 A requirement of informed consent for genetic testing arises from the broader societal value of respect for persons. It is generally accepted that the individual is free to decide whether to undergo any genetic testing, regardless of whether done in the context of screening, diagnosis or research. When the tissue samples provided for clinical use are intended also for research, informed consent for the

research is required in addition to the consent for taking the tissue for clinical use. Consent is also required if there is an intention to store the tissue for future use.

- 4.5 Consent is effective only if the person giving the consent is aware of the circumstances, conditions and consequences for which it was given. How an individual may be appropriately informed prior to giving consent to testing depends on the person, the situation in which consent is sought and the level of communication between the parties. In addition, the individual should be given sufficient time to understand the information provided and to decide whether or not to undergo genetic testing.
- 4.6 The individual should be given appropriate genetic counselling and informed about the nature of the test and risks of the procedure (if any) before giving consent. Pre-test counselling is thus intrinsic to the process of consent-taking. We discuss genetic counselling for clinical testing in Section D.

**Recommendation 3: Genetic testing should be voluntary. The individual should be given sufficient time and information to ensure informed consent before testing. Consent should also be obtained for the future use of tissue specimens.**

- 4.7 Obtaining consent and maintaining confidentiality are fundamental tenets of trust in the physician-patient relationship. They are also fundamental to the conduct of research. Third parties, however, may have a vested interest in knowing the genetic status of an individual, owing to the predictive power and hereditary nature of genetic information. It is easy to think of ways in which tissues can be taken from individuals without their knowledge, let alone their consent. The use of genetic information derived from tissues obtained without proper consent may result in harm not only to the individual, but possibly to his or her family members. We are strongly against the taking of an individual's tissues without consent or by deceit. We note the HGC's recommendation that "consideration be given to the creation of a criminal offence of the non-consensual or deceitful obtaining and/or analysis of personal genetic information for non-medical purposes."<sup>11</sup> This recommendation has since been accepted by the UK legislature and was enacted as law in November 2004.<sup>12</sup> We regard it as timely for Singapore to consider similar action.

**Recommendation 4: The non-consensual or deceitful taking of human tissues for the purpose of genetic testing should be prohibited.**

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<sup>11</sup> UK HGC, *Inside Information: Balancing interests in the use of personal genetic data* (2002), paragraph 3.60.

<sup>12</sup> *Human Tissue Act 2004*, Section 45.

***Respect for Vulnerable Persons***

4.8 There are certain categories of persons who are particularly vulnerable to circumstances that can compromise their volition and safety when undergoing genetic testing. Special procedures ought to be in place to safeguard their welfare. We consider three categories of vulnerable person in particular: children and adolescents, the mentally impaired and other persons in dependent relationships.

*Children and Adolescents*

4.9 Genetic testing of children and adolescents raises a number of difficult ethical and legal issues. Children and adolescents are dependent on their parents and guardians for survival and are limited in their ability to protect their own interests. As a result, it is generally recognised that persons responsible for the care of children or adolescents should only act in the best interest of the latter.

4.10 We appreciate that “best interest” is dependent on the specific circumstances and conditions of a child or adolescent. Physicians should always consider, together with the parents or legal guardians, the best interests of the child or adolescent and any possible harm before recommending genetic testing. In this regard, we note the recommendation of the European Society of Human Genetics (ESHG), that diagnostic genetic testing be permitted where it is necessary for the child’s or the adolescent’s own health, or where the information would be imperative to diagnose the existence of genetic disease in family members.<sup>13</sup> Similar recommendations have been made by the Council of Europe<sup>14</sup> and the UK HGC.<sup>15</sup>

4.11 Genetic testing is recommended in cases where preventive intervention or treatment is available and beneficial in childhood or adolescence. However, the informed consent of the parent or legal guardian of the child or adolescent should be obtained. In addition, the child or adolescent should be involved in the consent process as comprehensively as possible.

4.12 The ability of a child or an adolescent to comprehend the purpose and implications of genetic testing will differ from one child or adolescent to another. Therefore, the extent of involvement of a child or adolescent should be considered on a case-by-case basis, through the process of genetic counselling. An older child or adolescent who is sufficiently mature, should be involved in the consent process and his or her wish to undergo or to refuse a test should be respected. In Singapore, the law concerning the age at which a child is to be

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<sup>13</sup> ESHG, Provision of Genetic Services in Europe: Current Practices and Issues, *European Journal of Human Genetics*, Volume 11, Supplement 2, S2-S4, Recommendation 14 (2003).

<sup>14</sup> Council of Europe, *Recommendation No. R(92)3 on Genetic Testing and Screening for Health Care Purposes* (1992).

<sup>15</sup> HGC, *Inside Information: Balancing interests in the use of personal genetic data* (2002).

regarded as having the capacity to make medical decisions for himself or herself follows the English common law principles. However, as these principles have not been tested or expressly adopted by the Singapore courts, we think that clarifying legislation may be helpful in this context.<sup>16</sup> From an ethical perspective, we recommend that the capacity of a child or an adolescent to participate in the consent process be assessed according to his or her level of maturity rather than some arbitrary age.

- 4.13 We recognise that as a matter of principle, carrier testing in asymptomatic children should generally be deferred until the child is mature or required to make reproductive decisions. This is because to do otherwise is to risk pre-empting a later decision by the child, when adult, not to know his or her own genetic status or have it made known to others (paragraph 4.21 refers). However, the defence of this right must be weighed against the interests of other family members, the proper medical care of whom may depend on full and accurate information about a genetic condition in the family, as well as the wider public health interests of a given community. In Singapore, genetic screening programmes for at-risk groups aimed at lowering the incidence of lethal or disabling genetic conditions common in the local population, such as thalassaemia, are widely supported by both the medical profession and the public. Considerable success has been achieved over the years in reducing the incidence of affected children, born to parents who would not have been aware that they carried the risk, had they not been tested when children themselves. Where compelling interests of other family members or public health interests exist, we are of the view that the physician should be able to decide, together with the parents, whether or not to determine the carrier status of the child. In cases where the child shows symptoms, confirmatory testing is in any case appropriate.
- 4.14 Great caution has to be observed in predictive testing of children where there is no available preventive intervention or treatment, or where the intervention or treatment is only available during adulthood. It is generally discouraged because of potential harms that can arise. The potential harms include family and community stigmatisation, discrimination and adverse psychological reactions. Such predictive testing of children is best deferred until adulthood when they can make their own decisions.

**Recommendation 5: We do not recommend the broad use of genetic testing on children and adolescents. Confirmatory testing and predictive testing for genetic conditions where preventive intervention or treatment is available and beneficial in childhood are recommended. Carrier testing should generally be deferred until the child is mature or when required to make reproductive decisions, but where compelling interests of other family members or public health interests exist, the**

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<sup>16</sup> See Singapore Academy of Law, *Civil Inquiries into Mental Incapacity: The Report of the Sub-Committee of the Law Reform Committee of the Singapore Academy of Law for the Review of Proceedings under the Mental Disorders and Treatment Act (Cap 178) (1999)*.

**physician should be able to decide, together with the parents, whether or not to determine the carrier status of the child. Predictive testing where there is no preventive intervention or treatment, or where intervention or treatment is only available and beneficial during adulthood, should be discouraged.**

*The Mentally Impaired*

- 4.15 Additional safeguards should also be considered to protect the best interests of persons lacking the competence to agree to genetic testing. The ESHG identifies such persons as those suffering from mental disorders and adults placed under limited guardianship. Clinical genetic testing should only be permitted where it is necessary for their own health or where the information would be imperative to diagnose the existence of genetic disease in family members.<sup>17</sup>
- 4.16 In Singapore, the High Court has the power to appoint a legal guardian who may provide consent on behalf of a person lacking mental competence where it is appropriate to do so.<sup>18</sup> We also note the recommendation in the NMEC Gene Technology Guidelines that, in the case of an individual 21 years or older but mentally incapable of making a decision, a parent or guardian may consent on his or her behalf. In the main, we are of the view that genetic testing should not be conducted on a person who is mentally impaired unless consent has been obtained from a person who is legally authorised to decide on behalf of the mentally impaired.<sup>19</sup>

*Persons in Dependent Relationships*

- 4.17 Persons in dependent relationships require special consideration in the consent process. For example, prisoners who have been incarcerated may be under duress or some form of undue influence to give consent to those with authority over them, or they may hold some perception, which may or may not be real, that they have 'no choice' but to consent. Similarly, students or employees may be under duress or feel that they are under duress to agree to genetic testing. This category of dependent persons further includes poorly educated individuals, who are unable to fully understand what they are consenting to (due to language barriers for instance).
- 4.18 In cases of dependent relationships, it is important to ensure that consent is both informed and genuine. The Nuffield Council on Bioethics stated that special care is necessary when seeking consent from prisoners, student volunteers and individuals who do not speak English.<sup>20</sup> Similarly, the Human Genetics Society

<sup>17</sup> ESHG, Provision of Genetic Services in Europe: Current Practices and Issues, *European Journal of Human Genetics*, Volume 11, Supplement 2, S2-S4, Recommendation 14 (2003).

<sup>18</sup> *Supreme Court of Judicature Act (Cap 322)*, Section 17(e).

<sup>19</sup> Singapore Academy of Law, *Civil Inquiries into Mental Incapacity: The Report of the Sub-Committee of the Law Reform Committee of the Singapore Academy of Law for the Review of Proceedings under the Mental Disorders and Treatment Act (Cap 178)* (1999).

<sup>20</sup> Nuffield Council on Bioethics, *Genetic Screening: Ethical Issues* (1993), paragraph 4.27.

of Australasia (HGSA) stated that it would be unacceptable for those in positions of power to engage in actions that either coerce individuals into taking genetic tests or inhibit individuals from taking them for fear of social or economic disadvantage.<sup>21</sup> We agree with these statements. Where there are reasons to believe that a person agrees to genetic testing for fear of losing healthcare benefits, this misconception should be corrected. One way to do this is to expressly indicate when obtaining consent that however a person decides, no healthcare, employment, welfare, or other benefits that are currently provided or in prospect, will be jeopardised.

**Recommendation 6: Clinical genetic testing involving vulnerable persons should only be conducted if it is medically beneficial to the vulnerable persons and after informed consent has been obtained. In the case of persons in dependent relationships, extra care should be taken to ensure that such persons clearly understand that refusal to consent will not prejudice any current or prospective benefit.**

#### *Confidentiality and Privacy*

- 4.19 Healthcare professionals and researchers alike have an obligation to protect the confidentiality of genetic information. Article 7 of the 1997 *Universal Declaration on the Human Genome and Human Rights* of the United Nations Educational, Scientific and Cultural Organisation, states that: “Genetic data associated with an identifiable person and stored or processed for the purposes of research or any other purpose must be held confidential in the conditions set by law.” The WHO has similarly commented on the need for confidentiality and on the importance of ensuring that genetic data is only used to advantage and empower an individual or family, and for better treatment or prevention of disease.<sup>22</sup> We agree with these opinions. We further agree with the position of the HGC that: “Private genetic information should generally not be obtained, held or communicated without the free and informed consent of the individual.”<sup>23</sup>
- 4.20 We are of the view that genetic test results should not be disclosed to third parties without the informed consent of the individual. Individuals should be told how their privacy will be protected, before they consent to genetic testing.
- 4.21 Certain individuals may be unwilling to share or divulge their genetic test results with family members, other healthcare professionals or researchers. A difficult situation may arise when an individual refuses to disclose a test result which may be medically beneficial to a genetic relative, such as a high risk of

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<sup>21</sup> HGSA Policies, *Predictive Genetic Testing and Insurance* (1999).

<sup>22</sup> WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Executive Summary.

<sup>23</sup> HGC, *Inside Information: Balancing interests in the use of personal genetic data* (2002), page 42.

developing colon cancer. The genetic relative could adopt preventive health measures if he or she knew the test result. However, disregarding the wish of the patient would contravene confidentiality and breach the requirement of informed consent to disclose the test result to a third party. Generally, an individual's request for the confidentiality of his or her test result to be maintained should be respected, and the test result should not be disclosed without the individual's consent. It is nevertheless important that healthcare professionals point out clearly the important positive and negative consequences of not disclosing the test result, although the final decision must rest with the tested individual in most cases.

4.22 There may be exceptional circumstances when genetic information may be disclosed despite the individual's right to confidentiality. A situation may arise where harm to a third person could be averted if the relevant genetic information is disclosed. There is therefore a need to balance the risks of breaching confidentiality against the risks of non-disclosure. In this connection, we note and agree with NMEC's position<sup>24</sup> whereby a physician's ethical duty of confidentiality to a patient can be overridden if the following conditions are satisfied concurrently:

- “(a) Separate efforts by two physicians to elicit voluntary consent to disclosure have failed, despite the patient or client fully understanding the implications of such refusal;
- (b) there is a high probability both that harm will occur to identifiable individuals or society at large if the information is withheld and that the disclosed information can actually be used to avert harm;
- (c) the harm that identifiable individuals (if any) would suffer would be serious; and
- (d) appropriate precautions are taken to ensure that only the genetic information needed for diagnosis and/or treatment of the disease in question is disclosed.”

4.23 In the event that the above conditions are met, the patient concerned should be made aware that such a disclosure would take place and that only relevant information would be disclosed to individuals or entities that need to know in order to avert serious harm. A judgement of seriousness evidently has to be made by the physician in the light of the circumstances of the case.

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<sup>24</sup> NMEC, *Ethical Guidelines for Gene Technology*, Section 2.4.1. A similar position was recommended by the US President's Commission for the Study of Ethical Problems in Medicine and Medical and Behavioral Research (1983) and supported by the WHO (1998), the American Society of Human Genetics (1998) and the Institute of Medicine (1994).

**Recommendation 7: Results from clinical genetic testing should only be used to advantage or empower an individual or family and for the management or prevention of disease. Such information should not be disclosed to third parties without the informed consent of the individual unless in exceptional circumstances when the information is required to avert serious harm.**

*The Right Not To Know*

- 4.24 Generally, individuals would be interested to know the results of genetic tests that they have taken or the results of tests taken by their genetic relatives. Unless an individual has clearly indicated a wish not to know his or her genetic status after a test has been performed, and to address the individual's anxiety, the test result should be disclosed to the individual without undue delay.
- 4.25 However, there may be situations where an individual does not wish to know the test results of his or her genetic relatives or even his or her own genetic status and hence, decides not to take any genetic test. There may also be situations where an individual changes his or her mind about knowing the test result after the test has been conducted. In such situations, the individual's wish not to know should be respected.
- 4.26 An individual tested positive for a predisposition to developing a specific genetic condition has to decide whether this risk should be disclosed to other family members who may also be at risk of developing the same condition. The individual may be additionally burdened with considerations for the family members who may or may not be affected by the condition and their wish to know or not to know. Family members who are not affected by the genetic condition may nevertheless be affected psychologically (such as the condition of "survivor guilt"). In view of these considerations, we emphasise the importance of pre- and post-test genetic counselling.

**Recommendation 8: An individual should be informed of the result of a clinical genetic test without undue delay unless he or she has clearly indicated a wish not to know.**

**Section B: Specific Ethical Considerations**

- 4.27 Clinical genetic testing is usually carried out as part of the health management or treatment of an individual. Hence, the ethical management of such clinical genetic testing should not differ significantly from that of conventional medical service. We note and agree with the NMEC that the "introduction of a genetic test into routine clinical use must be based on evidence that the gene(s) being examined is associated with the disease in question, that the test itself has analytical and clinical validity, and that the test results will be useful to the

people being tested.”<sup>25</sup> In this section, we discuss ethical issues related to specific types of validated genetic tests.

### ***Carrier Testing***

- 4.28 Carrier testing identifies an individual who carries a genetic abnormality that generally does not affect the person’s health but puts him or her at a higher risk of having a child with a specific serious genetic disorder. Individuals who are identified as a carrier of a disorder such as thalassaemia or muscular dystrophy, can then be counselled about these risks and the options available to them when making reproductive decisions.
- 4.29 We emphasise the importance of genetic counselling both prior to and after the test. Proper counselling can prevent confusion over the difference between being an asymptomatic carrier for a genetic disorder and being affected with the disorder. Furthermore, the risk of stigmatisation, discrimination and adverse psychological reactions may also be minimised. Genetic counselling is considered in Section D below and issues concerning carrier testing in children have been discussed in paragraph 4.13.

### ***Preimplantation Genetic Testing***

- 4.30 Preimplantation genetic testing is the testing of early embryos created by IVF before they are implanted into the uterus. Preimplantation genetic diagnosis (PGD) is a procedure whereby early embryos created by IVF are evaluated to determine the presence or absence of one or more genetic conditions, of which the embryos are at risk due to a known family history. Unaffected embryos are then selected and implanted into the uterus. PGD was developed following the availability of IVF and new genetic testing techniques, primarily to help couples at risk of having a child with a genetic disorder have healthy children. Before this procedure was developed, PNGD and selective termination of an affected pregnancy were used to enable couples at risk to have healthy children. With PGD, these couples now have the option of starting out with unaffected pregnancies, thus avoiding the need to consider selective termination of an affected pregnancy subsequently.
- 4.31 Preimplantation genetic screening (PGS) differs from PGD in that the genetic tests are performed on embryos from patients who are considered to have a higher than average risk of conceiving abnormal embryos. These patients may have unexplained recurrent miscarriages or are in advanced maternal age. Unlike PGD, the tested embryos do not have a known family history of a specific genetic condition.
- 4.32 Preimplantation tissue typing (PTT) is a procedure whereby early embryos created by IVF are tested to determine if they have the same immunogenetic

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<sup>25</sup> NMEC, *Ethical Guidelines for Gene Technology*, Section 3.1.1.

status as an existing sick sibling. It can be performed with the sole objective of providing cord blood or bone marrow to a sick sibling with a compatible immunogenetic status, or in conjunction with PGD to avoid the risk of a serious genetic condition in a child.

*Preimplantation Genetic Screening and Diagnosis*

- 4.33 Since 1992, when PGD was successfully applied to avoid a specific genetic defect leading to cystic fibrosis, many clinics throughout the world have begun offering preimplantation genetic testing services. At present such testing can be used to screen for more than 100 genetic conditions, such as Down's syndrome, sickle-cell anaemia, thalassaemia and Huntington's disease. It has been estimated that about 2,000 embryo-screened babies have been born throughout the world.
- 4.34 Although preimplantation genetic testing is currently not available in Singapore as a clinical service, it is available in more than 100 clinics in many other countries including the US, the UK, Belgium, Australia, India, Israel, Japan and South Korea. In Cyprus and Greece, PNGD and PGD have been applied for the prevention of haemoglobin disorders and the number of children born with  $\beta$ -thalassaemia major has since been drastically reduced.
- 4.35 Preimplantation genetic testing can be used by fertile couples as well as those with fertility problems. It has been most commonly recommended for patients:
- (a) who have a child confirmed to have a genetic disease and with an increased risk of having another child with the same disease;
  - (b) of confirmed carrier status (in one or both partners) for a serious genetic condition; or
  - (c) of advanced maternal age.
- 4.36 Preimplantation genetic testing is a technically demanding procedure. While it presents an option for some couples to conceive a child without a specific genetic disease, its effectiveness is limited and success rates, in terms of "take home" babies, are not high. Current PGD pregnancy rates are estimated at about 20%, which is similar to the rates for IVF alone. Although there are some concerns relating to the safety and long-term health consequences of PGD, there have been no reports of increased foetal malformations or other identifiable problems arising from pregnancies involving PGD-tested embryos. A recent study of the past 12 years of data from the world's three largest PGD centres, comprising 4,748 PGD attempts and 754 successful pregnancies, led to the conclusion that PGD is safe.<sup>26</sup>

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<sup>26</sup> Verlinsky Y *et al*, Over a Decade of Experience with Preimplantation Genetic Diagnosis: A Multicenter Report, *Fertility and Sterility*, Volume 82, Issue 2, pages 292-294 (August 2004).

- 4.37 The possible compromise of the sanctity of life represented in an embryo touches one of the central moral and religious concerns of these assisted reproductive technologies. Other ethical concerns relate to the possible use of PGD for trait selection and the implied danger of leading society closer to positive eugenics. It is feared that PGD may be used to select certain desired traits (for example, intelligence, colour of hair, sports ability or musical talent) for the “enhancement” of children, which thereby devalue and alter the way in which society views those who do not possess the desirable traits. Ethical concerns regarding the use of PGD for trait selection is aggravated by the prospect that, even if such use becomes widely and ethically acceptable, only the rich can afford to have offspring with the desirable traits in view of the high cost of PGD. As a result, society could be further stratified into the economically rich and genetically desirable in the top layer, and the economically poor and genetically unaltered at the bottom.
- 4.38 We acknowledge these concerns and attempt to address them by drawing on the two broad guiding principles of ‘justness’ and ‘sustainability’, which were adopted in our Human Stem Cell Report.<sup>27</sup> In the first principle of ‘justness’ is the obligation to respect the common good and the fair sharing of social costs and benefits. The second principle of ‘sustainability’ reflects an obligation to respect the needs of generations yet unborn. Together, these two principles are compatible with the concepts of beneficence and non-maleficence. They encourage the pursuit of social benefits alongside efforts to avoid or ameliorate potential harm.
- 4.39 The UK is one of a few countries that have resolved the ethical debate in relation to human embryo research. The establishment of the Human Fertilisation and Embryology Authority (HFEA) under the Human Fertilisation and Embryology Act of 1990 (the 1990 Act) is a result of several years of discussion and deliberation on this subject. The HFEA licenses and monitors IVF clinics and the creation and handling of human embryos for research. At the time the 1990 Act was passed, PGD was only an experimental procedure. By the turn of this century, PGD has become an acceptable method employed to avoid the births of children with genetic disorders.
- 4.40 From the experiences of countries where preimplantation genetic testing is practised, there are indications that this technology is helpful in addressing the reproductive needs of couples who have a known family history of a genetic disorder, are carriers of a genetic disorder, or have unexplained infertility. For instance, doctors in the US have recently succeeded in using PGD to enable a woman to bear a child free of the gene mutation linked to an early-onset Alzheimer’s disease that she carries. The presence of this gene mutation in an individual confers an almost 100% probability of manifesting symptoms of the disease by the age of 40 years. The experiences of countries that allow the

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<sup>27</sup> BAC, *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning* (June 2002), Chapter 7, paragraph 3.

practice of preimplantation genetic testing also suggest that it is possible to guard against serious violations of moral and ethical standards through careful and effective regulation.

- 4.41 As preimplantation genetic testing is a special form of genetic testing connected with IVF, it should be viewed as a technology to help “at-risk” couples to have healthy children. We are of the view that PGS and PGD should be allowed, provided that they are subject to control by a relevant authority and limited to preventing serious genetic conditions. Generally, a disease is considered to be serious if it is life-threatening, incurable and/or severely debilitating. However, a judgement of the “seriousness” of a condition is subjective. It will vary with the individual and family circumstances, the nature of the condition and the degree of associated disability. Thus, the decision regarding the seriousness of a condition is best left to the parents and the medical team, with the parents being provided with sufficient information to help them decide.
- 4.42 In the multi-cultural and multi-religious society of Singapore, views on the ethics of preimplantation genetic testing are diverse. A segment of the medical community and the public may not wish to be involved in such activities because of religious or personal moral beliefs. Such conscientious objection should be respected and protected so that no one should be under a duty to be involved in preimplantation genetic testing. However, it should be equally open to other members of the medical community and the wider public to participate in or have recourse to preimplantation genetic testing in ways that are not harmful to the moral and social fabric of Singapore as a whole.
- 4.43 The relevant authority should license, monitor and assess preimplantation genetic testing to ensure that all activities are conducted by appropriately qualified personnel in accredited laboratories, and that individuals requesting such services receive sufficient counselling. As such, the authority should issue clear guidelines for the conduct of these activities, including acceptable uses for preimplantation genetic testing and the procedure for the disposal of unselected embryos. Acceptable uses for preimplantation genetic testing should be consistent with the current practice of prenatal genetic diagnosis. Provision should also be made so that no one shall be under any duty to be involved in preimplantation genetic testing to which he or she has a conscientious objection.

**Recommendation 9: Preimplantation genetic screening and diagnosis are permissible, subject to licensing and monitoring by a relevant authority and should be limited to preventing serious genetic conditions. Provision should also be made so that no one shall be under any duty to be involved in preimplantation genetic testing to which he or she has a conscientious objection.**

- 4.44 We do not consider it acceptable to use preimplantation genetic testing for the selection of certain desired traits on non-medical grounds. A child who is selected for a particular trait such as greater mental or physical potential may

experience increased pressure to fulfil the expectation of this genetic potential. The situation is worsened if the child fails to reveal the superior mental and/or physical qualities for which he or she was genetically selected. In both situations, the proper relationship between parent and child is undermined, that is, the ideal that parental love should not be dependent on a child having characteristics that the parents hoped for, but rather as individuals in their own right. Allowing parents to exercise their preference in making such a selection may introduce an element of control over the result of conception, thus making the “experience of parenthood very different from the present situation in which... parents are happy just to take their child as they find them.”<sup>28</sup> We note that some have argued that such concerns are unjustified. In their opinion, expanding control over human reproduction may be thought of as merely an extension of parental responsibility to care for offspring. The reasons behind a couple’s choice to have children are often personal and should not be open to public scrutiny. We do not agree with this view. Personal interest must always be balanced against public interest in any kind of society. In this case, there is public interest in maintaining a stable and harmonious relationship between parents and their children, and this interest far outweighs the right of parents to select certain traits in their children for non-medical reasons.

- 4.45 There may also be situations where a couple may wish to implant an affected embryo for what could be called “lifestyle” reasons. For example, a deaf couple with inherited deafness may wish to have a deaf child because they do not consider deafness as a disability and wish for a compatible family. We agree with the Ethics Task Force of the European Society of Human Reproduction and Embryology (ESHRE) that the implantation of affected embryos “can only be defended if the welfare of the child is strictly considered within the familial boundaries or subculture. However, the functioning of this child within society at large would be severely impaired due to the imposed disability. Therefore, such deliberate restriction of the autonomy of the child is not considered justifiable.”<sup>29</sup> Hence, we consider such a practice unacceptable and recommend it be prohibited.
- 4.46 It is technically possible to use preimplantation genetic testing for sex selection. Couples may desire this for medical reasons, since certain genetic disorders are sex-linked and only affect persons of a particular gender, for example, Duchenne muscular dystrophy is X-linked and affects only males. Sex selection may also be desired for non-medical reasons, such as balancing the gender ratio in the family, personal preference, or due to certain social, cultural, religious or economic motivations. We are of the view that sex selection for non-medical reasons is unacceptable, as it may promote or reinforce gender stereotyping and

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<sup>28</sup> Nuffield Council on Bioethics, *Genetics and Human Behaviour: The Ethical Context* (2002), page 154.

<sup>29</sup> Shenfield F *et al* (ESHRE Ethics Task Force), Taskforce 5: preimplantation genetic diagnosis, *Human Reproduction*, Volume 18, Issue 3, pages 649-651 (March 2003).

discrimination. It may also promote gender imbalance in the population structure, which in turn may have undesirable social implications.

**Recommendation 10: The use of preimplantation genetic testing for the selection of desired traits or gender for non-medical reasons should not be allowed.**

*Preimplantation Tissue Typing*

4.47 In recent years, PGD has been used in combination with tissue typing, which not only allows couples to have a healthy child, but also enables the selection of an immunogenetically compatible stem cell donor for a sick sibling. We find the experience of the HFEA with PTT to be instructive. In 2001, the HFEA adopted a cautious approach and permitted PTT on a case-by-case basis under the following conditions:<sup>30</sup>

- (a) the affected child's condition is severe or life-threatening and of sufficient seriousness to justify the use of PGD;
- (b) the embryos created for PTT are themselves at risk from the condition affecting the existing child;
- (c) all other possibilities of treatment and sources of tissue for the affected child have been explored;
- (d) parents are not the intended tissue recipient;
- (e) the intention is to obtain only cord blood for the purposes of treatment and not other tissues or organs;
- (f) couples receive appropriate counselling;
- (g) families encouraged to participate in follow-up studies and PGD clinics are to provide detailed information regarding treatment cycles and outcomes; and
- (h) the created embryos are not genetically modified to provide a tissue match.

4.48 However, in July 2004, the HFEA extended the rules to allow embryos not at risk of a genetic disorder to be tested for their compatibility as stem cell donors for a seriously ill sibling. The HFEA requires that such cases demonstrate "a genuine need for potentially life-saving tissue and a likelihood of therapeutic benefit for an affected child."<sup>31</sup> This extension was made after careful consideration of the medical, psychological and emotional implications for

<sup>30</sup> HFEA Report: *Preimplantation Tissue Typing* (July 2004), page 2.

<sup>31</sup> HFEA Report: *Preimplantation Tissue Typing* (July 2004), page 10.

children and their families, and the safety of the technique performed in the past three years.

- 4.49 Ethical concerns have been expressed over this use of PTT in that children may be used as a means to an end. However, it has been argued that parents who conceive a child to save a life may be on higher moral ground than those who procreate as an incidental consequence of sex or for some selfish purpose. Others have also argued that parents who would go to such length to save the life of their child would also afford equal affection for the child conceived through PTT.
- 4.50 We have earlier expressed our view that preimplantation genetic testing should be allowed in Singapore provided that proper and effective safeguards are in place. In light of the UK's experience with PTT, we consider PTT to be also acceptable provided that it is subject to regulation by a relevant authority and evaluated on a case-by-case basis. We want to emphasise that PTT should be a measure of last resort. The relevant authority should provide clear guidelines on the eligibility of families for PTT. In this connection, we are of the view that such families must have the capabilities to ensure that the welfare of both the child conceived by way of PTT and the sick child are not compromised. In addition, we agree with the HFEA that follow-up studies on the psychological, social and other longer-term implications in these families should be encouraged.

**Recommendation 11: Preimplantation tissue typing, whether as the sole objective or in conjunction with preimplantation genetic diagnosis to avoid a serious genetic disorder, is permissible but should be licensed and evaluated on a case-by-case basis.**

#### *Germline Genetic Modification*

- 4.51 Germline genetic modification is a type of gene technology that involves the alteration of a person's genetic makeup in a manner that is permanent and can be transmitted to his or her offspring. It is one of the rising gene technologies applicable at the preimplantation stage of an embryo. We note that germline genetic modification may also be brought about inadvertently in gene therapy or through other experimental techniques.
- 4.52 We are of the view that the clinical practice of germline genetic modification should not be allowed at this time. Germline genetic modification is at present still experimental and will require substantial research to establish its feasibility and safety in clinical application. In addition, the potentially great impact on future generations presents serious ethical concerns. We will monitor progress in germline genetic modification and reassess its clinical applicability at an appropriate time in the future.

**Recommendation 12: The clinical practice of germline genetic modification should not be allowed at this time.**

*Prenatal Genetic Diagnosis*

- 4.53 PNGD provides important information to couples who are at increased risk of having a baby with a genetic disorder. This information may help them decide whether or not to terminate the pregnancy and if they decide not to, the information may help them prepare for the birth of a child with a disability. The information may also be useful for the professional team to prepare for a difficult delivery. The risk factors for having a baby with a genetic disorder include:
- (a) advanced maternal age;
  - (b) a family history of a serious heritable medical condition;
  - (c) one or both parents are “carriers” of mutation(s) in the same gene;
  - (d) abnormal screening test results such as ultrasound or first and second trimester screening tests; and
  - (e) a history of a previous child affected by a serious growth, developmental or health problem.
- 4.54 Prenatal screening precedes PNGD and provides prospective parents and healthcare professionals with information regarding the health of the developing foetus. Prenatal screening procedures include:
- (a) determining whether there is a history of infertility, miscarriages, abnormal children, or a family history of genetic diseases;
  - (b) maternal serum screening tests, which are done either in the first or second trimester. These tests measure circulating levels of certain blood proteins or other metabolites where abnormal levels may indicate possible genetic and/or structural defects in the baby; and
  - (c) ultrasound scans of the foetus, usually between 12 and 22 weeks of pregnancy to detect structural abnormalities, which may indicate possible genetic defects in the baby.
- 4.55 In Singapore, prenatal screening in conjunction with pre- and post-test counselling is part of routine prenatal care and specific diagnostic tests are performed when indicated. PNGD can be carried out for various genetic conditions, including Down’s syndrome, thalassaemia and haemophilia. If the results of prenatal screening tests indicate that the foetus is likely to be affected

with a medical disorder, PNGD will be offered to verify the presence or absence of the disorder.

- 4.56 The range of available prenatal genetic tests is increasing as more knowledge is gained about genetic disorders through research. PNGD may require obtaining tissue specimens from the foetus. Acquiring these specimens involves an invasive procedure and hence poses a risk of miscarriage. It is therefore important that patients are fully informed of the risks, and their consent obtained prior to the tests being carried out.
- 4.57 If PNGD indicates that the foetus is or will likely be affected with a genetic disorder, the couple should be counselled about the disorder, its implications and the available options, to help them decide whether or not to continue the pregnancy.
- 4.58 It is possible to employ PNGD for trait or gender selection for non-medical purposes. For reasons similar to those that we have proffered in relation to preimplantation genetic testing, we are of the opinion that PNGD for gender or trait selection (whether physical, social or psychological characteristics or normal physical variations) should not be allowed. The current acceptable practice for PNGD is essentially confined to serious genetic disorders and we consider this to be appropriate. We note that the relevant professional bodies have guidelines on the practice of PNGD for their members.

**Recommendation 13: Prenatal genetic diagnosis should be limited to serious medical disorders. The use of prenatal genetic diagnosis for the selection of desired traits or gender for non-medical reasons should not be allowed.**

### *Predictive Testing*

- 4.59 Predictive testing identifies healthy individuals who have inherited a gene for a late-onset disease, which is a disease that normally manifests in adulthood, although there may be cases where symptoms arise during late childhood.
- 4.60 Predictive tests can be classified into two categories based on the predictive certainty of the information derived from the tests:
- (a) *Presymptomatic tests* identify healthy individuals who have inherited a defect in a specific gene for a late-onset disease which confers on the individual an almost 100% risk of developing the disease at a later stage in life. However, these tests do not provide information on the severity and onset of the disease. Examples of such diseases include Huntington's disease and familial adenomatous polyposis coli, which are due to defects in single genes.

- (b) *Susceptibility tests (or predisposition tests)* identify individuals who have inherited a genetic variant or variants which may increase their risk of developing a multi-factorial disease some time in the future. Such disorders are often the result of the interaction of multiple genes and environmental factors. Alzheimer's disease, diabetes and certain cancers and heart disease fall into this category. While their genetic predisposition indicates that these individuals have an increased risk of developing the disease, some individuals may ultimately not develop the disease.
- 4.61 Healthy individuals requesting for predictive testing often do so to determine their risk of developing a genetic disease or passing on the disease to their children. Hence, presymptomatic tests are usually performed on individuals with a family history of a specific genetic disease, while susceptibility tests may be performed because of a family history or as part of population screening. As our knowledge in medical genetics increases, it is likely that the number of susceptibility tests will also increase.
- 4.62 Testing for a late-onset disease before an individual develops any symptoms allows the individual in some cases to make life-style changes to either prevent the disease from developing or assist him or her in making reproductive choices to prevent transmitting the disease to the next generation. It may also allow affected individuals to take preventive measures or undergo regular examinations to achieve early diagnosis and treatment of the disease.
- 4.63 Presymptomatic testing is generally well established, both technically and in its clinical application. It should be available for adults at risk who request it, even in the absence of treatment, after proper counselling and informed consent.
- 4.64 Generally, susceptibility testing has not been sufficiently developed and validated to be used extensively in current clinical practice. Therefore, it should not be applied clinically until there is significant empirical evidence of validity and utility. However, when validated tests are available, such as for breast cancer genes, susceptibility testing may be considered.
- 4.65 Predictive genetic information may be burdensome or psychologically traumatic given the uncertainty of the disease. We reiterate the importance of pre- and post-test counselling and informed consent in genetic screening and testing. We further note the NMEC's recommendation that: "Testing must be voluntary and patients and/or families must not be coerced into undergoing predictive testing. Regardless of the decision made, the care of the patient should not be compromised."<sup>32</sup>

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<sup>32</sup> NMEC, *Ethical Guidelines for Gene Technology* (2001), Section 2.2.1 (b).

**Recommendation 14: Presymptomatic testing should be available for adults at risk who request it, even in the absence of treatment, after proper counselling and informed consent.**

**Recommendation 15: Susceptibility testing should not be applied clinically unless there is significant empirical evidence of validity and utility.**

### *Genetic Screening*

- 4.66 The WHO defined genetic screening as “tests offered to a population group to identify asymptomatic people at an increased risk from a particular adverse outcome.”<sup>33</sup> The main purpose of genetic screening is to prevent a disease or minimise morbidity and mortality through early diagnosis and treatment.
- 4.67 Screening tests are not definitive as they are designed to identify those at risk. A confirmatory diagnostic test should be performed as soon as possible after a positive screening test, so as to minimise unnecessary anxiety or to enable measures for the prevention or treatment of the condition to be instituted without delay.
- 4.68 Generally, population genetic screening programmes are offered only when there are proven methods of treatment or prevention. Such programmes are different from other types of medical screening, as there may be risk implications for family members of the person screened.
- 4.69 In Singapore, there are several prenatal and newborn screening programmes. Many pregnant women are screened prenatally for foetuses with Down’s syndrome. All newborn babies are screened for Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency to reduce the risk of neonatal jaundice and its complications. They are also screened for congenital hypothyroidism and for hearing defects, half the cases of which are likely to be genetic in origin. These routine newborn and prenatal screening programmes, which serve a public health function and provide information useful to patients and their physicians, have become socially acceptable and even expected in Singapore.

**Recommendation 16: In genetic screening programmes, a confirmatory diagnostic test should be performed as soon as possible after a positive screening test, so as to minimise unnecessary anxiety or to enable measures for the prevention or treatment of the condition to be instituted without delay.**

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<sup>33</sup> WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Section 6.

**Section C: Quality Control Issues in Clinical Genetic Testing**

- 4.70 In this section, our primary concern is the proper derivation and interpretation of genetic information in clinical genetic testing. This essentially rests on the quality of the genetic information, which in turn is dependent on the integrity of the diagnostic chain (this includes ensuring no sample switch or sample contamination) and the test methodology. As such, the sound practices of medical laboratories are directly relevant to the quality of the genetic information they provide and are a pre-requisite for accurate interpretation.
- 4.71 Accurate interpretation of genetic information presents one of the greatest challenges in clinical genetic testing. Another challenge is the presentation of genetic information in a comprehensible and empathetic manner. We address this latter challenge in the section on genetic counselling. Interpretation of genetic information, like other medical information, is as much an art as it is a science. Skill at interpretation depends on experience as well as up-to-date knowledge of the field.
- 4.72 As with other medical information, genetic information is likely to have psychological and social impact, or affect the reproductive choices of individuals. Given these concerns, we are particularly mindful of the care that is required in the accurate derivation and interpretation of genetic information.

***Standards and Quality of Genetic Test Providers***

- 4.73 As genetic information has far reaching implications, it is important to ensure its accuracy. The accuracy of a test is dependent on the integrity of the diagnostic chain and the test methodology. These aspects should be carefully monitored to ensure an acceptable level of confidence in the technical accuracy of test results. Generally, genetic tests are performed at laboratories selected by healthcare professionals. However, an individual may approach laboratories directly for testing to be done. We note in passing that such direct access may not be in the best interest of the individual as there is no assurance of the credibility of medical advice provided, if any, or of the quality of the test result.
- 4.74 Medical laboratories in Singapore are required to obtain a license from the MOH. Apart from minimum operational standards that the MOH prescribes, there are no binding standards for clinical genetic testing conducted by medical laboratories. There is however a system of voluntary accreditation for medical laboratories. Accreditation is often very helpful in providing greater assurance as to the overall competence of the testing laboratory, and thus the accuracy of the genetic information thereby derived.
- 4.75 In the US, the Clinical Laboratory Improvement Amendments establish quality standards for all clinical testing laboratories to ensure the accuracy, reliability and timeliness of the test result. In addition, professionals directing genetic

testing laboratories may be qualified under various mechanisms based on Federal laws and depending upon State laws. These mechanisms include holding licensure as a doctor of a particular field with laboratory experience, achieving board certification (from the American Board of Medical Genetics, etc.) and demonstrated specific experience as director of a clinical laboratory. Similarly in the UK, all laboratories providing genetic testing services need to be appropriately accredited and they take part in internal and external quality assurance programmes. Furthermore, it has been recommended that genetic testing be undertaken only by laboratories closely linked with other genetic services.<sup>34</sup> The Australian NHMRC stated that clinical genetic testing should be performed only by accredited laboratories.<sup>35</sup> Laboratories are required to be particularly sensitive to the possibility of error in the performance of genetic test.

- 4.76 Currently, the Singapore Accreditation Council (SAC) conducts general accreditation of medical laboratories. Although accreditation is not mandatory, the SAC actively encourages medical laboratories to be accredited. The SAC accredits medical laboratories as part of the Singapore Laboratory Accreditation Scheme (SINGLAS), which is essentially based on standards that are internationally accepted. SAC-SINGLAS is internationally recognised via mutual recognition arrangements such as the Asia-Pacific Laboratory Accreditation Cooperation, the International Laboratory Accreditation Cooperation and European Cooperation for Accreditation. It establishes best practices and standards for laboratories, including qualification requirements for the laboratory director and other technical personnel. In addition, SINGLAS also has specific criteria for accreditation in specialty areas such as molecular pathology and cytogenetics. Other than the SAC, accreditation of medical laboratories in Singapore has also been conducted by the College of American Pathologists (CAP), and jointly by the SAC and the CAP under the SAC-CAP Laboratory Accreditation Programme.
- 4.77 We propose that all laboratories conducting clinical genetic tests should be accredited by a body designated by the relevant authority, based on standards it considers appropriate. This is necessary to safeguard a high quality of genetic information derived from tests, which is in turn fundamental in safeguarding the welfare of tested individuals.

**Recommendation 17: All laboratories conducting clinical genetic tests should be accredited by a body designated by the relevant authority, based on standards it considers appropriate.**

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<sup>34</sup> UK Advisory Committee on Genetic Testing, *Report on Genetic Testing for Late-onset Disorders* (1998), pages 19 and 20.

<sup>35</sup> NHMRC, *Ethical Aspects of Human Genetic Testing: an Information Paper* (2000), section 2.5, page 23.

***Interpretation of Clinical Genetic Test Results***

- 4.78 There are several factors that affect the accurate interpretation of clinical genetic test results. These include:
- (a) the integrity of the diagnostic chain;
  - (b) the reliability of test methods;
  - (c) the technical competence of laboratory technicians;
  - (d) the ability of the individual to understand; and
  - (e) up-to-date knowledge, experience and competence of the genetic counsellor to interpret and communicate the test result and its implications effectively to the patient.

We believe that proper accreditation of medical laboratories should address factors (a) to (c). However, factors (d) and (e) will depend to a larger extent on the genetic counsellor conveying the test result to the patient.

- 4.79 The interpretation of clinical genetic test results is complex and dependent on many factors including the nature of the disease, the modality of testing, and the health status of the patient. Healthcare professionals have to ensure that sound interpretation is provided to patients, and so should be appropriately qualified and sufficiently experienced. Misinterpretation of results or misdiagnosis may lead to stress and unnecessary or inappropriate therapeutic interventions or changes to lifestyle for the patient and his or her family.
- 4.80 Genetic counselling should be provided in a timely manner. As far as is practicable, there should be no delay in counselling following the disclosure of a test result to a patient, to help the patient cope with any resultant psychological impact or emotional stress and the myriad medical, psychological, social, financial and legal implications that may arise. Sound and effective pre- and post-test counselling is thus particularly critical and should always be timely and integral to the practice of clinical genetic testing.

**Recommendation 18: Interpretation of clinical genetic test results should only be performed by healthcare professionals who are appropriately qualified or have sufficient experience. As far as is practicable, genetic counselling should immediately follow the disclosure of the test result, particularly if the test result is not favourable.**

**Section D: Genetic Counselling**

- 4.81 We have emphasised at various points in this report the importance of genetic counselling in the conduct of clinical genetic testing. Genetic counselling should seek to achieve the following objectives:
- (a) to provide sufficient and unbiased information to enable full and informed choices to be exercised; and
  - (b) to provide appropriate support to the patient and his or her family members.
- 4.82 In genetic counselling, the information provided should be adequate and comprehensible to the recipient, who will usually be a patient. It should be commensurate with the real and anticipated risks of the test, and the implications of the information it may yield. The patient should always be given sufficient time to consider the available options and have the opportunity to clarify doubts. Whenever practicable, counselling should be done in a face-to-face meeting. In addition, counselling should be conducted in an empathic manner and should be non-directive, especially if the condition is one where treatment is presently not available.
- 4.83 We have indicated that informed consent is dependent on the information that is provided to patients before genetic testing, and the manner in which such information is conveyed. For this reason, consent should be obtained after appropriate counselling. Taking into account the recommendations provided by the NMEC on this matter, we recommend that the following be considered in pre-test genetic counselling:
- (a) the nature of the condition to be tested;
  - (b) the potential consequences of not being tested;
  - (c) the alternatives to genetic testing and their pros and cons;
  - (d) the type of sample required, test procedure and possible risks;
  - (e) the consequences foreseeable as a result of testing, including implications for family members, and available support;
  - (f) test reliability and clinical validity, emphasising that not all mutations are detectable, that some mutations are of uncertain significance, and the extent to which results indicate probability, or degree of certainty of developing the disease;
  - (g) the treatment or management options;

- (h) the turn-around time and how the results will be conveyed to the patient; and
  - (i) an assurance to the patient of confidentiality of test results and counselling records, and explanation of circumstances that might require disclosure of the patient's test result (if necessary).
- 4.84 Where appropriate, it may be advisable also to consider the following in pre-test genetic counselling:
- (a) possible third parties' interest in the patient's genetic information, and the likely consequences;
  - (b) further use of genetic information and test samples, and their management; and
  - (c) the possibility of unexpected findings (such as parentage discrepancy even though the test is not a parentage test) and whether the patient will want to know such findings.

***Post-test Follow-up***

- 4.85 We are of the view that follow-up support should be provided to patients in the form of post-test counselling. Patients will often have queries on the result of their genetic tests and the implications. Healthcare professionals should attempt to address these queries in post-test counselling. In particular, we propose that the following concerns be anticipated and addressed:
- (a) the implications of the genetic test result for the patient himself or herself, whether the result is positive, negative or inconclusive;
  - (b) the treatment or management, and/or support options;
  - (c) the possible implications for family members;
  - (d) any psychological, social and ethical issues or concerns;
  - (e) any requirement or obligation to disclose the test result to a third party (if any); and
  - (f) the protection of the patient's privacy and confidentiality of his or her genetic test result.
- 4.86 Genetic test results may reveal cases that require long term follow-up. In such cases, the genetic counsellor is expected to:

- (a) conduct a periodic review of the management plan;
- (b) monitor the patient's adherence to the plan;
- (c) clarify any doubts and answer any questions;
- (d) give psychological support; and
- (e) inform the patient of relevant developments in genetic medicine.

4.87 In certain cases involving children tested positive for a serious genetic condition, it may be prudent to discuss the implications of the test result with the parents in the absence of the child. This is to allow parents to ask questions freely and to minimise any risk of misunderstanding on the part of the child.

**Recommendation 19: Genetic counselling should be offered to all individuals before and after they undergo clinical genetic testing.**

**Recommendation 20: Genetic counselling should generally be conducted in a non-directive manner and should provide sufficient information and appropriate support to the individual and his or her family members.**

#### *Professional Diversification and Development*

4.88 Currently in Singapore, there are no uniform standards or practice applicable to genetic counselling, which is usually carried out by physicians. However, genetic counselling can be a prolonged process and given the rapid development in medical genetics, specialised knowledge will increasingly be required. Individuals involved in genetic counselling must be committed and prepared to invest the time, and should possess and maintain up-to-date knowledge of gene technology. It may be desirable to involve others such as medical geneticists, nurses or healthcare therapists who have the necessary skills in counselling. However, the responsibility for overseeing the case, including counselling, remains with physicians as they carry ultimate clinical responsibility for their patients.

4.89 We propose that the relevant authority provides professional training and accreditation in medical genetics and genetic counselling to healthcare professionals working in this field.

**Recommendation 21: The relevant authority should provide professional training and accreditation in medical genetics and genetic counselling to healthcare professionals.**

## **V. Direct Supply of Genetic Tests to the Public**

- 5.1 In Singapore, as in many other countries, access to clinical genetic tests and services is mainly through healthcare professionals or healthcare institutions. Healthcare professionals are also responsible for interpreting genetic test results, providing pre- and post-test counselling to the patient regarding the value and implications of the test and the significance of the test results, and if need be, treatment and follow-up. However, recent developments in the availability of genetic testing kits and services direct to the public allow increasing access to genetic tests without a medical consultation.
- 5.2 Since the publication of the NMEC Gene Technology Guidelines in 2001, there have been important changes in the biomedical landscape in Singapore and elsewhere, including the development of advanced gene technologies and the provision of genetic services. A conventional demand-supply evaluation is illustrative. On the demand-side, the Singaporean public is gaining sophistication in knowledge of health and health-related matters. One factor that may have contributed to this social phenomenon is the increased availability of medical information from various sources, especially the Internet. When considered in light of hectic lifestyles, “face-saving” or privacy concerns and escalating healthcare costs, the prospect of a “do-it-yourself” approach to certain health-related matters may appear attractive. On the supply-side, advances in gene technology have simplified the usage of many genetic tests and enabled manufacturers to produce them at much lower cost. Considering these developments in the context of low-cost marketplaces such as the Internet, it is foreseeable that some may increasingly choose to bypass medical professionals to obtain direct access to genetic tests and services.
- 5.3 The commercialisation of genetic testing services and the ensuing direct supply of genetic testing kits to the public have become a growing concern in a number of countries. The UK HGC recently carried out an extensive review of this development and published a report, *Genes Direct: Ensuring the effective oversight of genetic tests supplied directly to the public* (2003). It found that commercial genetic testing services are likely to be increasingly marketed in the UK and in some other developed countries. In such direct supply, the public gains access to genetic tests without a conventional face-to-face consultation with a medical professional. It is possible, following a telephone call or an electronic mail, for an individual to post his or her tissue sample to a laboratory where genetic analysis is performed. Alternatively, certain do-it-yourself home test kits may be procured over the counter or through the Internet. In the absence of a medical consultation, the HGC was concerned that the possible harms far outweigh the interest of individuals in obtaining genetic information about themselves. Two possible harms from direct genetic testing were identified:

- (a) Misinformation, leading to false assurance and a delay in seeking proper medical assistance, or causing unnecessary alarm resulting in expensive unnecessary medical investigations or treatment, or a misguided reproductive decision; or
  - (b) inappropriate testing of children or other adults without proper consent.
- 5.4 We share the concerns of the HGC. If direct access to genetic testing is allowed in Singapore, the likelihood of misinformation is high. First, there is a lack of assurance that the genetic tests supplied by manufacturers are of a satisfactory quality and standard. Second, there is a high likelihood that the test result may be misinterpreted by an untrained person, with the probabilistic nature of predictions made from genetic information adding to interpretive difficulties. Third, it is unrealistic to expect suppliers of genetic testing kits to provide long-term counselling and other support services of satisfactory standards, particularly for the diagnosis or prediction of serious conditions.
- 5.5 There is no specific legislation regulating access to, or supply of, genetic testing kits and services in Singapore. The Centre for Medical Device Regulation of the Health Sciences Authority has established a system for the voluntary registration of medical devices and is currently in the process of setting up a framework for the regulation of medical devices.
- 5.6 The NMEC, in its Gene Technology Guidelines, strongly discouraged genetic testing by manufacturers and suppliers of genetic testing kits and the advertising or marketing of predictive genetic tests to the public. We agree that the advertising of predictive genetic tests to the public should be strongly discouraged. However, we are of the view that a more comprehensive system of control over public access to genetic testing should be devised in light of recent developments in gene technology. We propose that the relevant authority develop an oversight framework for the supply, direct to the public, of those genetic tests and services which are likely to cause serious harm if freely accessible. Consumers should on the other hand have easy access to accurate and impartial information to help them decide on the relevance of the tests or services. We reiterate that genetic testing should generally be conducted through the intermediation of a qualified healthcare professional and that tests that provide predictive health information should not be directly offered to the public.

**Recommendation 22: Genetic testing should generally be conducted through a qualified healthcare professional. Tests that provide predictive health information should not be offered directly to the public. The advertising of direct genetic tests to the public should be strongly discouraged. The relevant authority should develop an oversight framework for the supply of direct genetic tests, services and information to the public.**

## **VI. Ethical Considerations in Human Genetic Research**

- 6.1 Human genetic research is the study of genes, their functions, how they are associated with health and disease and how genetic and environmental factors influence health. The study may involve research participants or pre-existing records, or otherwise, genetic information derived from genetic tests, and may entail the use of tissue samples.<sup>36</sup> Tissue samples may be from healthy individuals, from patients or from people who have died.
- 6.2 Significant research is currently taking place throughout the world to examine the genetic basis of common diseases such as cancer, heart disease and diabetes, and important discoveries are emerging. Ultimately, it is hoped that human genetic research will enable or facilitate the development of new or more reliable ways of diagnosing, preventing and treating genetic disorders effectively. The treatments envisaged extend across a broad spectrum from pharmacological, gene or cell-based therapies, to simple changes in a person's environment or lifestyle.
- 6.3 Human genetic research is not conducted with the aim of providing research participants with specific information about their genetic status or health. Generally, genetic information derived from research is of unknown or uncertain predictive value. Therefore, special care must be taken to prevent inadvertent release of immature data.
- 6.4 If there is a likelihood that the research will yield individual data of clinical significance, the research participant should be told of this possibility prior to participation in the research, and whether he or she would be informed accordingly if desired. Where genetic tests of known clinical or predictive significance are used on research participants or on tissue samples that identify an individual, specific consent must be sought and appropriate counselling offered. In either case, if a research participant subsequently requests a test to confirm his or her genetic status, he or she should be advised to consult a physician.
- 6.5 Researchers have an obligation to protect the privacy of research participants and their family members, and to ensure confidentiality of all genetic information derived from the research, including information about the participant's relatives, who may not be part of the research project. Identifiable genetic information derived from the research should not be disclosed to any third party.

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<sup>36</sup> Human tissues refer to "all kinds of human biological materials derived from living or cadaveric donors, including solid body tissues, organs, fetuses, blood and other body fluids and their derivatives, cord blood, embryos, gametes (sperm or eggs) or any part or derivative thereof". BAC, *Human Tissue Research* (November 2002), paragraph 2.1.

- 6.6 The overall ethical framework for human biomedical research has been set out in our previous reports: the Human Stem Cell Report, the Human Tissue Research Report and the IRB Guidelines. We strongly encourage researchers to refer to these reports for further details. In particular, researchers should take note of the following:
- (a) All human genetic research requires the approval of an appropriately constituted research ethics committee or an IRB. In our IRB Guidelines, we emphasised the critical role that researchers, institutions and IRBs play in ensuring the protection of the safety, health, dignity, welfare and privacy of research participants. All the matters reviewed in this Part fall within the purview of IRBs approving human genetic research.
  - (b) As a general principle, where the research involves the use of stored tissue samples or genetic information, consent is required from the person from whom the tissue was derived or to whom the information relates. Such consent would normally have been taken at the time tissue was donated. The IRB should consider if any consent requirement arises where the research involves legacy tissue, stored human tissue or genetic information, that has been anonymised.
  - (c) Tissue donors should be free to choose between making a general gift, which means that the tissue may be used for any type of research, or a restricted gift, which restricts the use of the tissue to types of research specified by the donor.<sup>37</sup> Research participants should be informed that when they donate any tissue for research, including genetic research, they will no longer have any claim to property rights in the tissue.
  - (d) When researchers plan to use tissue samples from abroad, both the researchers and the IRB reviewing the proposal must be satisfied that the tissue samples have been ethically obtained.
  - (e) Participation in genetic research is voluntary. Researchers need to seek the informed consent of prospective research participants, whether or not they are also patients. In particular:
    - (i) where an attending physician is also the researcher, it is necessary for consent to be taken separately through an independent third party to avoid conflicts of interest and to ensure that the patient's participation in the research is genuinely voluntary;
    - (ii) where tissue samples provided for clinical use are also intended for research, informed consent for the research is required in addition to the consent for taking the tissue for clinical use.

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<sup>37</sup> BAC, *Human Tissue Research* (November 2002), Section 13.1.9.

Consent is also required if there is an intention to store the tissue for other future research; and

- (iii) where vulnerable persons are involved, their informed consent or that of their legally authorised guardians must be sought. In such cases, the IRB should be satisfied that there is no appropriate alternative test population and that the research is dependent on their participation.

6.7 When the research involves human embryos for reproductive purposes, written approval from the MOH is required in addition to approval by the IRB. In any case, no research should be performed on any embryo more than 14 days old.<sup>38</sup>

6.8 Researchers conducting human genetic research should provide research participants with sufficient information in an understandable form to enable them to make an informed decision. The participant should be informed of the following prior to the research:

- (a) the experimental nature and purpose of the study;
- (b) the possible benefits to others and to science;
- (c) why he or she is invited to participate, and the voluntary nature of the participation;
- (d) the procedure and the risks (if any);
- (e) whether he or she will be informed (if desired) if clinically relevant information is obtained from the research;
- (f) where relevant, the significance and implications of the genetic information derived from the research for the participant and his or her family, in which case counselling provisions as per Part IV Section D would apply;
- (g) the possibility of being re-contacted in the future;
- (h) the use and storage of the tissue contributed for current and any future IRB approved research;
- (i) the arrangement to ensure the participant's privacy and the confidentiality of records;

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<sup>38</sup> MOH, *Guidelines for Private Healthcare Institutions Providing Assisted Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248, Rg 1)* (2001).

- (j) who to contact for questions about the research or in the event of an adverse occurrence arising from it;
  - (k) the right to withdraw from the research at any time;
  - (l) assurance that refusal to consent without giving any reasons, or withdrawal from the research at any time, will not compromise the quality of any care that may be given to the participant and/or the family;
  - (m) the procedure for the disposal of the participant's information or tissue upon withdrawal or completion of the research, if not stored for future research; and
  - (n) possible commercial uses, if any.
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