

ETHICAL, LEGAL AND SOCIAL ISSUES IN GENETIC TESTING AND GENETICS RESEARCH

A CONSULTATION PAPER

THE BIOETHICS ADVISORY COMMITTEE

SINGAPORE

5 April 2005

THE BIOETHICS ADVISORY COMMITTEE

Chairman

Professor Lim Pin

*University Professor
National University of Singapore*

Deputy Chairman

Judge Richard Magnus

Senior District Judge, Subordinate Courts of Singapore

Members

Associate Professor John Elliott

Department of Social Work & Psychology, National University of Singapore

Mr Han Fook Kwang

Editor, The Straits Times

Associate Professor Terry Kaan Sheung-Hung

Faculty of Law, National University of Singapore

Mr Ahmad Khalis Bin Abdul Ghani

Member of Parliament, Hong Kah Group Representation Constituency

Professor Lee Eng Hin

Professor and Director, Division of Graduate Medical Studies, National University of Singapore

Mr Lim Aeng Cheng Charles

Principal Senior State Counsel (Law Reform & Revision), Attorney-General's Chambers

Professor Edison Liu

Executive Director, Genome Institute of Singapore

Mr Niam Chiang Meng

Permanent Secretary, Ministry of Community Development, Youth and Sports

Mr Nuyen Anh Tuan

Department of Philosophy, National University of Singapore

Professor Kandiah Satkunanantham

Director of Medical Services, Ministry of Health

Professor Tan Chorh Chuan

Provost, National University of Singapore

About the Bioethics Advisory Committee

The Bioethics Advisory Committee (BAC) was appointed 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 Ministerial Committee for Life Sciences. For further information about the BAC and its work, please visit <http://www.bioethics-singapore.org>

Contacting the Bioethics Advisory Committee

The BAC welcomes views, comments, suggestions and other feedback on the issues raised in this Consultation Paper and on any bioethical issues within the BAC's remit. All feedback should be addressed to:

Bioethics Advisory Committee

20 Biopolis Way

#08-01 Centros

Singapore 138668

Web: <http://www.bioethics-singapore.org/>

E-mail: contactus@bioethics-singapore.org

CONTENTS

PART I.	Introduction	1
PART II.	Genetic Testing and Genetic Information	4
	Defining Genetic Testing	4
	Defining Genetic Information	5
PART III.	General Ethical Considerations	8
	Respect for Welfare, Safety, Religious and Cultural Perspectives and Traditions	8
	Free and Informed Consent: Freedom of Consent and the Right to Information	9
	Respect for Vulnerable Persons	11
	• Children and Adolescents	11
	• The Mentally Impaired	13
	• Persons in Relationship of Dependence	13
	Confidentiality and Privacy	14
PART IV.	Public Access to Genetic Testing	16
	Direct Supply of Genetic Testing to the Public	16
	Prohibition Against Involuntary Genetic Testing	18
PART V.	Specific Ethical Considerations for Human Genetics Research	19
PART VI.	Specific Ethical Considerations for Clinical Genetic Testing	21
Section A:	Specific Ethical Considerations	21
	Carrier Testing	21
	Preimplantation Genetic Diagnosis	21
	Preimplantation Tissue Typing	25
	Germline Genetic Modification	26

	Prenatal Genetic Diagnosis	27
	Predictive Testing	28
	Genetic Screening	30
Section B:	Ensuring the Proper Derivation and Interpretation of Genetic Information in Clinical Genetic Testing	31
	Standards and Quality of Genetic Test Providers	31
	Results Interpretation	33
Section C:	Genetic Counselling	33
	Post-test Follow-up	35
	Professional Diversification and Development	35
PART VII.	Summary of Recommendations	37
ANNEXES		
Annex A:	The Human Genetics Subcommittee	41
Annex B:	Abbreviations	42
Annex C:	Glossary	43
Annex D:	References	48

ETHICAL, LEGAL AND SOCIAL ISSUES IN GENETIC TESTING AND GENETICS RESEARCH

I. Introduction

- 1.1 The Bioethics Advisory Committee (BAC) was established by the Cabinet in December 2000 to examine the potential ethical, legal and social issues arising from research in the biomedical sciences in Singapore, and to recommend policies to the Life Sciences Ministerial Committee.
- 1.2 Three sets of recommendations have since been published and accepted by the government:
 - (a) on human cloning and human stem cell research - *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning*, June 2002 (Human Stem Cell Report);
 - (b) on human tissue banking and human tissue research - *Human Tissue Research*, November 2002; and
 - (c) on the ethics governance of human biomedical research - *Research Involving Human Subjects: Guidelines for IRBs*, November 2004 (IRB Guidelines Report).
- 1.3 We believe that human welfare can be elevated through the responsible development and application of biomedical science. The mapping of the human genome 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.
- 1.4 Genetic tests can help in the diagnosis, prevention and treatment of serious genetic disorders but they also present ethical, legal and social concerns to both 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.
- 1.5 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. It provides information that has broader implications extending to family members¹ and future generations. Occasionally, unexpected information, for instance, information about parentage or information on the likelihood that an apparently healthy individual may develop a serious genetic condition later in life, may be revealed. The result of a genetic test, especially one that is positive for a serious genetic disorder for which there is no treatment, may have

¹ For the purposes of this Consultation Paper, the terms "family" or "family members" refer not only to persons who are biologically or 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.

significant psychological impact on an individual and possibly on his or her family. Due to the shared and predictive nature of genetic information, family members and third parties such 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.

- 1.6 In light of the broad scope of genetic testing, we focus on two main aspects in this Consultation Paper:
 - (a) genetic testing for certain specified purposes; and
 - (b) the genetic information thereby derived.
- 1.7 The use of genetic testing and genetic information for non-medical purposes can give rise to 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. However, we do not consider it appropriate to address these issues in this Consultation Paper but will continue to closely monitor them. Another aspect of genetic testing that is not considered in this Paper is the use of genetic information from linked medical registries and genetic databases for research. The ethical, legal and social issues that may arise are manifold and likely to have long-term implications for all levels of society. We intend to address these issues separately.
- 1.8 While some view genetic information as distinct from other medical information, our preference is for it to be treated as similar to medical information. We believe that the conduct of genetic testing should be limited to medical or related purposes. Healthcare professionals and biomedical researchers must ensure the safety, health, dignity and welfare of their patients or human subjects.
- 1.9 Ethical issues arising from genetic testing in Singapore has been considered by the National Medical Ethics Committee (NMEC)² in its *Ethical Guidelines for Gene Technology* (NMEC Gene Technology Guidelines) published in February 2001. In this Paper, we build on some of NMEC's Guidelines and provide specific recommendations relating to the ethical conduct of genetic testing in a clinical setting, the direct supply of genetic tests to the public and the proper derivation and interpretation of genetic information. We have placed particular emphasis on the importance of sound and effective counselling, which we regard as indispensable to the ethical conduct of genetic testing.
- 1.10 This Consultation Paper is prepared by the Human Genetics Subcommittee (HGS)³ with the following objectives:

² The NMEC was established in January 1994 to assist the Ministry of Health in addressing ethical issues in medical practice and to ensure a high standard of ethical practice in Singapore.

³ The HGS was constituted by the BAC in March 2001 to specifically address the ethical, legal and social issues relating to research and development in human genetics and gene technology. Members of the HGS are listed in Annex A.

- (a) to consider the ethical, legal and social issues arising from the conduct of genetic testing in Singapore; and
- (b) to seek public feedback on the proposed recommendations.

1.11 After thorough consideration of all the views and comments received, we will present our final recommendations to the Life Sciences Ministerial Committee.

II. Genetic Testing and Genetic Information

- 2.1 The demand for genetic testing 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 1,000 different genetic tests may now be conducted by clinical and research laboratories.
- 2.2 In recognition of the growing importance of genetic testing in the healthcare sector, the NMEC Gene Technology Guidelines were issued to assist physicians in managing this development. The Guidelines defined “gene technology” as “the use of techniques for the analysis and/or manipulation of DNA (deoxyribonucleic acid), RNA (ribonucleic acid) and/or chromosomes”⁴ and focused on gene technology in the context of medical practice and doctor-patient relationship.

Defining Genetic Testing

- 2.3 In this Consultation Paper, we seek to address some of the more pertinent ethical, legal and social issues in the conduct of genetic testing for clinical and research purposes. **Genetic Testing** is the use of tests which are designed specifically to detect genetic differences, for purposes that 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 definitive genetic cause of the disorder;
 - (b) *Carrier Testing* conducted to identify individuals with a genetic or chromosomal abnormality that generally does not affect the person’s health but puts him or her at higher risk of having a child with a specific genetic disorder;
 - (c) *Prenatal Genetic Diagnosis (PND)* conducted on a foetus or a pregnant woman so as to identify a specific genetic disorder;
 - (d) *Preimplantation Genetic Diagnosis (PGD)* conducted on an early embryo so as to identify a specific genetic disorder prior to the transfer of the embryo to the womb;
 - (e) *Predictive Testing* conducted on asymptomatic individuals to determine if they are at risk of developing a genetic disorder in the future;
 - (f) *Genetic Screening* conducted on healthy individuals to determine their status with regards to a specific genetic disorder; and
 - (g) *Genetic Testing* for research.

⁴ NMEC Gene Technology Guidelines, Section 1.1

Accordingly, **Clinical Genetic Testing** is genetic testing conducted for the diagnosis, prevention or treatment of a genetic disorder in a patient for purposes (a) to (f) of the above paragraph.

2.4 Genetic tests are commonly accomplished by the following methods:

- (a) direct testing, where tests are performed on the DNA or RNA specific for a gene;
- (b) cytogenetic testing, where the chromosomes are examined; and
- (c) linkage testing, where markers co-inherited with a disease-causing gene are examined.

Biochemical, functional, or immunological methods have also been used in Genetic Testing. However, for the purposes of this paper, Genetic Testing does not include these methods when they are not primarily designed to detect specific genetic defects but are instead used to screen for overall biochemical, physiological, or anatomical abnormalities.

Defining Genetic Information

2.5 The practice of Genetic Testing in Singapore has largely been directed at addressing 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 Genetic Testing, are filed together with other medical records of the patient. Generally, the law requires 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 is not treated any differently from regular medical records.

2.6 The ethical, legal and social 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 Testing⁵ 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.⁶ 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).

⁵ US Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States* (1997). The Task Force is established by the National Institutes of Health-Department of Energy Joint Working Group on the Ethical, Legal and Social Implications of Human Genome Research.

⁶ European Commission Expert Group, *25 Recommendations on the Ethical, Legal and Social Implications of Genetic Testing* (2004).

2.7 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 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 a 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 so it is 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, which may be given exaggerated symbolic significance;
- (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 stable DNA recovered from stored specimens or even archaeological material after many years.

2.8 The ALRC and the AHEC adopted a similar analysis and crystallised these features 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 ready availability in various forms (such as hair or fingernail) for genetic test to be conducted by various parties;
- (b) It has a familial dimension so that it is important not only to the individual but also to that individual's family due to the possible hereditary impact; and
- (c) It is predictive in its informational impact on the individual's future health.

While the ALRC and the AHEC stop 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 and the

Bioethics Committee of Japan's Council for Science and Technology have stated similar positions.

- 2.9 The most distinctive feature of Genetic Information is perhaps its predictive value. However, we note that other information such as a smoking habit, which is related to the cancer-causing effect of tobacco, and exposure to certain toxic substances are also predictive health information. Nevertheless, we recognise that a potential misuse of Genetic Information may be attributed to the failure to properly comprehend its predictive nature. For instance, mutations in some disease genes (such as in Huntington's disease) are definite in giving expression to "disease" conditions or symptoms within the normal average lifetime of carriers. But for many other disease genes, mutations only confer a percentage chance of developing a particular genetic disease. Even if it is known that this genetic disease will occur within the lifetime of the carrier, it is uncertain when this will occur, or how severe it will be, since scientists do not yet know what conditions influence disease onset and severity. Where the prediction based on Genetic Information is uncertain, an unnecessary psychological burden (and possibly economic and social burdens as well) may be imposed on the carrier and his or her family.
- 2.10 The current practice of Clinical Genetic Testing in Singapore is through physicians registered under the Medical Registration Act. Such a "physician-based" system is also found in many leading scientific jurisdictions. Consequently, 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 a system of ethical procedures. In most cases, physicians are the main points of contact with patients and accordingly bear ultimate responsibility towards them.
- 2.11 In light of the current practice of Genetic Testing in Singapore, as well as the current use of Genetic Information thereby derived, we are of the view that Genetic Information should not be treated differently from medical information. By this, we refer to Genetic Information as accessed and managed through the intermediation or under the supervision of a physician for a healthcare or health-related purpose. We do, however, recognise that there are occasions when Genetic Information – especially sensitive and non-observable Genetic Information – should be accorded greater ethical and legal safeguards when it is accessed and used by third parties for non-medical purposes. Indeed, history informs us that misuse of Genetic Testing and Genetic Information can lead to grave injustice and immense hardship not only for those immediately affected, but for their family members as well. For these reasons, many jurisdictions have introduced, or are considering, regulatory measures for governing access to, and the use of, Genetic Testing and Genetic Information outside of the healthcare context. Accordingly, we focus on the ethical conduct of Genetic Testing that provides non-observable and sensitive Genetic Information.

Recommendation 1: Genetic Information derived from Clinical Genetic Testing should be confined to a healthcare context, owing to its complex nature and the need for professional input. Accordingly, it should be regarded as medical information and the highest ethical standard should be applied in its derivation, management and use.

III. General Ethical Considerations

- 3.1 As with many other types of technologies, Genetic Testing not only presents healthcare benefits, but also possible harms if misused. In this Part, we discuss ethical considerations that are generally applicable to all types of Genetic Testing, whether in a research or clinical setting. While we are of the view that healthcare professionals may be entrusted with the ethical conduct of Genetic Testing, the increasing commercialisation and ease of access to certain Genetic Testing may lead to compromising situations for members of the public. In this respect, we are particularly concerned with non-consensual Genetic Testing. This and other related issues are discussed in Part IV. In Parts V and VI, we consider the more specific ethical considerations that are applicable to human genetics research and Clinical Genetic Testing respectively.
- 3.2 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) Free and informed consent;
 - (c) Respect for vulnerable persons; and
 - (d) Privacy and confidentiality.

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

- 3.3 Where Genetic Testing is conducted primarily for a clinical purpose, research considerations should not compromise or prejudice the primary purpose. If there is a possibility that the sample taken for clinical purposes may be used for research, this must be made known to the patient and his or her free and informed consent must be obtained. The more specific recommendations in our *Human Tissue Research* report for donations of human tissue for research to be made as gifts will then apply.⁷
- 3.4 In a multi-cultural and multi-religious society, healthcare professionals and researchers 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 should be carefully managed. Similarly, in selecting a population group to be screened, it is important to avoid stigmatisation of the entire group.

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.

⁷

“**Donations to be Outright Gifts.** Gifts of tissues should be accepted only on the basis that the donor renounces any property rights or claims to the tissue that they choose to donate. Donors should be informed of this principle, and if they do not agree, then their donation should not be accepted.” *Human Tissue Research* (2002), Recommendation 1D.

Free and Informed Consent: Freedom of Consent and the Right to Information

- 3.5 The requirement of free and informed consent to be obtained before 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 it being done in the context of screening, diagnosis or research.
- 3.6 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 situation in which consent is sought and the comprehensibility of the language used in the interactive process. In addition, the individual should be given sufficient time to understand the information provided and to decide whether or not to undergo Genetic Testing.
- 3.7 We propose that information to be provided to individuals before any Genetic Testing should include:
- (a) purpose of the test;
 - (b) procedure;
 - (c) discomforts and risks (if any) of the test to both the individual and the family;
 - (d) accuracy or predictive value of the test;
 - (e) implications (including social risks) of the test result (negative and positive) for the individual and his or her family members;
 - (f) treatment or management options;
 - (g) alternatives to Genetic Testing and their pros and cons;
 - (h) whether unexpected findings resulting from the test should be disclosed and the likely extent of the disclosure; and
 - (i) that the confidentiality of the test result would be maintained.
- 3.8 In some instances, healthcare personnel or scientists may want to store specimens provided for clinical testing for possible future uses in research. In such cases, informed consent for the future use of tissue specimens for research is required in addition to the consent to undergo Genetic Testing. The World Health Organization (WHO) stated that: “People should be informed of possible future uses of the specimens, whether identifiers will be retained, and if so, whether individuals will be re-contacted about new developments concerning their health care.”⁸ We agree with this statement.

⁸ WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Section 7.

- 3.9 In addition to the information in paragraph 3.7 that is to be provided to individuals before Genetic Testing, participants in Genetic Testing for research should be provided with the following additional information:
- (a) the experimental nature and purpose of the study;
 - (b) why the individual is invited to participate, and that participation is voluntary;
 - (c) the uncertainty of the results of the test for prediction and accurate genetic counselling;
 - (d) the possible benefits to others and to science;
 - (e) the confidentiality of records identifying the tested individual;
 - (f) who to contact for questions about research or in the event of a research injury;
 - (g) the right of the individual to withdraw from the research at any time;
 - (h) that refusal to consent, or withdrawal from the research at any time, will not compromise the quality of care that will be given to the individual and the family; and
 - (i) possible commercial uses.

Recommendation 3: Genetic Testing should be voluntary and conducted only after free and informed consent has been obtained. Consent must be based on sufficient information, which includes the nature, purpose, risks and implications of the test. Consent should also be obtained for future clinical and/or research use of tissue specimens.

- 3.10 A difficult situation may arise when an individual refuses to disclose a test result that may be medically beneficial to a third person. For instance, a genetic relative of the tested individual may benefit from knowing that the latter has a high risk of developing a genetic disorder such as colon cancer. The relative may then decide to undergo Genetic Testing, which may allow him or her to adopt beneficial practices, such as making lifestyle changes or going for regular medical check-ups. Such a scenario would encroach on the ethical principle of free and informed consent. Generally, an individual's request for the confidentiality of his or her test result to be maintained should be respected, and the test result is not to be disclosed without the individual's consent. It is nevertheless important that attending healthcare professionals point out clearly, through appropriate counselling, the important positive and negative consequences of disclosing the test result, although the final decision must rest with the tested individual. However, we emphasise that the ethical principle of privacy and confidentiality of an individual is not an absolute right. We address in greater detail the circumstance where disclosure may be made without consent of the individual in our discussion on the ethical principle of privacy and confidentiality below.

- 3.11 Where an individual has agreed to undergo Genetic Testing, this individual should be informed of the test result without undue delay unless he or she has clearly indicated the wish not to know after appropriate counselling. However, in cases where newborn babies and children are tested for treatable conditions, the test results should be disclosed to their parents or guardians. In addition, a healthcare professional may decide to postpone disclosure of the test result if the individual is not in a suitable condition to receive such information. This may arise when the test result reveals a condition that cannot be medically treated or alleviated. In research involving Genetic Testing, researchers should inform the individual prior to participation in the research whether the Genetic Information so derived will be disclosed to him or her.

Recommendation 4: An individual should be informed of the test result without undue delay unless he or she has clearly indicated the wish not to know. However, the test results of newborn babies and children for treatable conditions should be disclosed. In research involving Genetic Testing, researchers should inform the individual prior to participation in the research whether the Genetic Information so derived will be disclosed to him or her.

Respect for Vulnerable Persons

- 3.12 There are certain categories of persons where special procedures should be in place to ensure their voluntary and safe participation in Genetic Testing and to safeguard their welfare. Generally, it is inappropriate for such vulnerable persons to be involved in research. Exceptions can be made when the outcome of the research is greatly or critically dependent on their participation and when there is no appropriate alternative test population. In such cases, special safeguards should be assured to the greatest extent possible. We consider three categories of vulnerable persons in particular: children and adolescents, the mentally impaired and persons in dependent relationships.

Children and Adolescents

- 3.13 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 all persons responsible for the care of children or adolescents should only act in the latter's best interest.
- 3.14 We appreciate that "best interest" is dependent on the specific circumstances and conditions of a child or adolescent. When considering whether the child or adolescent's best interest is met by Genetic Testing, it should be considered in the context of the family. Physicians should always consider, together with the parents or legal guardians, any possible harm before recommending Genetic Testing. However, the "best interest" approach is not an absolute one. In this regard, we note the recommendation of the European Society of Human Genetics (ESHG), indicating that Genetic Testing is permitted where it is necessary for the child's or adolescent's own health, or where the information would be imperative to diagnose the existence of

genetic disease in family members.⁹ Similar recommendations have been made by the Council of Europe and the UK HGC.^{10 11}

- 3.15 Genetic Testing is recommended or required in certain cases, for conditions 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.
- 3.16 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 Genetic Testing should be respected. While we recognise the general perception that a person reaches maturity when he or she attains the age of 21 years, we consider a child or adolescent to be mature if he or she is capable of understanding the purpose and implications of Genetic Testing. We consider the capacity of a child or an adolescent to participate in the consent process to be dependent on his or her level of maturity rather than some arbitrary age. In this connection, we note and agree with the WHO's statement: "An adequate explanation for a child's assent should describe the potential harms and benefits of testing in a simple manner appropriate to the child's age."¹²
- 3.17 Carrier Testing should generally be deferred until the child is mature or required to make reproductive decisions. He or she should then be fully informed of the benefits, risks and implications of the test. Predictive Testing in children for late-onset diseases where there is no available preventive intervention or treatment, or where the intervention or treatment is only available during adulthood, should likewise be deferred. However, there may be exceptional situations where Carrier and Predictive Testing may be considered in children. For instance, the parents of a child at risk may find it extremely difficult to bear the psychological burden of not knowing the genetic status of their child. We consider that in such circumstances, psychological and emotional burdens may prevent or have a negative impact on the provision of the best possible care to the child or the adolescent. A conceivable event is when parents overreact to the possibility of their child developing the disease. The physician should take into consideration unique family circumstances and have the discretion to decide, together with the parents, if it is in the best interest of the child or adolescent to conduct Genetic Testing. For mature children or adolescents, we reiterate that their decision to undergo or refuse Genetic Testing should be respected. We emphasise that in such circumstances, genetic counselling is particularly important.

⁹ European Society of Human Genetics, *Provision of Genetic Services in Europe: Current Practices and Issues* (2001).

¹⁰ Council of Europe, *Recommendation No. R(92)3 on Genetic Testing and Screening for Health Care Purposes* (1992).

¹¹ HGC, *Inside Information: Balancing Interests in the Use of Personal Genetic Data* (2002).

¹² WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Section 7.

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 till the child is mature or when required to make reproductive decisions. Predictive Testing should generally be deferred where there is no preventive intervention or treatment, or where intervention or treatment is only available and beneficial during adulthood. However, in exceptional circumstances, parents and the physician should have the discretion to decide regarding Carrier and Predictive Testing, and counselling should be an intrinsic part of the testing process.

The Mentally Impaired

- 3.18 Additional safeguards should also be considered for 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.¹³ In cases where mentally impaired persons are the most suitable candidates to undergo Genetic Testing for research, special safeguards should be in place to ensure that free and informed consent of persons having legal charge over them is obtained. In addition, the welfare and safety of the mentally impaired research subject must be ensured at all times and to the furthest extent possible.
- 3.19 In Singapore, the Supreme Court of Judicature Act empowers the High Court to appoint and control guardians and keepers of “idiots, mentally disordered persons and persons of unsound mind”.¹⁴ Hence, 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. 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 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.

Persons in Relationship of Dependence

- 3.20 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).

¹³ European Society of Human Genetics, *Provision of Genetic Services in Europe: Current Practices and Issues* (2001), at Recommendation 14.

¹⁴ *Supreme Court of Judicature Act* (Cap 322), Section 17(e).

- 3.21 In cases of dependent relationships, it is important to ensure that consent is both informed and freely given. 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.¹⁵ Similarly, 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 the same for fear of social or economic disadvantage as stated by the Human Genetics Society of Australasia.¹⁶ 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, any healthcare, employment, welfare, or other benefits that are currently provided or in prospect, will not be jeopardised.

Recommendation 6: Genetic Testing involving vulnerable persons should be conducted only if appropriate free and informed consent has been obtained. In the case of persons in special relationships, extra care should be taken to ensure that the consent is freely given. Clinical Genetic Testing should only be conducted if it is medically beneficial. Genetic Testing for research should only be conducted if the research is considered of sufficient importance and there is no appropriate alternative test population.

Confidentiality and Privacy

- 3.22 Healthcare professionals and researchers involved in Genetic Testing have an obligation to protect the confidentiality of Genetic Information. We note Article 7 of the 1997 *Universal Declaration on the Human Genome and Human Rights* of the United Nations Educational, Scientific and Cultural Organisation (UNESCO), which states: “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 stated: “Genetic data should only be used to advantage and empower an individual or family, and for better treatment or prevention of disease. Data relevant to health care should be collected and kept by medical geneticists in secure confidential files.”¹⁷ We agree with these statements and we are of the view that genetic test results should not be disclosed to third parties, including insurers and employers, without the free and informed consent of the individual.
- 3.23 Individuals should be provided information on how their privacy will be protected, before they consent to Genetic Testing. We agree with the HGC’s position that Genetic Information should generally not be obtained, held or communicated without the free and informed consent of the individual.¹⁸ Certain individuals may be unwilling to share or divulge their Genetic Information to their family members, other healthcare professionals or researchers. Hence, healthcare professionals and researchers should exercise special care in protecting the individual’s privacy and the confidentiality of such information. However, we reiterate our view that the ethical principle of privacy and confidentiality is not an absolute right in itself. There may be

¹⁵ Nuffield Council on Bioethics, *Genetic Screening: Ethical Issues* (1993), paragraph 4.27.

¹⁶ Human Genetics Society of Australasia, *Predictive Genetic Testing and Insurance* (1999).

¹⁷ WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Executive Summary.

¹⁸ HGC, *Inside Information: Balancing Interests in the Use of Personal Genetic Data* (2002), at page 42.

exceptional circumstances when Genetic Information may be disclosed notwithstanding its confidentiality or the individual's privacy. One such circumstance may be where the Genetic Information will be of direct benefit to society on the whole if its use in research is permissible. However, the reasons for the disclosure should be clearly explained to the individual concerned and his or her privacy should be safeguarded to the furthest extent possible (for instance, through anonymisation of the Genetic Information).

3.24 In addition, a situation may arise where the life of a third person will be endangered if the relevant Genetic Information is not 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 position¹⁹ whereby a physician's ethical duty of confidentiality to a patient can be overridden if the following conditions are satisfied concurrently:²⁰

- (a) Separate efforts by two healthcare professionals 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 the 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.

3.25 In the event that the above conditions are met, the physician should ensure that the patient concerned is aware that such a disclosure would take place and only relevant information would be disclosed.

Recommendation 7: Genetic test results should not be disclosed to third parties, including employers and insurers, without the free and informed consent of the individual.

¹⁹ NMEC Gene Technology Guidelines, Section 2.4.1.

²⁰ 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).

IV. Public Access to Genetic Testing

- 4.1 In Singapore, as in many other countries, access to Genetic Testing is mainly through healthcare professionals or healthcare institutions. Healthcare professionals are also responsible for interpreting the results of genetic tests, providing pre-test and post-test counselling to the patient regarding the value and implications of the test, the significance of the test results and, if need be, treatment and other follow-up actions.
- 4.2 Generally, an individual will not obtain direct access to Genetic Testing. However, recent developments in the public availability of Genetic Testing services indicate that it is possible for an individual to conduct Genetic Testing either on himself or herself, or on another person, in Singapore or overseas.

Direct Supply of Genetic Testing to the Public

- 4.3 Since the publication of the NMEC Gene Technology Guidelines, there have been important changes in the biomedical landscape in Singapore and elsewhere, especially in genetic testing devices and services. A conventional demand-supply evaluation is illustrative. On the demand-side, the Singaporean public is, on average, 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 and health-related matters may appear attractive. On the supply-side, advances in gene technology have simplified the usage of many devices for Genetic Testing and further 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 a significant number of Singaporeans may choose to by-pass medical professionals to obtain direct access to Genetic Testing for various reasons.
- 4.4 The commercialisation of Genetic Testing services and ensuing “direct supply” of Genetic Testing devices and services to the general public have become a growing concern in a number of countries. The UK HGC has recently carried out an extensive review of this development in its report *Genes Direct: Ensuring the Effective Oversight of Genetic Tests Supplied Directly to the Public* (2003). It found that devices and services for Genetic Testing are increasingly being marketed directly to the public in the UK and in some other developed countries. In such “direct supply”, the public gains access to Genetic Testing without the conventional face-to-face consultation with a medical professional so that, following a telephone call or electronic mail, an individual can post his or her tissue sample to a laboratory where the genetic analysis is performed. Alternatively, certain do-it-yourself genetic test devices can be procured over-the-counter or through the Internet. In the absence of a medical consultation, the HGC is concerned that the possible harms far outweigh the interest of an individual in obtaining information about himself or herself. Two possible “harms” from direct Genetic Testing were identified:
- (a) misinformation leading to a delay in seeking proper medical assistance or seeking unnecessary medical assistance; or

- (b) inappropriate Genetic Testing of children or other adults without proper consent.

- 4.5 We share the concerns of the HGC. If free 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 or devices 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. The predictive nature of Genetic Information discussed in Part II of this Consultation Paper contributes to the interpretive difficulties. Third, it is unrealistic to expect suppliers of Genetic Testing kits and devices to provide long-term counselling and other support services of satisfactory standards, particularly for the diagnosis and/or prediction of serious conditions. It should be noted that even if such devices and services are not intended for the diagnosis and/or prediction of serious conditions, they might nevertheless provide Genetic Information that is indicative of the possibility of some serious condition.
- 4.6 There is a further possibility of grave harm arising from inappropriate Genetic Testing. In recent years, the supply of Genetic Testing services to establish family relationships or historical roots is a growing industry and several such services are available through the Internet. While harm is unlikely to arise where such tests are voluntarily undertaken by fully informed adults, the same cannot be said if children or unsuspecting adults are tested. The knowledge of mistaken family ties can exert a heavy psychological burden on adults, let alone children who will have to come to terms with this information without proper counselling and support. The broader impact on the relationship between the individual and his or her family members is likely to complicate matters further.
- 4.7 We envisage another possible “harm” in the potential discrimination of individuals whose Genetic Information may be acquired by third parties. While insurers or employers do not have the right to require genetic tests to be undertaken by a potential client or employee, there is presently nothing to prevent them from requiring the test results to be disclosed where available. It is arguable that disclosure of a genetic condition by a person seeking to be insured becomes necessary if he or she is aware of this condition through Genetic Testing, even if the test was conducted for some other purpose. Failure to disclose this condition may render the insurance legally ineffective, although disclosure may lead to higher premiums or preclusion from insurance coverage altogether. We will continue to review these complex issues which presently cannot be satisfactorily resolved and will consider them separately.
- 4.8 The NMEC has strongly discouraged genetic testing by manufacturers and suppliers of genetic testing kits, unless it is conducted under the direction of a physician.²¹ However, we are of the view that a more comprehensive system of control over public access should be devised in light of recent developments in gene technology and the consequences that they entail. While it is not necessary to restrict access to all kinds of Genetic Testing, we think that it is timely to develop an appropriate regulatory framework for the oversight of Genetic Testing that is likely to cause serious harm to the public if freely accessible.

²¹ NMEC Gene Technology Guidelines, Section 3.2.1.

- 4.9 There is currently no specific legislation regulating access to, or supply of, Genetic Testing devices and services. The Centre for Medical Device Regulation (CMDR) of the Health Sciences Authority (HSA) 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.
- 4.10 We recommend that a comprehensive regulatory framework for the direct supply of genetic tests to the public be established, taking into consideration the likely harm that may arise if access is not controlled. Genetic tests that are predictive of serious health conditions should be accessible only through qualified healthcare professionals.
- 4.11 We emphasise that genetic tests, especially those associated with possible serious health conditions, should generally be regarded as part of medical service. For a similar reason, the advertising of direct genetic tests to the public should be strongly discouraged.

Recommendation 8: Genetic Testing should be conducted through the intermediation of a qualified healthcare professional. Accordingly, the advertising of genetic tests by manufacturers or suppliers to the public is strongly discouraged. A comprehensive regulatory framework should be established for access to Genetic Testing services. Genetic tests that provide predictive health information should not be directly offered to the public.

Prohibition Against Involuntary Genetic Testing

- 4.12 It is difficult to regulate access where Genetic Testing devices and services may be easily procured via the Internet. We are concerned that such devices and services may be used on individuals without their consent as it is relatively easy for body samples to be taken from individuals without their knowledge, let alone their consent. In view of the harms that may arise from the misuse of Genetic Information, we are strongly against the taking and testing of an individual's tissues without consent. 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."²² This recommendation has since been accepted by the UK legislature and enacted as law in November 2004.²³ We regard it as timely for Singapore to adopt a similar legislation.

Recommendation 9: The non-consensual or deceitful obtaining of body samples for the purpose of Genetic Testing should be legally prohibited.

²² UK HGC, *Inside Information: Balancing Interests in the Use of Personal Genetic Data* (2002), at paragraph 3.60.

²³ *Human Tissue Act* 2004, Section 45 (Non-consensual analysis of DNA)

V. Specific Ethical Considerations for Human Genetics Research

- 5.1 Human genetics research is the study of genes and how they are associated with health and disease. It may involve processes leading to more effective methods for the diagnosis and treatment of genetic diseases or the development of genetic tests for clinical use. Human genetics research enhances our understanding of the genetic basis of disease and how genetic and environmental factors influence one's health. Hence, its primary objective is not to provide research participants or their families with specific information about their genetic status or health.
- 5.2 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 genetics 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.
- 5.3 The overall ethical framework for human biomedical research has been set out in our previous reports. This framework applies to all biomedical research that involves human subjects or the use of any kind of human biological materials, including solid body tissues, organs, foetuses, blood and other bodily fluids and their derivatives, cord blood, embryos, gametes (sperm or eggs) or any part or derivative of such materials, and whether they are derived from living or cadaveric donors.
- 5.4 Human genetics research may involve research subjects, tissue samples or genetic information derived from genetic tests. As genetic materials are shared by biological relatives, genetic information derived from research using a person's tissue will have implications extending to his or her relatives. In addition to ethical considerations that apply to all research involving humans, genetic research poses unique ethical issues arising from the shared nature of genes and genetic information. The misuse of genetic information may lead to harm, including stigmatisation and unfair discrimination. Thus, privacy and confidentiality issues are important considerations for researchers involved in human genetics research.
- 5.5 In our IRB Guidelines Report, we emphasised the critical role that researchers, institutions and Institutional Review Boards (IRBs) play in ensuring the protection of the safety, health, dignity, welfare and privacy of research subjects.
- 5.6 Researchers conducting human genetics research must also observe the following:
 - (a) Obtain the approval of a research ethics committee (or IRB) before proceeding with the research;
 - (b) Seek the free and informed consent of the research subjects. Information to be provided to research subjects prior to seeking consent is outlined in Part III of this Paper. Where an attending physician is also the researcher, it may be necessary for consent to be taken separately through an independent third party to ensure the voluntary involvement of the individual. Where the research

involves human tissue that have been appropriately anonymised or can no longer be traced to an individual (such as legacy tissues), the consent requirement may be waived. However, ethics review of the research project is still required;

- (c) Protect the privacy of research participants and the confidentiality of the genetic information so derived;
- (d) When vulnerable people are involved, the principle of acting in their best interest applies; and
- (e) When the research involves using human embryos, written approval from the Ministry of Health (MOH) is required in addition to approval by the IRB. No research should be performed on any embryos more than 14 days old.

VI. Specific Ethical Considerations for Clinical Genetic Testing

- 6.1 Clinical Genetic Testing is usually carried out as part of the health management or treatment of an individual. As such, the ethical management of Clinical Genetic Testing should not differ significantly from conventional medical service. While Genetic Information derived from Clinical Genetic Testing may be utilised in research that is independent of any human subject, such as research using genetic databases and medical registries, the ethical, legal and social issues arising from such research will be addressed in a separate paper.
- 6.2 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.”²⁴ In addition, the choice of a genetic test should be based on the individual’s best interest. In the following section, we discuss ethical issues related to specific types of genetic tests.

Section A: Specific Ethical Considerations

Carrier Testing

- 6.3 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.
- 6.4 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 C below.

Preimplantation Genetic Diagnosis

- 6.5 Preimplantation genetic diagnosis (PGD) is a procedure whereby early embryos created by *in vitro* fertilisation (IVF) are evaluated to determine the presence of one or more genetic conditions. It is then followed by the selection and implantation of unaffected embryos into the uterus. PGD was developed following the availability of IVF and new genetic testing techniques, primarily to help couples where one or both partners are known carriers of genetic disorders to have healthy children. Before this procedure was developed, PND and selective termination of an affected pregnancy were used to enable “at-risk” couples to have healthy children. With PGD, these couples have the option of starting out with unaffected pregnancies, thus avoiding the need to consider selective termination of an affected pregnancy subsequently.

²⁴ NMEC Gene Technology Guidelines, Section 3.1.1.

- 6.6 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 PGD services. At present PGD can be used to screen for more than 100 genetic conditions, including 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.
- 6.7 Although PGD is currently not available in Singapore as a clinical service, it is available in more than 100 clinics in many countries including the US, the UK, India, Israel, Japan and South Korea. In Cyprus and Greece, PND and PGD have been applied for the prevention of haemoglobin disorders and the number of children born with β -thalassaemia major has since been drastically reduced.
- 6.8 PGD has most commonly been recommended for patients with:
- (a) a child confirmed with a genetic disease and with an increased risk of having another child with the same disease;
 - (b) confirmed carrier status (in one or both partners) for a serious genetic condition; or
 - (c) advanced maternal age.
- 6.9 PGD is a technically demanding procedure. Although it presents an option for some couples to conceive a child without a 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 4748 PGD attempts and 754 successful pregnancies, led to the conclusion that PGD is safe.²⁵
- 6.10 As PGD is a special form of Genetic Testing connected with IVF, it should be viewed as a technology to help couples who do not wish their children to be affected by a genetic disorder. We do not dispute the generally accepted assumption that parents will only wish to act in the best interest of their children. There is no reason to believe that this assumption should not apply generally to couples in reproductive decisions.
- 6.11 In a multi-cultural and multi-religious society, views on the ethics of PGD in Singapore are likely to be as diverse as views on human therapeutic cloning and embryonic stem cell research. Indeed, a segment of the medical community and the public may not wish to be involved in PGD, in the same way as they avoid involvement in human therapeutic cloning and embryonic stem cell research. Such conscientious objection should be respected and no one should be under a duty to

²⁵ Y. Verlinsky 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)

undergo or perform PGD. However, it should be equally open for other members of the medical community and the greater public who do not hold the same view to participate in, or have recourse to, PGD in ways that are not harmful to the moral and social fabric of Singapore on the whole.

- 6.12 Although the intent for which PGD is employed differs significantly from that in human cloning and embryonic stem cell research, the possible compromise of the sanctity of life represented in an embryo touches one of the central moral and religious concerns of these technologies. Other ethical concerns relate to the possible use of PGD for trait selection and the danger of leading society closer to eugenics. It is feared that PGD may be used to select for or against certain non-medical traits for the “enhancement” of the newborn, which thereby devalue and alter the way in which society views those who nonetheless possess the “undesirable” 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 will be further stratified into the economically rich and genetically desirable at one end, and the economically poor and genetically unaltered at the other end.
- 6.13 We acknowledge these concerns and attempt to address them by drawing on the two broad guiding principles of ‘justness’ and ‘sustainability’, which were first articulated and adopted in our Human Stem Cell Report. 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 also advance the concepts of beneficence and non-maleficence. They in turn encourage the pursuit of social benefits along-side efforts to avoid or ameliorate potential harm.
- 6.14 From the experiences of countries where PGD is practiced, 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 America 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 practice of PGD also suggest that it is possible to guard against serious violations of moral and ethical standards through careful and effective regulation.
- 6.15 We are of the view that PGD should be allowed, provided that it is subject to control by a relevant authority and limited to serious medical conditions. The relevant authority should license, monitor and assess PGD to ensure that it is employed within legal and ethical limits. As such, the authority should issue regulations and guidelines for this purpose.

Recommendation 10: Preimplantation genetic diagnosis is permissible provided that it is subject to control by a relevant authority and limited to serious medical conditions. The relevant authority should license, monitor and assess preimplantation genetic diagnosis to ensure that it is employed within legal and ethical limits.

- 6.16 We do not consider it to be acceptable at the present time to use PGD in trait selection on non-medical grounds. A child who is selected for a particular trait such as greater mental or physical potential thought to be in some manner superior may experience increased pressure to fulfil that genetic “potential” in his or her parents’ expectations. The situation is worsened if the child fails to attain these “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.”²⁶ 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 the parental responsibility to care for their 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 relationship between parents and their children, and this interest far outweighs the desire of parents to select for certain traits in their children for non-medical reasons. There may be situations where a couple may wish to implant an affected embryo for “lifestyle” reasons. In a recent case in the US, a deaf couple has deliberately conceived a deaf child because they do not consider deafness as a disability. We are of the view that such use of PGD is unfair to the child and is, accordingly, unacceptable and should be prohibited.
- 6.17 It is technically possible to use PGD 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 a family, personal preference, or certain social, cultural, religious or economic motivations. We agree with the position of the International Bioethics Committee of the UNESCO that sex selection for non-medical reasons is generally unethical. Such selection tends to promote gender stereotyping and discrimination.

Recommendation 11: Use of preimplantation genetic diagnosis for sex selection and the selection of certain desired traits for non-medical reasons should be prohibited.

- 6.18 It is beyond our remit and premature at the present time to determine the extent that PGD should be made available to couples who are unable to afford this means of assisted conception. It is more appropriate for the relevant authority to deliberate on this issue, taking into account the economic consequences, at a time it determines to be appropriate.

²⁶ Nuffield Council on Bioethics, *Genetics and Human Behaviour: The Ethical Context* (2002), at page 154.

Preimplantation Tissue Typing

- 6.19 The UK is one of a few countries that have moved beyond the impasse of 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 birth of children with genetic disorders. 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 a potential tissue donor for a sick sibling. Preimplantation tissue typing (PTT) is described by the HFEA as “a new technique which allows the selection of embryos in order to bring about the birth of a child who can provide a matched tissue donation to an existing sibling, either as the sole clinical objective or in combination with [PGD] to avoid a serious genetic condition in the resulting child.”²⁷ We find the experience of the HFEA with PTT to be instructive.
- 6.20 In 2001, the HFEA adopted a cautious approach and permitted PTT on a case-by-case basis under the following conditions: ²⁸
- (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 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 match.
- 6.21 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 tissue 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

²⁷ HFEA Report: *PreImplantation Tissue Typing* (2004) at page 1.

²⁸ HFEA Report: *PreImplantation Tissue Typing* (2004) at page 2.

child.”²⁹ This extension was made after the HFEA had carefully considered the medical, psychological and emotional implications for children and their families, and the safety of the technique performed in the past three years.

- 6.22 Ethical concerns have been expressed over PTT in that children may be used as a means to an end rather than having children for no other purpose. We note that such concerns are not supported by evidence. 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 unanticipated consequence of sexual pleasure or for some selfish purpose.
- 6.23 We have earlier expressed our view that the conduct of PGD 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 generally 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 sibling 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 12: 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

- 6.24 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. We note that germline genetic modification may also be brought about inadvertently in gene therapy or through other experimental techniques.
- 6.25 While the technologies capable of rendering germline genetic modification do not fall within our definition of Genetic Testing, we are of the view that 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 13: Clinical practice of germline genetic modification should not be allowed at this time.

²⁹ HFEA Report: *PreImplantation Tissue Typing* (2004) at page 10.

Prenatal Genetic Diagnosis

- 6.26 Prenatal genetic diagnosis (PND) 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 of having a baby with a genetic disorder include:
- (a) advanced maternal age;
 - (b) 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) history of a previous child affected by a serious growth, developmental or health problem.
- 6.27 Prenatal screening precedes PND 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 at 12 and 22 weeks of pregnancy to detect structural abnormalities, which may indicate possible genetic defects in the baby.
- 6.28 In Singapore, prenatal screening in conjunction with pre- and post-test counselling is part of the routine prenatal care and specific diagnostic tests are performed when indicated. PND can be carried out for various genetic conditions, including Down’s syndrome, thalassaemia and haemophilia. If prenatal screening tests indicate that the foetus is likely to be affected with a disorder, PND will be offered to verify the presence or absence of a genetic disorder.
- 6.29 The range of available prenatal genetic tests is increasing as more knowledge is gained about genetic disorders through research. PND 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 this and other risks, and their consent is obtained prior to the tests being carried out.

- 6.30 If PND indicates that the foetus is or will likely be affected with a genetic disorder, the couple should be counselled about the disorder and its implications, in order to make an informed decision as to whether or not to continue with the pregnancy.
- 6.31 PND for late-onset diseases poses difficult ethical problems. If parents are strongly against abortion, the information derived from the PND provides no benefits to them or the child and may even cause the child to suffer from stigmatisation and discrimination by family and society. Hence, we propose that performing a test for late-onset diseases on a foetus should be discouraged. However, if parents are undecided and would like to consider abortion, it may be appropriate to respect their autonomy.

Recommendation 14: Prenatal genetic diagnosis should be voluntary, conducted with informed consent and with appropriate pre- and post-test counselling. The prospective parents' choice of whether a genetic disorder warrants a prenatal genetic diagnosis or termination of the pregnancy should be respected.

- 6.32 It is possible to employ PND for gender or trait selection for non-medical purposes. For reasons similar to those that we have proffered in relation to PGD, we are of the opinion that PND for gender or trait selection (whether physical, social or psychological characteristics or normal physical variations) should not be allowed. The practice of PND is essentially confined to serious genetic disorders and we consider this to be appropriate. We recommend that appropriate professional bodies prescribe detailed ethical guidelines on the practice of PND for their members.

Recommendation 15: Prenatal genetic diagnosis should be limited to serious genetic diseases. The use of prenatal genetic diagnosis for gender selection, apart from sex-linked disorders is unacceptable. Similarly, it is unacceptable to use prenatal genetic diagnosis for the selection of any physical, social or psychological characteristics or normal physical variations.

Recommendation 16: The appropriate professional bodies should prescribe detailed ethical guidelines on the practice of prenatal genetic diagnosis for their members.

Predictive Testing

- 6.33 Predictive testing identifies healthy individuals who have inherited a gene for a late-onset disease, which is a disease that normally becomes symptomatic in adulthood, although there are cases where symptoms may arise during late childhood.
- 6.34 Predictive tests can be classified into two categories based on the predictive nature 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, which are due to defects in single genes.

- (b) *Susceptibility (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 generally due to the interaction of genes and the environment. 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.
- 6.35 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 or predisposition tests will increase.
- 6.36 Testing for a late-onset disease before an individual develops any symptoms allows the individual 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.
- 6.37 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.
- 6.38 Susceptibility testing is at the moment not in clinical practice to any extent, largely because such tests have not been sufficiently developed and validated. Therefore, susceptibility testing should not be applied clinically unless there is unequivocal empirical evidence of validity and utility.
- 6.39 Predictive Genetic Information may be burdensome or psychologically traumatic given the uncertainty of the disease. We reiterate the importance of voluntariness and free and informed consent in genetic screening and further note NMEC's recommendation: "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."³⁰

Recommendation 17: Presymptomatic testing should be available for adults at risk who request it, even in the absence of treatment, after proper counselling and informed consent.

³⁰ NMEC Gene Technology Guidelines, Section 2.2.1 (b).

Recommendation 18: Susceptibility testing should not be applied clinically unless there is unequivocal empirical evidence of validity and utility.

Genetic Screening

- 6.40 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.”³¹ The main purpose of genetic screening is to prevent a disease or minimise morbidity and mortality through early diagnosis and treatment.
- 6.41 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.
- 6.42 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.
- 6.43 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 of the cases of which are likely to be genetic in origin. These routine newborn and prenatal screening programmes have become socially acceptable in Singapore and hence informed consent is not explicitly taken. However, with new tests being developed, leading to an expansion of screening programmes, we recommend that free and informed consent should be obtained. The process of giving information and obtaining consent should be tailored to the level of risk and benefit to the individual and the society. For newborn screening programmes which have well-established scientific and clinical validity, the process of giving information and obtaining consent should not be too complex to the extent that it discourages participation in such programmes. The healthcare professional should explain the reasons for performing the genetic tests to parents before taking a blood sample from the baby. Institutions may consider providing additional information through means such as pamphlets for mothers or large notices displayed in clinics. Testing should not proceed if parents object to the tests after being provided with adequate information.

Recommendation 19: In genetic screening programmes, the appropriate free and informed consent should be obtained from the individual to be tested or parents (or legally designated persons) as the case may be. 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.

³¹ WHO, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services* (1998), Section 6.

Section B. Ensuring the Proper Derivation and Interpretation of Genetic Information in Clinical Genetic Testing

- 6.44 In this Consultation Paper, 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, and are a pre-condition to accurate interpretation.
- 6.45 Accurate interpretation of Genetic Information presents one of the greatest challenges in 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 very much an art as it is a science. Skill at interpretation depends on experience as well as up-to-date knowledge of the field.
- 6.46 As with other medical information, Genetic Information is likely to have psychological impact on patients. However, this impact may be greater if the Genetic Information suggests that a patient has a predisposition to developing a serious condition some time in the future and/or the condition is likely to affect his or her genetic relatives. A predisposition indicates that the patient has a risk of developing the genetic condition, although he or she may eventually not develop the disease. Where other family members may also be at risk of developing the genetic condition, the patient will have the additional burden of having to decide if this risk should be disclosed to them. Family members who are not affected by the genetic condition may nevertheless be affected psychologically (such as the condition of “survivor’s guilt”). This is further complicated where the patient is a member of an identical twin or a triplet. Genetic Testing of the patient will at the same time reveal the genetic status of the other member(s). In this case, there may be a conflict of wishes. For instance, the patient may wish to know the Genetic Information but his or her twin may not. It is difficult to reach a common position whereby the patient’s right to know may be balanced against his or her twin’s right ‘not to know’, since both wishes should be respected. Adding to all these difficulties are broader social implications that may arise, such as reproductive choices that a patient may be faced with. 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

- 6.47 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 as to 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 are concerned that such direct access may not be in the best interest of the individual as there is no assurance of the quality of the test result.

- 6.48 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 generally binding standards for Genetic Testing that is 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, as well as the accuracy of the Genetic Information thereby derived.
- 6.49 In the US, the Clinical Laboratory Improvement Amendments of 1988 establishes quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of the test results. In addition, professionals involved in Genetic Testing are usually certified by the American Board of Medical Genetics (ABMG) and/or are members of the American College of Medical Genetics (ACMG). ABMG and ACMG also regularly issue policy statements on important issues in Genetic Testing. 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.³² The Australian NHMRC stated that Clinical Genetic Testing should be performed only by accredited laboratories.³³ Laboratories are required to be particularly sensitive to the possibility of error in the performance of genetic test.
- 6.50 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.
- 6.51 We propose that all laboratories conducting Clinical Genetic Tests should be accredited by an accreditation body designated by the relevant authority, based on standards as it considers appropriate. This is necessary to maintain a high quality of Genetic Information thereby derived, which is in turn fundamental in safeguarding the welfare of tested individuals.

Recommendation 20: All laboratories conducting Clinical Genetic Tests should be accredited by an accreditation body designated by the relevant authority, based on standards it considers appropriate.

³² UK Advisory Committee on Genetic Testing, *Report on Genetic Testing for Late-onset Disorders* (1998) at pages 19 and 20.

³³ NHMRC, *Ethical Aspects of Human Genetic Testing: an Information Paper* (2000).

Results Interpretation

- 6.52 There are several factors that affect the accurate interpretation of Genetic Information. These include (a) integrity of the diagnostic chain, (b) reliability of test methods, (c) technical competence of laboratory technicians, (d) ability of the individual to understand, and (e) up-to-date knowledge of the interpreter. 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 interpreter of the Genetic Information.
- 6.53 The interpretation of 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. As we have discussed, healthcare professionals are to ensure that sound interpretation is provided to patients, and so healthcare professionals should be appropriately qualified or sufficiently experienced. Misinterpretation of results or misdiagnosis may lead to psychological trauma, and unnecessary or inappropriate therapeutic interventions or changes to lifestyle for the patient and his or her family.
- 6.54 It should also be highlighted that genetic counselling should be provided in a timely manner. As far as practicable, there should be no delay in counselling following the disclosure of the test result to the patient, so as to help the patient cope with any resultant psychological impact or emotional stress. Given these, together with the myriad of medical, psychological, social, financial and legal implications that may arise, sound and effective pre- and post-test counselling is particularly critical and should always be timely and integral to the practice of Genetic Testing.

Recommendation 21: Interpretation of genetic test results should only be performed by healthcare professionals who are appropriately qualified or have sufficient experience. Genetic counselling should immediately follow the disclosure of the test result, particularly if the test result is not favourable.

Section C. Genetic Counselling

- 6.55 We have emphasised at various points in this Consultation Paper the importance of genetic counselling in the conduct of Genetic Testing. Genetic counselling should seek to achieve the following objectives:
- (a) provide sufficient and unbiased information, as well as appropriate support, to enable full and informed choices to be exercised; and
 - (b) assist the patient and his or her family members cope with the situation.
- 6.56 In genetic counselling, information provided should be adequate and comprehensible to the patient. The patient should always be given sufficient time to consider the available options and the opportunity to clarify doubts. In addition, counselling should be conducted in an empathetic manner and should be non-directive, especially if the condition is one where treatment is presently not available. Whenever practicable, counselling should be done in a face-to-face meeting.

- 6.57 We have indicated that free and 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, we consider counselling to be intrinsic to the consent process. Taking into account the recommendations provided by the NMEC on this matter, we recommend that the following considerations be taken into account in pre-test genetic counselling:
- (a) nature of the condition to be tested;
 - (b) potential consequences of not being tested;
 - (c) foreseeable consequences as a result of testing, including implications for family members, and available support;
 - (d) test reliability and clinical validity, emphasising that not all mutations are detectable, that some mutations are of uncertain significance, and that results indicate probability, not certainty, of developing the disease;
 - (e) the nature and efficacy of any interventions that might follow after the genetic testing, including the quality of evidence concerning the efficacy of treatments, or other strategies for avoiding the consequences of mutations that might be detected;
 - (f) type of sample required, test procedure and possible risks;
 - (g) turnaround time and how the results will be conveyed to the patient;
 - (h) treatment or management options; and
 - (i) alternatives to Genetic Testing and their pros and cons.
- 6.58 Where appropriate, it may be beneficial to also take into consideration 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;
 - (c) 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; and
 - (d) assure patient of confidentiality of test result, but explain circumstances that might require disclosure of the patient's test result (if necessary).

Recommendation 22: Genetic counselling should be offered to all individuals prior to and after they undergo Genetic Testing.

Recommendation 23: 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.

Post-test Follow-up

6.59 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 recommend that the following considerations be undertaken:

- (a) discussion on the implications of the genetic test result, whether the result is a positive, negative or inconclusive one;
- (b) treatment or management, and/or support options;
- (c) possible implications for family members;
- (d) address psychological, social and ethical issues or concerns;
- (e) requirement or obligation to disclose the Genetic Information to a third party (if any); and
- (f) management of Genetic Information.

6.60 Genetic Information may reveal cases that require long term follow-up attention. In such cases, the genetic counsellor concerned is expected to:

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

6.61 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.

Professional Diversification and Development

6.62 Currently in Singapore, there is no uniform practice or standards applicable to genetic counselling, which is usually carried out by physicians. However, genetic counselling is a time consuming process. Thus, it may not be practical for genetic counselling to be solely conducted by physicians. Furthermore, in light of rapid development in

medical genetics, specialised knowledge may be required. This may mean that certain individuals who are not physicians may be better skilled at conducting genetic counselling. Such individuals may be medical geneticists, nurses or other healthcare therapists. Individuals involved in genetic counselling must be committed and prepared to invest the time and should possess up-to-date knowledge of gene technology. However, it should be noted that the responsibility for overseeing the case, including counselling, rests ultimately on physicians, as they carry ultimate clinical responsibility for patients.

- 6.63 The relevant authority should consider providing professional training in medical genetics and counselling to scientific and healthcare professionals working in this field.

Recommendation 24: Individuals involved in genetic counselling should possess up-to-date knowledge of medical genetics and should be appropriately trained in both medical genetics and counselling.

VII. Summary of Recommendations

Genetic Information

Recommendation 1:

Genetic Information derived from Clinical Genetic Testing should be confined to a healthcare context, owing to its complex nature and need for professional input. Accordingly, it should be regarded as medical information and the highest ethical standard should be applied 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 and conducted only after free and informed consent has been obtained. Consent must be based on sufficient information, which includes the nature, purpose, risks and implications of the test. Consent should also be obtained for future clinical and/or research use of tissue specimens.

Recommendation 4:

An individual should be informed of the test result without undue delay unless he or she has clearly indicated the wish not to know. However, the test results of newborn babies and children for treatable conditions should be disclosed. In research involving Genetic Testing, researchers should inform the individual prior to participation in the research, whether the Genetic Information so derived will be disclosed to him or her.

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 till the child is mature or when required to make reproductive decisions. Predictive Testing should generally be deferred where there is no preventive intervention or treatment, or where intervention or treatment is only available and beneficial during adulthood. However, in exceptional circumstances, parents and the physician should have the discretion to decide regarding Carrier and Predictive Testing, and genetic counselling should be an intrinsic part of the testing process.

Recommendation 6:

Genetic Testing involving vulnerable persons should be conducted only if appropriate free and informed consent has been obtained. In the case of persons in special relationships, extra care should be taken to ensure that the consent is freely given. Clinical Genetic Testing should only be conducted if it is medically beneficial. Genetic Testing for research should only be conducted if the research is considered of sufficient importance and there is no appropriate alternative test population.

Privacy and Public Access to Genetic Testing

Recommendation 7:

Genetic test results should not be disclosed to third parties, including employers and insurers, without the free and informed consent of the individual.

Recommendation 8:

Genetic Testing should be conducted through the intermediation of a qualified healthcare professional. Accordingly, the advertising of genetic tests by manufacturers or suppliers to the public is strongly discouraged. A comprehensive regulatory framework should be established for access to Genetic Testing services. Genetic tests that provide predictive health information should not be directly offered to the public.

Recommendation 9:

The non-consensual or deceitful obtaining of body samples for the purpose of Genetic Testing should be legally prohibited.

Preimplantation Genetic Testing

Recommendation 10:

Preimplantation genetic diagnosis is permissible provided that it is subject to control by a relevant authority and limited to serious medical conditions. The relevant authority should license, monitor and assess preimplantation genetic diagnosis to ensure that it is employed within legal and ethical limits.

Recommendation 11:

Use of preimplantation genetic diagnosis for sex selection and the selection of certain desired traits for non-medical reasons should be prohibited.

Recommendation 12:

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 13:

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

Prenatal Genetic Diagnosis

Recommendation 14:

Prenatal genetic diagnosis should be voluntary, conducted with informed consent and with appropriate pre- and post-test counselling. The prospective parents' choice of whether a genetic disorder warrants a prenatal genetic diagnosis or termination of the pregnancy should be respected.

Recommendation 15:

Prenatal genetic diagnosis should be limited to serious genetic diseases. The use of prenatal genetic diagnosis for gender selection, apart from sex-linked disorders is unacceptable. Similarly, it is unacceptable to use prenatal genetic diagnosis for the selection of any physical, social or psychological characteristics or normal physical variations.

Recommendation 16:

The appropriate professional bodies should prescribe detailed ethical guidelines on the practice of prenatal genetic diagnosis for their members.

*Predictive Testing***Recommendation 17:**

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 18:

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

*Genetic Screening***Recommendation 19:**

In genetic screening programmes, the appropriate free and informed consent should be obtained from the individual to be tested or parents (or legally designated persons) as the case may be. 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 20:**

All laboratories conducting Clinical Genetic Tests should be accredited by an accreditation body designated by the relevant authority, based on standards it considers appropriate.

Recommendation 21:

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

*Genetic Counselling***Recommendation 22:**

Genetic counselling should be offered to all individuals prior to and after they undergo Genetic Testing.

Recommendation 23:

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 Development

Recommendation 24:

Individuals involved in genetic counselling should possess up-to-date knowledge of medical genetics and should be appropriately trained in both medical genetics and counselling.

HUMAN GENETICS SUBCOMMITTEE

Chairman

Associate Professor Terry Kaan Sheung-Hung
Faculty of Law
National University of Singapore

Members

Professor Yap Hui Kim
Senior Consultant, National University Hospital
Professor in Paediatrics, National University of Singapore

Associate Professor Samuel Chong
Department of Paediatrics
National University of Singapore

Associate Professor Chia Kee Seng (from September 2004)
Department of Community, Occupational and Family Medicine
Faculty of Medicine
National University of Singapore

Dr Denise Goh Li Meng (from September 2004)
Consultant
The Children's Medical Institute
National University Hospital

Dr Lee Soo Chin (from September 2004)
Consultant
Department of Haematology-Oncology
National University Hospital

Mr Charles Lim Aeng Cheng (from January 2005)
Principal Senior State Counsel (Law Reform and Revision)
Attorney-General's Chambers

Mr Jeffrey Chan Wah Teck (January 2001 to December 2004)
Principal Senior State Counsel (Civil)
Attorney-General's Chambers

ABBREVIATIONS

ABMG	American Board of Medical Genetics
ACMG	American College of Medical Genetics
AHEC	Australian Health Ethics Committee
ALRC	Australian Law Reform Commission
BAC	Bioethics Advisory Committee (Singapore)
CAP	College of American Pathologists
CMDR	Centre for Medical Device Regulation
DNA	Deoxyribonucleic acid
ESHG	European Society of Human Genetics
HFEA	Human Fertilisation and Embryology Authority (UK)
HGC	Human Genetics Commission (UK)
HGS	Human Genetics Subcommittee (BAC)
HSA	Health Sciences Authority
IRB	Institutional Review Board
IVF	<i>In vitro</i> fertilisation
MOH	Ministry of Health (Singapore)
NMEC	National Medical Ethics Committee (Singapore)
PGD	Preimplantation genetic diagnosis
PND	Prenatal diagnosis (a.k.a. Prenatal genetic diagnosis)
PTT	Preimplantation tissue typing
RNA	Ribonucleic acid
SAC	Singapore Accreditation Council
SINGLAS	Singapore Laboratory Accreditation Scheme
UNESCO	United Nations Educational, Scientific and Cultural Organisation
WHO	World Health Organisation

GLOSSARY

Assisted reproduction	The use of clinical and laboratory techniques to increase chances of conceiving a baby. An example is <i>in vitro</i> fertilisation, or IVF.
Asymptomatic	Having no signs or symptoms of disease.
Alzheimer's disease	A degenerative brain disease of unknown cause that is the most common form of dementia, that usually starts in late middle age or in old age as a memory loss for recent events spreading to memories for more distant events and progressing over the course of five to ten years to a profound intellectual decline characterized by dementia and personal helplessness, and that is marked histologically by the degeneration of brain neurons especially in the cerebral cortex and by the presence of neurofibrillary tangles and plaques containing beta-amyloid.*
Carrier	Someone who carries only one copy of a mutant gene in question. A carrier usually shows no symptoms or very mild symptoms for the disease gene that he or she carries, as two copies of the disease gene are required for a full-blown manifestation of the disease. A carrier has the risk of transmitting the mutant gene to the next generation.
Chromosome	Structure in a cell that contains DNA and proteins. With the exception of sperm and egg cells and red blood cells, each human cell with a nucleus contains two sets of chromosomes, one inherited from the mother and one from the father. Each set consists of 23 chromosomes, 22 autosomes (non-sex chromosomes) and one sex chromosome, either X or Y. These human cells thus contain 46 chromosomes and are termed diploid. A male diploid cell has an X and a Y chromosome, whereas a female diploid cell contains two X chromosomes. Sperm and egg cells are haploid and contain only 23 chromosomes. Each chromosome contains genes arranged linearly, and is made up of proteins and DNA .
Clinical validity	The accuracy with which a test determines the presence or absence of a clinical condition or which a test predicts a predisposition.
Congenital	Existing at or dating from birth.
Diagnostic chain	The chain of events or procedures that begins from the collection of sample and ends with a diagnosis based on analyses of the sample.
DNA	DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms. Each DNA is a linear molecule made up of nucleotides or bases. There are four different types of bases in DNA and the order in which these bases are arranged determines the protein to be formed.

Each individual's body contains an identical set of DNA in nearly all of its cells. A great fraction of cellular DNA is located in the cell nucleus (where it is called nuclear DNA), while the remaining can be found in the mitochondria (where it is called mitochondrial DNA).

Down's syndrome A congenital condition characterized by moderate to severe mental retardation, slanting eyes, a broad short skull, broad hands with short fingers, and by trisomy of the human chromosome numbered 21.*

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

Early-onset The early manifestation or occurrence of a disease normally characterised by delayed development. For example, Alzheimer's disease usually occurs in late middle-age years or old age, but early-onset Alzheimer's disease may occur in early middle-age years.

Familial adenomatous polyposis A disease of the large intestine that is marked by the formation especially in the colon and rectum of numerous adenomatous polyps which typically become malignant if left untreated, that may be either asymptomatic or accompanied by diarrhoea or bleeding, and that is inherited as an autosomal dominant trait.*

Gene A gene is the basic physical and functional unit of heredity. It is made up of DNA which carries instructions to make molecules of **RNA** and proteins. Every person has two copies of each gene, one inherited from each parent. Most genes are commonly found in all people, but about one percent of each person's **genome** is slightly different from that of another. The slight difference is what makes people physically unique.

Gene therapy Treatment of a genetic disorder by inserting functional genes in order to replace, supplement, or manipulate the expression of non-functional or abnormal genes. Gene therapy has thus far only advanced into clinical trials and is not yet an established therapy.

Genome The complete set of genetic instructions for making an organism is called its genome. The genome contains the master blueprint for all cellular structures and activities for the lifetime of the cell or organism. Found in every nucleus of a person's many trillions of cells, the human genome consists of tightly coiled threads of DNA and associated protein molecules, organised into structures called chromosomes.

Genotype A specific set of alleles (variant forms of a gene) at particular position on the chromosome.

Germ cell (Germline)	The cell (or cell line) from which sperm and egg (gametes) are derived.
Glucose-6-phosphate dehydrogenase deficiency	A hereditary metabolic disorder affecting red blood cells that is controlled by a variable gene on the X chromosome, that is characterized by a deficiency of glucose-6-phosphate dehydrogenase conferring marked susceptibility to haemolytic anaemia which may be chronic, episodic, or induced by certain foods (as broad beans) or drugs (as primaquine), and that occurs especially in individuals of Mediterranean or African descent.*
Haemoglobin	The substance inside red blood cells which binds oxygen molecules and transport them from the lungs to other tissues.
Haemophilia	A sex-linked hereditary blood defect that occurs almost exclusively in males and is characterized by delayed clotting of the blood and consequent difficulty in controlling haemorrhage even after minor injuries.*
Huntington's disease	A progressive chorea that is inherited as an autosomal dominant trait, that usually begins in middle age, that is characterized by choreiform movements and mental deterioration leading to dementia, and that is accompanied by atrophy of the caudate nucleus and the loss of certain brain cells with a decrease in the level of several neurotransmitters.*
Hypothyroidism	Deficient activity of the thyroid gland; <i>also</i> : a resultant bodily condition characterized by lowered metabolic rate and general loss of vigour.*
Institutional Review Board (IRB)	A committee appointed by an institution to review the ethical standards of biomedical research proposals.
<i>In vitro</i> fertilisation (IVF)	A clinical and laboratory procedure whereby the eggs and sperms from a couple are extracted and fertilised outside their bodies. Such a procedure is a kind of assisted reproduction aimed at increasing the chances of a couple conceiving a baby.
Jaundice	A yellowish pigmentation of the skin, tissues, and certain body fluids caused by the deposition of bile pigments that follows interference with normal production and discharge of bile (as in certain liver diseases) or excessive breakdown of red blood cells (as after internal haemorrhage or in various haemolytic states).*
Karyotype	The chromosomes of a cell can be stained by a dye to become observable under the microscope and to display characteristic banding patterns. The analysis of a set of chromosomes arranged in corresponding sizes and banding patterns is called a karyotype.

Late-onset	The development of a hereditary disorder beginning only in late childhood or adulthood.
Metabolite	A product of biochemical processes in a cell or organism.
Muscular dystrophy	Any of a group of hereditary diseases characterized by progressive wasting of muscles.*
Mutation	<p>A gene mutation is a permanent change in the DNA sequence that makes up a gene. It ranges in size from one DNA base to a large segment of a chromosome.</p> <p>Gene mutations can be inherited from a parent or acquired during a person's lifetime. If a mutation occurs in an egg or sperm cell during a person's life, there is a chance that the person's children will inherit the mutation.</p> <p>Most mutations do not cause genetic disorders. For example, some mutations alter a gene's DNA base sequence but don't change the function of the protein made by the gene.</p>
Neonatal	Of, relating to, or affecting the newborn and especially the human infant during the first month after birth.
Phenotype	The observable characteristics of the expression of a gene.
Preimplantation genetic diagnosis (PGD)	A procedure whereby early embryos created by IVF are evaluated to determine the presence of one or more genetic conditions. It is then followed by the selection and implantation of unaffected embryos into the uterus.
Preimplantation tissue typing	A procedure whereby early embryos created by IVF are tested for tissue compatibility with an existing sibling. This is then followed by the selection and implantation of tissue compatible embryos into the uterus with the aim of bringing about the birth of a child who can provide a matched tissue donation. It can be used as the sole clinical objective or in combination with PGD to avoid a serious genetic condition in the resulting child.
Prenatal diagnosis	Tests performed during pregnancy to determine if a foetus is affected with a particular disorder.
Presymptomatic testing	Testing of an asymptomatic individual to determine if the individual has inherited a defect in a specific gene for a late-onset disease which confers on him or her an almost 100% risk of developing the disease at a later stage in life.
Protein	Large and complex molecules that play many critical roles in the body. They do most of the work in cells and are required for the structure, function and regulation of the body's tissues and organs.

RNA	RNA, or ribonucleic acid, is mainly involved in the translation of genetic information coded in DNA to make protein molecules in the cell.
Scientific validity	The reliability of a test performed in the laboratory. A validated test should consistently detect the presence of its gene substrate and should consistently show negative results in the absence of its gene substrate.
Sex-linked	A disease gene that is situated on either the X or Y chromosome is said to be sex-linked.
Sickle-cell anaemia	A chronic anaemia that occurs primarily in individuals of African descent who are homozygous for the gene controlling haemoglobin S and that is characterized by destruction of red blood cells and by episodic blocking of blood vessels by the adherence of sickle cells to the vascular endothelium which causes the serious complications of the disease (as organ failure).*
Somatic cell	All the body cells except the reproductive (germ) cells.
Susceptibility (Predisposition) testing	Testing of an asymptomatic individual to determine if the individual has inherited a genetic variant or variants, which may increase his or her risk of developing a multi-factorial disease such as Alzheimer's disease, diabetes and certain cancers, some time in the future.
Thalassaemia	Any of a group of inherited hypochromic anaemias and especially Cooley's anaemia controlled by a series of allelic genes that cause reduction in or failure of synthesis of one of the globin chains making up haemoglobin and that tend to occur especially in individuals of Mediterranean, African, or southeastern Asian ancestry – sometimes used with a prefix (as alpha-, beta-, or delta-) to indicate the haemoglobin chain affected; called also <i>Mediterranean anaemia</i> .*

* *From Merriam-Webster Medical Dictionary*

REFERENCES

- Advisory Committee on Genetic Testing (UK), *Code of Practice and Guidance on Human Genetic Testing Services Supplied Direct to the Public*, 1997
- Advisory Committee on Genetic Testing (UK), *Report on Genetic Testing for Late-Onset Disorders*, 1998
- American Academy of Pediatrics, *Policy Statement of Ethical Issues with Genetic Testing in Pediatrics*, 2001
- American College of Medical Genetics / American Society of Human Genetics, *Policy Joint Statement of Genetic Testing in Adoption*, 2003
- American Society of Clinical Oncology, *Policy Statement of Genetic Testing for Cancer Susceptibility*, 2003
- American Society of Human Genetics, *ASHG Statement on Professional Disclosure of Familial Genetic Information*, 1998
- Australian Law Reform Commission / Australian Health Ethics Committee of the National Health and Medical Research Council, *Essentially Yours: the Protection of Human Genetic Information in Australia*, 2003
- Australian Medical Association, *Policy Statement of Human Genetic Issues*, 1998 (Revised 2002)
- Bioethics Advisory Committee (Singapore), *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning*, 2002
- Bioethics Advisory Committee (Singapore), *Human Tissue Research*, 2002
- Bioethics Committee, Council for Science and Technology (Japan) *Fundamental Principles of Research on the Human Genome*, 2000
- Canadian Paediatric Society, *Policy Statement of Guidelines for genetic testing of healthy children*, 2003
- Committee for the Study of Ethical Aspects of Human Reproduction and Women's Health, International Federation of Gynecology and Obstetrics (FIGO), *Recommendations on Ethical Issues in Obstetrics and Gynecology by the FIGO Committee for the Study of Ethical Aspects of Human Reproduction*, 2003
- Council of Europe, *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, 1997

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

Council of Europe, *Recommendation No. R (94) 11 on Screening as a Tool of Preventive Medicine*, 1994

Department of Health (UK), *Preimplantation Genetic Diagnosis (PGD)* –

European Commission, *25 Recommendations on the ethical, legal and social implications of genetic testing*, 2004

European Commission, *Report on the Ethical, Legal and Social Aspects of Genetic Testing: Research, Development and Clinical Applications*, 2004

European Society of Human Genetics, *Provision of Genetic Services in Europe: Current Practices and Issues*, 2001

Gene CRC (Australia), *Ethical Issues in Genetic Research*, 2003

Guiding Principles for Commissioners of NHS services, 2002

Human Fertilisation and Embryology Authority (UK), *Human Fertilisation and Embryology Authority Report: Preimplantation Tissue Typing*, 2004

Human Fertilisation and Embryology Authority and Human Genetics Commission (UK), *Outcome of the Public Consultation on Preimplantation Genetic Diagnosis*, 2001

Human Genetics Commission (UK), *Genes Direct: Ensuring the Effective Oversight of Direct Supply to the Public*, 2003

Human Genetics Commission (UK), *Genetic Testing Services supplied Direct to the Public* (A consultation document), 2002

Human Genetics Commission (UK), *Inside Information: Balancing Interests in the Use of Personal Genetic Data*, 2002

Human Genetics Society of Australasia, *Predictive Genetic Testing and Insurance*, 1999

Human Genome Organisation, *International Declaration on Human Genetic Data*, 2003

Institute of Medicine, *Assessing Genetic Risks: Implications for Health and Social Policy*, 1994

International Bioethics Committee (IBC) of the United Nations Educational, Scientific and Cultural Organisation, *Report of the IBC on Pre-implantation Genetic Diagnosis and Germ-line Intervention*, 2003

National Health and Medical Research Council (Australia), *Ethical Aspects of Human Genetic Testing: an Information Paper*, 2000

National Medical Ethics Committee (Singapore), *Ethical Guidelines for Gene Technology*, 1998

Nuffield Council on Bioethics, *Genetic Screening: Ethical Issues*, 1993

Nuffield Council on Bioethics, *Genetics and Human Behaviour: the Ethical Context*, 2002

Society of Obstetricians and Gynaecologists of Canada, *Canadian Guidelines for Prenatal Diagnosis: Genetic Indications for Prenatal Diagnosis*, 2001

Task Force on Genetic Testing (US), *Promoting Safe and Effective Genetic Testing in the United States*, 1997

United Nations Educational, Scientific and Cultural Organisation, *Universal Declaration on the Human Genome and Human Rights*, 1997

United Nations Educational, Scientific and Cultural Organisation, *Report on Genetic Screening and Testing*, 1994

US President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions: The Ethical, Social, and Legal Implications of Genetic Screening, Counseling, and Education Programs*, 1983

US Secretary's Advisory Committee on Genetic Testing, *Enhancing the Oversight of Genetic Tests*, 2000

World Health Organization, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services*, 1998

World Health Organization, *Review of Ethical Issues in Medical Genetics*, 2003

POSITION PAPERS

Dr. Ann Tan, *Prenatal Genetic Screening and Testing*

Dr. Christine Yap, *Legal and Ethical Issues Pertaining to Pre-implantation Genetic Diagnosis*

Dr. Christine Yap, *Pre-implantation Genetic Diagnosis*

Dr. Denise Goh, *Ethical, Legal and Social Issues in Genetic Testing and the Supply of Genetic Tests Direct to the Public*

Dr. Eric Yap, *Ethical, Legal, Social and Policy Issues in Medical Genetic Testing of Relevance to Singapore: Personal Perspectives*

Dr. Lee Soo Chin, *Genetic Counselling and Genetic Testing: Hereditary Cancer Syndromes*

Dr. Ong Toon Hui, *Social Implications of Genetic Research and its Applications*

Dr. Peter Ang, *Genetic Testing in Oncology*

Dr. Tan Eng King, *Molecular Diagnosis of Neurodegenerative Diseases and Movement Disorders*