THE USE OF PERSONAL INFORMATION IN BIOMEDICAL RESEARCH

A CONSULTATION PAPER

THE BIOETHICS ADVISORY COMMITTEE

SINGAPORE

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This Consultation Paper is prepared by the Human Genetics Subcommittee

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

The BAC reports to the Steering Committee on Life Sciences (formerly the Life Sciences Ministerial Committee). 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
11 Biopolis Way, #10-12 Helios
Singapore 138667
Web: http://www.bioethics-singapore.org
Email: contactus@bioethics-singapore.org

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Executive Summary

Part I: Introduction

1. Biomedical research is a public good. Without it, advances in medicine would be impossible. This Consultation Paper discusses the need to use personal information in biomedical research and makes recommendations aimed at establishing principles for privacy protection and confidentiality consistent with legitimate research needs.

2. We identify five issues for discussion:

   (a) What is personal information?

   (b) Do we require a legal framework for the protection of privacy and confidentiality?

   (c) Issues of informed consent;

   (d) Issues of privacy and confidentiality; and

   (e) Issues of access by third parties such as employers or insurance companies.

Part II: Personal Information

3. A broad definition of personal information is adopted. The Paper treats as personal any information that is information about a particular person. It is not just information of an inherently private or personal nature. For example, a blood sample yields information about a person's blood group. However, the type of blood group is not considered personal information, unless the identity of the person providing the sample is known. Information about the blood group of a known person would be information about that person. It would be personal information.

4. Only if proper steps are taken to protect the identity of research participants can their personal information be used for research purposes without breach of privacy. For this reason, de-identified information is used where possible in research; and sometimes, the de-identification is done in such a way that it is

permanent and irreversible, so that the identity of the person concerned cannot be known. There are various ways in which a greater or lesser degree of security can be obtained using de-identification procedures. In general, the more sensitive the information, the more care is needed to ensure that the identity of the person concerned is protected and their personal information kept secure.

5. Sometimes the information needed is patients' medical information, that is, information provided to a physician for purposes of diagnosis or treatment. Such information is kept in medical records. Sometimes personal information needed in research is obtained from volunteers who are not patients. Sometimes the needed information is genetic information, which may or may not be medical information. Medical and genetic information are also examples of personal information.

Part III: The Legal Protection of Personal Information

6. In paragraphs 3.1-3.6 the Paper considers whether or not some general legal framework is needed, and concludes that it is. A legal framework that protects privacy while allowing the legitimate use and exchange of information may be valuable in its own right, and may be essential if researchers in Singapore are to collaborate with researchers in other jurisdictions.

7. Singapore's existing laws provide for privacy protection in specific circumstances, such as between banks and their customers, and between solicitors and clients, but currently there is no overall statutory framework for the protection of personal information. A legal regime for personal information protection could provide a general framework for public engagement and for policy development.

8. A general privacy protection law could also assist the development of realistic expectations on the part of researchers and prospective research participants regarding the use of personal information in biomedical research. In particular, the management of de-identified information, the right of access to research data by participants, and the use of information for epidemiological research and public health research, are all matters where particular provisions may be helpful.

Recommendation 1: We recommend that the relevant authorities consider establishing a legal framework for the use of personal information in biomedical research.

Part IV: Informed Consent

9. In paragraphs 4.1-4.5 the Paper briefly considers the issue of informed consent and confidentiality, which are the fundamental means to privacy protection, and explains specific and general consent.

Section A: Consent and Proportionality

10. When a researcher asks a person to provide tissue or personal information for research, specific informed consent for the research is needed. However, an additional general consent for future research may also be taken. When general consent for future research is given, it relieves the researcher of the need to re-contact the individual concerned for a fresh consent, provided that the information or tissue is stored and used as de-identified material. Generally, the process of obtaining informed consent and details of information to be provided should be in proportion to the sensitivity of the information and risk of harm to the individual. The approval of a research ethics committee or an Institutional Review Board (IRB) is required before research can proceed. Paragraphs 4.6-4.16 discuss this.

Recommendation 2: Specific consent should be obtained when research involves identifiable personal information or tissue samples. General consent may be obtained for subsequent research involving the use of de-identified information or remnant tissue. The information to be provided to the individual when taking consent should depend on the sensitivity of the information and the risk of harm.

Section B: Reciprocity, Disease Registries, Epidemiological Research and Public Health Research

Disease Registries

11. Paragraphs 4.17-4.29 relate to the use of information held in disease registries. Such information is essential to disease prevention, public health planning and policy-making, as well as research aimed at improving public health. Accordingly, we consider it to be ethically proper for medical information to be disclosed by physicians to disease registries without patients' consent, provided that adequate privacy and other ethical safeguards are in place, and patients are appropriately informed.

12. In addition to the ethical basis for this position, there are a number of practical difficulties that will make a strict requirement of consent inappropriate for research using information from such registries, including the very large numbers of patients often involved and the likely desire of some patients not to be contacted. These reasons were also identified by the UK Academy of Medical Sciences.

13. Disclosure of medical information to a disease registry could be in breach of medical confidentiality if done without the patients' explicit consent. In other jurisdictions, there has been a move towards legal regulation of disclosure. We are of the view that public health purposes could justify a similar move in Singapore.

Recommendation 3: We recommend that the relevant authorities clarify the legal basis for the disclosure of medical information to disease registries by health care institutions and physicians; and establish mechanisms enabling the registries and healthcare institutions to increase the accessibility of personal information for research that can significantly advance public welfare, while safeguarding privacy concerns.

Epidemiological Research and Public Health Research

14. Paragraphs 4.30-4.34 consider non-disease public registries, such as the Registry of Births and Deaths, which are an invaluable resource for biomedical research. Where disclosure of identifiable information by a public registry is permitted by law or regulation, the ethical principles of informed consent and confidentiality should apply in the same manner as they do for medical registries, which include disease registries, custodians of medical records, and other similar registries of medical information.

15. However, while a consent requirement exists before identifiable personal information is used in research, it should arguably not extend to the use of reversibly de-identified information provided there are adequate provisions to protect privacy and confidentiality. It is possible to link data between registries and allow research access to personal information without compromising confidentiality and privacy concerns.

16. While informed consent should generally be obtained for the research use of personal information, the procurement of consent may not be possible or practicable in every situation. There may be cases where there is public health justification for certain research to proceed even where the consent requirement is not satisfied, if it poses minimal risk to individual privacy and confidentiality of personal information. The types of research that typically qualify for such special treatment are epidemiological research and public health research, either of which may include the use of medical records. However, appropriate mechanisms for this may only be put in place through legislative means and we recommend that the relevant authorities consider establishing them.

Recommendation 4: We recommend that the relevant authorities consider establishing legal mechanisms to facilitate the use of personal information in registries, databases and medical records for epidemiological research and public health research. These mechanisms should also ensure that there is minimal risk to individual privacy and confidentiality.

Section C: Clinical Audit and the Electronic Medical Record Exchange

17. Paragraphs 4.35-4.43 deal with the use of medical records for clinical audits carried out by physicians or healthcare institutions to monitor and evaluate the quality of the medical services provided. Audits may entail access to the medical records of patients, and will increasingly extend to cover more than one institution as the Electronic Medical Record Exchange (EMRX) comes into use.

18. When physicians report their own cases in the medical literature, it has usually been accepted that such clinical reviews need not entail consent and IRB review. Clinical reviews are primarily the means by which physicians maintain and improve their clinical knowledge and skills. We are of the view that existing custom and practice need not be changed in this regard, as it already contains privacy and confidentiality safeguards.

Recommendation 5: We recommend that the relevant authorities consider legal provisions necessary to ensure that the potentially increased scope of clinical audit does not violate medical confidentiality and to assure the public that privacy and confidentiality interests in personal information will be safeguarded.

Section D: Additional Considerations about Consent

19. Certain additional considerations about consent are covered in paragraphs 4.44-4.52, specifically vulnerability and withdrawal of consent. Vulnerability may be thought to occur if one's ability to give informed and voluntary consent is compromised or if one would be at heightened risk for adverse consequences of the research. Three common categories of vulnerable persons are:

    (a) children and adolescents;

    (b) the mentally impaired; and

    (c) persons in dependent relationships.

20. When vulnerable persons are involved in research, they are entitled, as a general rule, to the same considerations of privacy and protection as any other research participants, and this principle needs to be kept in mind when consent is taken, whether directly or by proxy.

Recommendation 6: We recommend that IRBs, when reviewing research, ensure that any concerns in regard to vulnerable persons are appropriately addressed.

Recommendation 7: Research participants should be allowed to withdraw their consent to participate in a research at any time without explanation and without prejudice. They should be assured that upon withdrawal their personal

information and/or tissue samples will either be destroyed or irreversibly de-identified.

Part V: Privacy and Confidentiality

21. Paragraphs 5.1-5.5 deal with the need to store and manage personal information in ways that provide proper security and confidentiality, and a number of specific suggestions are made. The two most important are:

    (a) that research data should not be made available to insurance companies or employers, because it is not obtained for health purposes and can be misleading if used outside the research; and

    (b) that while a researcher collecting data from consenting individuals will know their identities, such information should be stored and managed as de-identified information as far and as early as possible.

Recommendation 8: Personal information should be de-identified as far and as early as possible and should be stored or transferred as de-identified information.

22. Paragraphs 5.6 & 5.7 are a reminder that confidentiality requires that researchers not only take proper security safeguards with data, but refrain from trying to identify an individual from de-identified information.

Recommendation 9: Researchers should not attempt to identify an individual from de-identified information as it is a serious breach of ethics to do so.

23. Paragraphs 5.8-5.11 are concerned with irreversibly de-identified personal information. Irreversibly de-identified information should not be subject to privacy and confidentiality requirements, provided that proper measures are taken to ensure that the de-identification really is irreversible. In particular, this means protecting participants whose anonymity might otherwise be threatened by the uniqueness of the information, or the availability of a detailed and complete profile however anonymous.

Recommendation 10: Irreversibly de-identified personal information generally need not be subject to privacy and confidentiality requirements.

24. When personal information is reversibly de-identified, the extent and thoroughness of de-identification should be balanced against the likely harm that would follow in the event that an individual is identified. It is the responsibility of the IRB to consider the extent and means of de-identification proposed. Paragraphs 5.12 & 5.13 consider this.

Recommendation 11: When reversibly de-identified information is used for research, IRBs should consider the adequacy of the extent and means of the de-identification in proportion to the risk. Should a person be identified from de-identified information, the person should still enjoy confidentiality and privacy entitlements.

25. Paragraphs 5.14-5.16 deal with the principle of proportionality as applied to the use of personal information in medical or public registries. The level of confidentiality safeguards, whether in the extent of de-identification or otherwise, should be commensurate with the potential risk to research participants. Generally, the confidentiality obligation of research institutions involved in large-scale research initiatives will be more wide-ranging than research performed by a single researcher.

Recommendation 12: The ethical principle of confidentiality should apply to the use of personal information from medical or public registries. Confidentiality safeguards should be commensurate with the potential risk of harm from inadvertent disclosure.

Part VI: Access to Medical Information by Employers and Insurers

26. Paragraphs 6.1-6.15 discuss third party access to medical information. Medical information should not be disclosed to third parties without the individual's consent, although there are circumstances when an employer or an insurance company may reasonably expect disclosure of health conditions. Research information should not be disclosed to third parties at all.

27. The main ethical difficulties arise when predictive information is involved, especially genetic information. Predictive health testing, even for monogenic disorders, often entails a high level of uncertainty. There is a conflict of interest between the desire of an employer or an insurer not to take an unnecessary risk at a possible cost, and the desire of employees, applicants, or prospective policy holders not to experience discrimination in eligibility for jobs or insurance cover on the basis of slender evidence or a probability.

28. The key issue is perhaps the concealment of immediately relevant information. In the case of employment, the use of valid genetic or other health testing by employers is appropriate to address imminent health and safety concerns, or where the detected or predicted condition is incompatible with the requirements of the job.

29. In the case of insurance, we recognise the potential 'adverse selection' problem that may arise as if relevant information is withheld, and that risk evaluation for the purposes of determining insurance coverage inherently involves

discriminating between applicants. However, we empathise with the public's concern of possible discrimination in the availability of insurance coverage. Nor do we wish to see individuals deterred from obtaining needed information about their medical conditions on the grounds that they might then be obliged to disclose it.

30. In our view much of the difficulty arises from uncertainty as to the actuarial value of genetic information, and our preferred solution is a moratorium, as in the UK, whereby predictive genetic test results will not be used by insurers, although certain exceptions apply.

Recommendation 13: We recommend that the government consider implementing a moratorium on the use of predictive genetic information for insurance purposes and appoint an authority to consider long-term implications of the accessibility of predictive genetic test results by employers and the insurance industry and to monitor developments in this area.

The Use of Personal Information in Biomedical Research

Consultation Paper

I. Introduction

1.1 Modern scientific medicine, in its entirety, is a research-based enterprise, and biomedical research has been critical to advances in medical science and public health. Research has improved understanding of the effects of medication, of how our environment and/or lifestyle relates to diseases (such as smoking and cancer, heart and lung diseases), and longevity, and of the effectiveness of preventive and therapeutic practices. Sound research promotes public good and the facilitation of biomedical research is a public interest. Such research critically depends on the use of personal information[1] from research participants.

1.2 Personal information may be medical information, genetic information, demographic information, or other information of a personal and private nature. The people from whom it is obtained include patients and volunteers who agree to participate in research (i.e. research participants); they may be alive, or deceased. The information may be derived from tissue samples, medical records, researchers' data files, or institutional databases; and these institutions may be of a public or private character. In all cases, the privacy of the persons concerned needs to be protected, since the information is personal and may be sensitive. Consequently, there are rules and conventions regarding the confidentiality and use of research data in general, and medical records in particular.

1.3 Despite these rules and conventions, people may nevertheless be concerned that information about them will be used against their interests. This is a general concern, fed by awareness of the extent to which information can be captured, stored and used by electronic means, and it is also a specific concern in the case of research. Such a concern is not unique to Singapore. It drives privacy and data protection issues in many parts of the world.

1.4 The modern view is that there should be explicit regulation of who may access personal information, and what it can be used for. In the case of research, many scientifically advanced countries have established ethical and legal frameworks to maintain public confidence in and support for the research enterprise. In addition, efforts directed at engaging the public in consultation and education have significantly increased in Australia, Japan, North America and Western Europe.

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[1] The term "personal information" is explained in paragraph 2.1.

1.5 This Consultation Paper considers the need for similar provisions in Singapore, where despite a commitment to developing biomedical research capabilities, the ethical and legal standards for the use of personal information for biomedical research are not always clear. It strikes a balance between ensuring appropriate privacy safeguards and public confidence on the one hand, and facilitating access for research of legitimate public interest on the other. We identify five important issues that serve to structure the Paper as a whole:

(a) What is personal information?

(b) Do we require a legal framework for the protection of privacy and confidentiality?

(c) Issues of informed consent;

(d) Issues of privacy and confidentiality; and

(e) Issues of access by parties such as employers or insurance companies.

1.6 The purpose of this Consultation Paper is to set out these issues as a basis for obtaining feedback from healthcare, research and governmental institutions, relevant professions, religious organisations, as well as members of the public. Feedback received will be considered by the BAC and a final report will be submitted to the Steering Committee on Life Sciences.

1.7 In preparing this Consultation Paper, we have been mindful of the need to distinguish between ethical issues, and the limitations of the current legal or regulatory frameworks arising from recent advances in biomedical science. For this reason, we have not only made recommendations on ethical issues, but have at several points proposed clarifying the legal framework within which ethical decisions are made and implemented.

1.8 Many of the ethical issues reviewed in this Paper will have relevance to the work of research ethics committees or Institutional Review Boards (IRBs). It is important that IRBs, whose primary function is to safeguard research participants, feel able to make the best decision, having regard to the needs of the researchers and the value of the research. They must feel able to do this, without pressure to adopt the safest and most conservative decision just to avoid legal repercussions, either for themselves or the institutions that appoint them.

1.9 The aim of this Paper is to explicitly outline ethical principles and best practices in the use of personal information for biomedical research. This will enable researchers to be clear as to acceptable legal and ethical boundaries, and it will help to assure the public that proper safeguards are in place or contemplated.

1.10 In addition to the consent and privacy concerns discussed in this Consultation Paper, we note, as a general ethical requirement, that research must be conducted in ways that ensure the welfare and safety of individuals. In a multi-cultural and multi-religious society, researchers and healthcare professionals should also be sensitive to the religious and cultural perspectives and traditions of individuals.

II. Personal Information

2.1 Generally, personal information is data relating to an individual who can be identified from that data or from a combination of that data and other information which is in the possession of, or is likely to come into the possession of, a data controller or custodian.[2] It is a very broad term, including personal particulars, details of medical conditions and health care management, physical or psychological measures, dietary, religious or other beliefs, identifying particulars such as National Registration Identity Card (NRIC) number, or any other information which is linked to a specific identifiable person.

2.2 The most restrictive treatment of personal information is often reserved for the most sensitive information. To determine the sensitivity of the information, it may be important to distinguish between information that *identifies* an individual (such as a person's name), and information *about* an individual (such as that person's medical history). Personal information may be obtained through written or electronic records, opinions, survey questionnaires, images, interviews, recordings and biochemical or other tests, or from analysis of human tissue.[3] Some of the information may not be especially sensitive (like height and weight), but very often, it may be sensitive and should be regarded as private. However, such information should only be considered private if it is linked to information that *identifies* the individual. Information that identifies an individual includes personal particulars such as name, address, date of birth, image (such as picture, photograph, video), voice recording, NRIC number or other means of identification. In most cases, sensitive personal information relates to living individuals. However, personal information of deceased persons can also be sensitive.

2.3 Identifying information can also be some combination of personal data and other information in the possession of whoever keeps the data. In addition, there are unusual situations where an extremely rare condition in a small community

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2 This definition is based on that given in the UK Data Protection Act 1998, Section 1(1).

3 Human tissue is defined in paragraph 2.1 of our report on Human Tissue Research (BAC, 2002) as "all kinds of human biological materials derived from living or cadaveric donors, including solid body tissues, organs, foetuses, blood and other body fluids and their derivatives, cord blood, embryos, gametes (sperm and eggs) or any part or derivative thereof."

can identify an individual. Information that identifies an individual in this way may thus be sensitive and raises privacy concerns even when it is not linked to other identifying information.

2.4 Medical information is a particular kind of personal information. It refers to all information about a patient that is provided to a physician[4] or derived for the purpose of diagnosis or treatment, and includes the results of medical investigations ordered by the physician. Information so collected is typically recorded, managed and used as medical records, which are governed by a system of ethical and legal requirements, notably those set out by the Singapore Medical Council.[5]

2.5 Certain personal information, such as genetic information, blood group, or current medication, may or may not be considered medical information, since this depends on whether or not it was provided to a physician for purposes of treatment or diagnosis. Genetic information broadly refers to any information about the genetic makeup of an individual. It can be derived from genetic testing or from any other sources, including a family history of genetic disease.[6] The term "personal information" in this Consultation Paper includes all personal genetic information used in biomedical research.[7] In our Genetic Testing and

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4 A physician is a person qualified to practice medicine under the Medical Registration Act.

5 Paragraph 4.1.2 of the *Ethical Code and Ethical Guidelines* of the Singapore Medical Council states the general content of clinically relevant information that should be documented as medical records: "All clinical details, investigation results, discussion of treatment options, informed consents and treatment by drugs or procedures should be documented." The same paragraph stipulates that medical records be kept in a manner that is clear, accurate and legible, made during consultation or shortly thereafter, and of "sufficient detail so that any other doctor reading them would be able to take over the management of a case." In addition, a physician is to "respect the principle of medical confidentiality and not disclose without a patient's consent, information obtained in confidence or in the course of attending to the patient" (paragraph 4.2.3.1).

6 Paragraph 3.1 of *Genetic Testing and Genetic Research* (BAC, 2005).

7 The term "biomedical research" in this Consultation Paper refers to "human biomedical research", which includes Direct Human Biomedical Research and Indirect Human Biomedical Research as defined in paragraph 3.7 of our IRB Report (*Research Involving Human Subjects: Guidelines for IRBs*, BAC 2004). It does not include research in the social sciences or humanities. Direct Human Biomedical Research is "any kind of human biomedical research that involves any direct interference or interaction with the physical body of a human subject, and that involves a concomitant risk of physical injury or harm, however remote or minor" (paragraph 3.7(a) of the IRB Report). Indirect Human Biomedical Research is "any research (not qualifying as Direct Human Biomedical Research) involving human subjects, human tissue, or medical, personal or genetic information relating to both identifiable and anonymous individuals, undertaken with a view to generating data about medical, genetic or biological processes, diseases or conditions in human subjects, or of human physiology or about the safety, efficacy, effect or function of any device, drug, diagnostic, surgical or therapeutic procedure (whether invasive, observational or otherwise) in human subjects whether as one of the objectives or the sole objective, of the research study, trial or activity, and which research, study, trial or activity has the potential to affect the safety, health, welfare, dignity or privacy of the human subjects involved in the study, or of the donors of human tissue or information used in

Genetic Research Report, we focused on issues relating to the derivation of genetic information, and we provided recommendations for the ethical derivation, management and use of genetic information. In many respects, considerations in this Consultation Paper follow from points made in that report.

2.6 When personal information is used in research, it is necessary that the confidentiality of the information is ensured and thus the privacy of the person is protected, throughout the research process and in any publication resulting from it. Both these aims are usually achieved by de-identification of the information.

2.7 For the purposes of this Consultation Paper, we distinguish identifiable personal information from de-identified personal information, as follows:

(a) *Identifiable personal information*: Information that allows the identification of an individual;

(b) *De-identified personal information*:

(i) Reversibly de-identified information, in which personal identity information has been removed, and a code substituted, so that the identity of the person could be restored under strict conditions; and

(ii) Irreversibly de-identified information, which is information that has been permanently stripped of identifying details and therefore cannot be used to identify an individual.[8]

2.8 In this Consultation Paper, we consider the use of personal information for the purposes of biomedical research. We also briefly address the use of personal information for clinical audit. We are not otherwise concerned with the collection, management and use of medical information in clinical contexts, since these are already subject to clear ethical and legal standards.

III. The Legal Protection of Personal Information

3.1 The trend in many countries is towards the establishment of a uniform legal framework for the privacy protection of personal information. Much impetus to

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research, or of the family members of any of the human subjects or donors thereof, or to which such medical, personal or genetic information relates" (paragraph 3.7(b) of the IRB Report).

[8] The concept embodied in the terminology is consistent with that adopted by the Ethics Committee of the Human Genome Organization in 1998 (Genome Digest, 86 (1)). See Knoppers and Saginur (Nature Biotechnology, 23 (8) p.925) for a discussion of the terminological confusion in this area.

such a trend arises from unprecedented advances in information technology, allowing the enhanced accessibility and manipulation of electronically stored information. This creates new research opportunities, but poses new risks to the violation of privacy and confidentiality.[9] Scientifically advanced countries have considered it necessary to establish legal regimes for privacy protection in order to facilitate the exchange of personal information. Their experiences have been instructive and their most relevant provisions for the use of personal information in biomedical research are as follows:

(a) Research use of personal information is regulated within a comprehensive personal information protection regime. Consequently, a minimum privacy standard applies across various ways of using information, including those for medical and research purposes. Personal information that ceases to be identifiable or is unlikely to cause harm to anyone is generally exempted from the requirements of the regime. Such exempted information is typically irreversibly de-identified personal information or aggregate information that cannot identify any particular individual. The extent to which personal information protection regimes should apply to reversibly de-identified information, however, has been a contentious issue. We address this concern in Part V below;

(b) Personal information protection regimes generally allow individuals the right of access to their identifiable personal information held in a databank or register, to ensure correctness of the information. However, access is not feasible in the case of biomedical research databases held in de-identified form since the researcher is unable to identify an individual;

(c) Privacy provisions usually limit information collection, storage and use to specific purposes, but such provisions may not be applicable in research, since it is not possible to foresee all the research uses of the information. Similarly, while the destruction of information after a suitable period is usually mandated under privacy protection laws, research data should normally be preserved in case fresh information or theories require re-analysis; and

(d) Many personal information protection regimes explicitly recognise the public interest as including certain kinds of research. Special mechanisms have been established to make available personal

[9] By "privacy" we mean "the quality of being secluded from the presence or view of others", thus, the keeping of one's personal information away from others. By "confidentiality" we mean "treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not without permission be divulged to others in ways inconsistent with the understanding of the original disclosure". In other words, one has some right to privacy, and one has the right to expect that proper safeguards will operate to ensure that private information is treated as confidential by those to whom it is divulged.

information for epidemiological research and public health research. We consider this aspect in greater detail in Part IV below.

3.2 With the globalisation of research, we anticipate that the collaborative exchange of de-identified personal information will become increasingly necessary. If this occurs, countries with privacy protection regimes will expect equivalent protection in countries with which such information is exchanged. We are therefore of the view that this is an appropriate time for the relevant authorities in Singapore to consider establishing a legal regime for the protection of personal information in biomedical research. This regime should address issues relating to the transfer of personal information to a third party and should provide judicial remedies and sanctions for any breach. We note that in many jurisdictions a public authority or agency is established to administer the regime.

3.3 We believe that most Singaporeans expect that their personal information will be kept confidential and that physicians and researchers alike will act responsibly and sensitively in managing it. However, the current level of public awareness in relation to the use of personal information in biomedical research is likely to be low. The establishment of a personal information protection regime carries a two-fold benefit: first, it provides a framework for public engagement and for policy development. We note that policy-makers in Australia, Japan, North America and Western Europe rely heavily on various forms of public consultation for formulating appropriate levels of privacy protection. Given the nature of the subject matter, this process of public engagement is an ongoing one. Second, it promotes the development of realistic expectations on the part of both researchers and prospective research participants regarding the use of personal information in biomedical research. Even though internationally recognised standards and best practices are available, every jurisdiction that has established a personal information protection regime has had to decide for itself the fundamental concerns it has in relation to personal privacy and the kinds of public interest that can override these concerns. A clear and realistic appreciation of privacy concerns is the foundation of public confidence.

3.4 While we support the establishment of a personal information protection regime in Singapore, both regulators and the public should understand that the objective of the regime is to facilitate (rather than limit) the appropriate use of personal information through the provision of proper safeguards. Regulators, IRBs and information custodians should guard against a disproportionate emphasis on certain requirements under the regime, notably the requirement of informed consent for the use of personal information, which is a general requirement in such regimes. This occurred in Germany, Japan, the United Kingdom and the United States, and it severely limited important public health research, necessitating subsequent remedial regulatory action.

3.5 The reputation of Singapore as a centre for responsible biomedical research requires the development of a robust but sensible legal framework for personal information protection, taking into account internationally recognised standards and best practices.

3.6 Personal information is widely used in biomedical research. As with other leading jurisdictions, we consider the ethical principles of informed consent and confidentiality to be the key principles in such use, because it is these principles that protect the privacy of the individual. Wherever possible, individuals should know how their personal information which they have provided in the course of medical care or for research may be used, how their privacy will be protected, and should be given the opportunity to withhold consent if they so wish.

Recommendation 1: We recommend that the relevant authorities consider establishing a legal framework for the use of personal information in biomedical research.

IV. Informed Consent

4.1 Generally, the use of personal information in biomedical research requires the informed consent of the individual concerned and the approval of an IRB. In most situations, researchers will only require access to de-identified personal information. In these cases, specific consent need not be obtained if the individuals have earlier provided a general consent for their personal information to be used for research, and the research has been approved by an IRB.

4.2 Specific consent is consent for a specific research project or for a specific purpose. General consent is consent that does not limit the use of the information or tissue contributed to a specific project or purpose. General consent is thus usually taken for future research, when no specific project has been planned. When a general consent is to be taken, patients or research participants must be provided with sufficient information to make an informed decision and be assured that all future research has to be approved by an IRB and that there will be safeguards to protect their privacy and the confidentiality of their personal information.

4.3 Medical confidentiality requires that a patient's informed consent be obtained before his or her medical information may be used in research. For consent to be valid, sufficient information must be provided to the individual. This obligation arises from the requirement that an individual's involvement in research must be voluntary. Even if the information is de-identified, the individual concerned must at some point have consented to the use of his or her information in research unless such research falls within the limited exceptions discussed below.

4.4 The need for informed consent and for privacy and confidentiality are two separate and necessary requirements for the use of personal information in research. The fact that consent has been obtained does not mean that privacy and confidentiality obligations are abrogated. Similarly, even if the confidentiality of personal information is assured, informed consent must still be obtained in order for it to be used in research.

4.5 While the general ethical requirement is that informed consent must be obtained for the use of personal information in biomedical research, there are arguably certain exceptions. The provision of medical information by physicians to disease registries is one such case that we discuss in Section B below. In addition, the experience of scientifically advanced countries suggests the need of a mechanism whereby the consent requirement may be dispensed with in exceptional situations involving research that poses minimal risk to the individuals concerned and advances public benefit. Such research usually relates to public health, and certain bodies or authorities (such as an IRB or a government agency) are empowered by legislation to determine if research access should be permitted. In Section B below, we propose a similar mechanism be established in Singapore. But first, we consider the manner in which requirements in consent taking should take into account the principle of proportionality.

Section A: Consent and Proportionality

4.6 Informed consent is generally required for obtaining personal information or tissue samples for research. When personal information or tissue is to be stored or used for future research, additional consent should be obtained. This additional consent may be a general consent, in that no specific type of research need be identified at the time of consent-taking.

4.7 When a research participant is also a patient, his or her specific consent for research use of personal information or tissue samples should be separate from the consent needed for any medical treatment. If information or tissue obtained in the course of medical treatment is to be stored and used for future research, consent should also be sought. This additional consent for future research use may be a general consent.

4.8 In instances where a patient may also be a potential research subject, we reiterate that particular caution is necessary when the attending physician is also the researcher. As we have discussed in our previous reports on human tissue research and guidelines for IRBs, patients may feel under obligation to their physicians. For this reason, we recommend that consent for research participation in such a situation be obtained by a competent third party.

4.9 When personal information or tissue obtained specifically for research (but not in the course of medical treatment) is to be stored or used for future research, additional consent should be obtained. This additional consent may be a general consent.

4.10 At the time when a general consent is taken, researchers should provide the assurance that all subsequent research use of information or tissue would require approval of an IRB, that such materials would not be used in ways likely to identify the research participant individually, that the research participant has the right to withdraw his or her consent at any time without giving any reasons and that if he or she is a patient, refusal to consent will not affect the quality of the medical care to which he or she is entitled. In addition, any reasonable possibility of commercial use of the information or tissue should be indicated. The extent of information to be provided will depend on the degree of actual or perceived risk.

4.11 Researchers and IRBs should be mindful of possible public sensitivity towards certain types of research. If it is likely that personal information or tissue contributed by research participants may be used in any type of sensitive research, specific consent must be obtained. General consent is inappropriate for research involving the use of identifiable personal information or for sensitive research. The Nuffield Council on Bioethics has considered certain types of genetic research that may be of public concern, such as those relating to personality, behavioural characteristics, sexual orientation or intelligence.[10] Where it appears to an IRB that an issue of public sensitivity may arise, the IRB may require specific consent to be obtained for the use of personal information or tissue sample, unless it is irreversibly de-identified.

4.12 We stress that biomedical research using personal information tends to serve public welfare. It mostly requires the use of de-identified information, which carries little risk of harm. It would not be prudent to constrain such research by always imposing the particularly stringent standards needed to manage exceptionally sensitive information. In general, under the principle of reciprocity, one might presume that irreversibly de-identified information should be readily available for benevolent purposes, though the individual should be able to opt out. The goal of ethics guidelines is to ensure ethical propriety in the conduct and regulation of biomedical research. Such guidelines are intended to promote a culture of confidence that facilitates rather than hampers responsible research.

4.13 Accordingly, the process of obtaining informed consent should be detailed in proportion to the sensitivity of the information and the actual or perceived risk of harm to the individual concerned. Informed consent should be explicit and in

[10] Nuffield Council on Bioethics, Genetics and Human Behaviour: *The Ethical Context* (October 2002).

writing[11] where the risk of harm to the individual is appreciable, for example if tissue is sought for research from an at-risk individual undergoing elective surgery, and the information provided should be correspondingly detailed. Where the risk is low or non-existent, less information may suffice for the participant to feel able to give consent.

4.14 Personal information or tissue that is provided for research by way of a general consent may be used in subsequent research without further consent. This relieves the researcher of the need to re-contact the individual concerned. So long as the individual was fully informed and agreed to the future research application of his or her personal information or tissue, we are of the view that consent has been obtained, although the other ethical obligations (such as to require IRB review and to keep the information secure and confidential) will continue to apply. If the participant is also a patient, the consent-taking process must allow for the patient's dissent without prejudice to his or her treatment.

4.15 If personal information or tissue is to be stored or used in a form that allows an individual to be identified (rather than as de-identified material), then specific consent must be taken and it will be necessary to provide more detailed information to the individual at the time of consent-taking.

4.16 In summary, we are of the view that specific consent is required when research involves identifiable personal information or tissue samples. General consent may be obtained for subsequent unspecified research, subject to de-identification of the information and tissue as well as IRB review. Re-consent for future research is generally not necessary.

Recommendation 2: Specific consent should be obtained when research involves identifiable personal information or tissue samples. General consent may be obtained for subsequent research involving the use of de-identified information or remnant tissue. The information to be provided to the individual when taking consent should depend on the sensitivity of the information and the risk of harm.

Section B: Reciprocity, Disease Registries, Epidemiological Research and Public Health Research

4.17 Essentially, the consent requirement ensures that an individual's decision to participate in research by providing personal information (whether subsequently de-identified or not) is a free choice. However, the value of free choice does not supersede all other values in our society. Similarly, freedom from intrusion into

[11] Consent is legally valid whether it is in writing or not. However, putting consent in writing makes for easier resolution in the event of any dispute over whether consent was taken or what was consented to. It is generally desirable in research, where the researcher is the party requesting information or tissue samples. In the case of consent for clinical procedures, existing clinical procedures and conventions for taking consent will apply.

one's private life is not an absolute value. There are instances where other legitimate public interests take priority.

4.18 In our Human Stem Cell[12] and Genetic Testing and Genetic Research[13] reports, the guiding principles of 'justness' and 'sustainability' highlighted the need to respect the common good of both present and future generations, together with the importance of fair sharing of social costs and benefits. The reciprocity implied in these principles also applies in research; research depends on informed voluntary contributions or participation, and need not benefit the participants, though it benefits others in the future.

4.19 While it is generally accepted that the requirement of informed consent is important, as it acknowledges the principle of autonomy, there is growing recognition that this principle should not be strictly applied where important public interest may be served. Procedures for obtaining consent from research participants were considered in a UK report, in this case for the collection and retention of biological samples that could be used for genetic analysis.[14] The report recommended that consent procedures include notice to prospective research participants that:

> "(i) the medical treatment that all receive is based on studies carried out on very many earlier patients and that the request is for them to provide similar help for future generations;
>
> (ii) because medical science is changing very rapidly, some of the valuable uses to which the data could sooner or later be put are not foreseeable".

4.20 These recommendations entail the principle of reciprocity, the idea that accepting benefit from past medical research, inherent in the utilisation of medical services, carries some expectation of a willingness to participate in research for the common good or public interest. This is an especially important consideration in societies where individuals are seen incurring obligations to others through their membership and roles in society. In the wider public interest, therefore, we see the principles of autonomy and reciprocity as complementary.

4.21 There are many important uses of personal information that do not contribute directly to the healthcare of individuals, but are beneficial to society. These uses include epidemiological research,[15] public health protection requirements and health service management. We consider the use of medical records for health service management in Section C below. First, however, we focus on

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12 BAC (2002) *Ethical, Legal and Social Issues in Human Stem Cell Research, Reproductive and Therapeutic Cloning,* Chapter 7, paragraph 3.

13 BAC (2005) *Genetic Testing and Genetic Research*, paragraph 4.38.

14 House of Lords' Select Committee on Science and Technology, Fourth Report, *Human Genetic Databases: Challenges and Opportunities* (2001), paragraph 7.65.

15 Epidemiology is the study of the causes and distribution of diseases or epidemics in populations.

exceptional instances where personal information may be applied in biomedical research without the explicit consent of individuals concerned. These are typically certain types of biomedical research that are likely to promote public welfare without posing risk of serious harm to individuals concerned. Internationally, such research is gaining ethical endorsement under the principle of reciprocity.

Disease Registries

4.22 The National Disease Registries Office (NDRO) was established in 2001 as a department under the Health Promotion Board to manage and develop the Singapore Cancer Registry, the Singapore Renal Registry and the Singapore Stroke Registry. Apart from these registries managed by the NDRO, other disease registries in Singapore include the Singapore Myocardial Infarction Registry, the National Thalassaemia registry, the Singapore Myopia Registry and the National Birth Defects Registry. These registries collect patient information, analyse the data and report incidence and trends of diseases in Singapore. Their work is critical to sound public health policy formulation and programme planning, as well as for research in general. For example:

(a) A recent study on trends in cancer incidence in Singapore from 1968 to 2002 relied on data derived from the Singapore Cancer Registry and other sources. In the last 35 years several types of cancer have increased, but cancers of the stomach, liver, oesophagus and nasopharynx have declined substantially;[16]

(b) About 10,000 Singaporeans are admitted into hospitals for strokes and transient ischaemic attacks[17] every year, thereby making stroke the fourth leading cause of death;[18]

(c) Research using data drawn from the Singapore Myocardial Infarction Registry from 1988 through 1997 indicated that women who have heart attack tend to be older than men and are more likely to have prior ischaemic heart disease, atypical symptoms and worse prognosis than men if they are 64 years and below;[19] and

(d) In 2000, it was found that 47% of all new cases of end-stage kidney disease in Singapore were due to complications of diabetes, making

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16 *Trends in Cancer Incidence in Singapore 1968 – 2002*, A Seow, WP Koh, KS Chia, LM Shi, HP Lee, K Shanmugaratnam, Singapore Cancer Registry, Report No. 6, 2004.

17 A transient stroke lasting only a few minutes.

18 *Community-Based, Tri-Racial, Cross-Sectional Study on prevalence of Stroke among Chinese, Malay and Indian Singaporeans*, National Neuroscience Institute, Media Release, 27 April 2005.

19 "Gender Differences in Outcome After an Acute Myocardial Infarction in Singapore, R Kam, J Cutter, SK Chew, A Tan, S Emmanuel, KH Mak, CNS Chan, TH Koh, YL Lim, *Singapore Med J* 2002 Vol 43(5): 243-248.

Singapore the country with the second highest incidence of such cases of kidney failure in the world. This finding is important for devising preventive measures to halt the epidemic of kidney failure in Singapore.[20]

4.23 Not surprisingly, all major scientific countries have established disease registries. However, when many of these countries first implemented personal information protection regimes, a disproportionate emphasis was placed on the need to obtain specific consent from patients before information in their medical records could be disclosed by physicians to disease registries. In many of these countries, epidemiological research, as well as public health research, was severely affected. In Part III above, we have noted our concern in order to prevent a similar occurrence in Singapore.

4.24 Medical information is protected by medical confidentiality and may not ordinarily be disclosed without the consent of the patient concerned. However, it is important to understand that it is inappropriate to apply a strict informed consent requirement for every kind of biomedical research using medical information. The UK Academy of Medical Sciences clearly identified problems that can arise:[21]

(a) It may be impracticable to seek consent for a number of reasons, including temporal or geographical distance, and insupportable time and expense. Researchers have in the past analysed and linked thousands of medical records with data from other sources (including death records). These patients were not contacted for consent to use their information for research, and it would have been impossible to do so since many had died. However, confidentiality safeguards were observed so that the privacy interests of these patients were protected. Such research allowed the identification of risk factors for diseases, enabling preventive measures to be taken;

(b) Strict insistence on informed consent may compromise effective population coverage, which is critical for population studies and disease registries. If many people opt out, the data may no longer be representative, especially since higher refusal rates are common for certain segments of populations, such as the elderly or the socially disadvantaged. In such circumstances, a requirement for informed consent can lead to a significant diminution in the quality of the data, which may be rendered useless;

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[20] "Preventive Nephrology: A Time for Action", by A Vathsala and HK Yap, *Annals of the Academy of Medicine*, January 2005, Vol 34 No. 1, 1-2.

[21] *Personal data for public good: using health information in medical research* (January 2006), pages 58 to 61.

(c) Patients may be inconvenienced or distressed at being contacted for the use of their personal information in research. There are also patients who do not wish to dwell on a disease diagnosis or may be in denial;

(d) Bias in the research may arise if there is a significant or systematic difference between the proportion of individuals in different groups who consent to participate in the research. As suggested above, certain segments of populations may be more willing to give consent for research access to their personal information than others; and

(e) The reliability and generalisability of studies may be reduced, since a strict consent requirement will increase the cost of such studies, thereby leading to smaller study size and larger random errors. In some cases, consent may introduce unacceptable bias into the research findings and penalise some patients (such as schizophrenic patients).

4.25 As a matter of ethics, the use of medical information to secure or advance public health in a way that does not prejudice the patients concerned is an important practical expression of a principle of reciprocity. Existing patients are receiving the benefits of improved medical care through the contributions of past patients who have volunteered their medical information for research, and there is little ethical justification for them to refuse a similar contribution where their interest is not likely to be compromised. The principle of autonomy should not be applied rigidly, such that epidemiological and public health research directed at advancing the "common good" of improving medical care for future patients is hampered without good cause. Accordingly, we consider it to be ethically acceptable for medical information to be disclosed by physicians to disease registries provided that adequate privacy and other ethical safeguards that we have discussed in this Consultation Paper are in place, and that patients are appropriately informed. The essential principle is that the privacy interest of the patient should be primarily protected by appropriate privacy safeguards, rather than protected by the exercise of patient discretion in the use of information for the general good.

4.26 From the experience of scientifically advanced countries that share a common legal heritage with Singapore, we recognise that an ethical position on the disclosure of medical information for the purposes of important epidemiological and public health research may not be adequate in the absence of clear common law precedents, and legislative action may be required. Recently, the provision of medical information to a cancer registry for public health purposes became the subject of controversy in the UK. The question was whether the provision of medical information to such a registry and its subsequent use in research required patients' consent, and if it did, at what point and in what form. The main concern was the possibility that individuals might be identified. As a result, the UK Parliament had to introduce new legislative and regulatory guidelines in 2001 to put transfer of medical information to these registries on a sound legal

footing. Safeguards were proposed to ensure the anonymity of those on the registry to the fullest extent possible. These guidelines allow disclosure of personal information to the cancer registry and for the registry to use such information for biomedical research that serves a public interest, even without consent.

4.27 Similar developments have also been observed in the legal and regulatory landscapes of Australia and Canada, and in certain non-common law countries. For instance, the Swedish Personal Data Act (1998) provides that sensitive personal data may be processed for research and statistics purposes, even without the consent of patients, provided that the processing is necessary and that the interest of society is greater than the risk of improper violation of the integrity of the patients concerned. It further provides that research ethics committees or IRBs must approve the processing of personal information. Integral to this arrangement is that hospitals and custodians of personal information must consider privacy and confidentiality concerns before allowing access to personal information.

4.28 We generally consider these developments to be positive. In the past, it may have been acceptable for public healthcare institutions in Singapore to provide medical information to government entities for epidemiological or public health purposes. However, many healthcare institutions have been privatised in recent years and it has become unclear if government entities are able to require disclosure of personal information without the explicit consent of the patients concerned. In addition, legality of non-consensual disclosure of sensitive personal information to public health authorities for the protection of public health has long been recognised and provided for under the Infectious Diseases Act. Under this legislative regime, a physician, or indeed anyone who has reason to believe or to suspect that an individual is suffering from a specified infectious disease (such as the Severe Acute Respiratory Syndrome or SARS) or is a carrier of that disease, is required to notify the Director of Medical Services. While infectious diseases continue to be of grave concern to public health authorities, many more Singaporeans are today affected by conditions that are serious but not infectious, such as cancer, heart disease, renal disease and stroke. These conditions are the primary interest of disease registries, and they are of no less public health significance.

4.29 As such, we recommend that the relevant authorities consider adopting measures similar to those in the abovementioned countries, in order to enable the disclosure of personal information to public health entities (such as disease registries) within reasonable bounds and subject to reasonable safeguards. These measures should include mechanisms to allow the use of medical information in important public health research that poses minimal or no risk of harm to those concerned, in situations where it is impossible or impractical to obtain consent or if patients have previously objected to such research use.

Recommendation 3: We recommend that the relevant authorities clarify the legal basis for the disclosure of medical information to disease registries by health care institutions and physicians; and establish mechanisms enabling the registries and healthcare institutions to increase the accessibility of personal information for research that can significantly advance public welfare, while safeguarding privacy concerns.

Epidemiological Research and Public Health Research

4.30 Apart from medical information, other personal information held in public registries, such as the Registry of Births & Deaths, is also an invaluable resource for important biomedical research (typically epidemiological research). Disclosure of identifiable information held by public registries may be regulated by law (for example, in the case of information from the national census conducted by the Department of Statistics) or by in-house rules. Where disclosure of identifiable information by a public registry is permitted by law or regulation, the ethical principles of informed consent and confidentiality should apply in the same manner as they do for medical registries which include disease registries, custodians of medical records, and other similar registries of medical information.

4.31 The informed consent of individuals concerned is required before identifiable information about them may be used. In addition, if it is anticipated that such identifiable information would be shared with other researchers or used in other research, then the consent of the participant should reflect his or her agreement to such extended use.

4.32 However, this consent requirement should not apply to the use of reversibly de-identified information in epidemiological research and public health research. From an ethical perspective, it can be argued that reversibly de-identified information could be released from such registries for such research, provided that adequate de-identification and privacy safeguards are in place. Systems that nonetheless permit linkage of data do exist, such that information needed for research can be made available without prejudicing the privacy of the persons to whom the data relate. Some system of this kind is needed, because it may not be practical to require consent to be sought from the individuals concerned in every situation.

4.33 Important public health justification, with low risk of harm to individuals, has been considered in some jurisdictions to provide sufficient justification for the research use of personal information without the need to obtain informed consent. The types of research that typically qualify for such special treatment are epidemiological research and public health research, either of which may include the use of medical records. However, IRB review is still required and approval must be obtained from the custodian of the medical records (if used) as there are ethical and legal responsibilities in the proper management of these

records. In many of the scientifically advanced countries, legal mechanisms have been implemented to facilitate such use. For instance, in Australia and Sweden, ethics review committees are empowered to make such public interest valuation. Sections 60 and 61 of the UK Health and Social Care Act (UK HSC Act) were similarly enacted to mitigate the strict consent requirement.

4.34 Various mechanisms are possible to allow research access to personal information in ways that do not significantly compromise confidentiality and privacy concerns.[22] We consider the availability of such mechanisms to be beneficial to public welfare. While informed consent should generally be obtained for the research use of personal information, the procurement of consent may not be possible or practicable in every situation. There may be exceptional cases where important public health justification for certain research to proceed even where the consent requirement is not satisfied, if it poses minimal risk to individual privacy and confidentiality of personal information. These mechanisms may only be put in place through legislative means and we recommend that the relevant authorities consider establishing them.

Recommendation 4: We recommend that the relevant authorities consider establishing legal mechanisms to facilitate the use of personal information in registries, databases and medical records for epidemiological research and public health research. These mechanisms should also ensure that there is minimal risk to individual privacy and confidentiality.

Section C: Clinical Audit and the Electronic Medical Record Exchange

4.35 Broadly speaking, clinical audits are activities carried out by physicians or healthcare institutions to monitor and evaluate or to otherwise improve the quality and appropriateness of the medical services provided and the practices and procedures carried out by them. These activities can also be undertaken to identify and resolve problems that may have arisen in connection with such services, practices or procedures, and may entail access to the medical records of patients.

4.36 These records are likely to be increasingly electronic in nature. The Electronic Medical Record Exchange (EMRX) is an initiative of the Ministry of Health (MOH) and the two healthcare clusters – Singapore Health Services and National Healthcare Group – to facilitate the sharing of electronic medical records among public hospitals and polyclinics in Singapore. In 2004, the MOH commenced its first phase of implementation with the sharing of the Hospital Inpatient Discharge Summary.

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[22] The ethical requirement of privacy and confidentiality safeguards is discussed in Part VI below.

4.37 The MOH has identified the benefits of the EMRX to be:

(a) improvement to the quality of care provided;

(b) increase in safety, since patients' drug allergies and current medications will be readily accessible to attending physicians; and

(c) reduction to medical cost, as physicians can now view the results of any recent blood tests, X-rays and investigations online without having the need to repeat such tests.

4.38 These benefits are clearly relevant to clinical audit. Although the facilitation of clinical audit is not given as an advantage of EMRX, it is unlikely that effective audit can proceed without some use of it. Currently, only physicians and healthcare staff involved in the care of a patient have access to medical information in the EMRX and information protection safeguards have been implemented.

4.39 The Ministry of Health does not currently permit research access to information in the EMRX. However, medical information in the EMRX may be a potential source of personal information for research. If research access were to be considered, the ethical principles of informed consent and confidentiality would apply.

4.40 Physicians may at times wish to use the medical records of their own patients to review the quality and effectiveness of their clinical services, to determine any new trends, or to study the diseases of their patients. They may subsequently publish their findings, which should not include any identifiable patient information. This anonymity is also required by journal editors. Although such use of medical information does not directly or necessarily benefit the patients whose records are reviewed, it is not so different an application that it should require patients to provide explicit consent. Moreover, the privacy interest of patients is not compromised as there is no disclosure to third parties. We consider such clinical reviews as extensions of medical care and hence ethically desirable. Such work, whether published or unpublished, need not fall within the remit of an IRB.

4.41 Section 11 of the Private Hospitals and Medical Clinics Act provides a mechanism for the conduct of clinical audit by quality assurance committees. While the provision does not explicitly address the issue of medical confidentiality, it is implicit that the use of medical information for clinical audit by such a committee, within the confines of a healthcare institution, does not amount to inappropriate disclosure of medical information.

4.42 However, it is legally unclear whether those who are not members of the quality assurance committee may be involved in such audit activities without the

explicit consent of the patients concerned. While we do not consider clinical audit to be ethically contentious when carried out in a limited context that poses minimal risk to individuals concerned, the scope of clinical audit has greatly expanded in many leading scientific jurisdictions. Under an expanded clinical audit, other healthcare and non-healthcare professionals can be involved in reviewing medical information.

4.43 From the experience of these countries, there is reason to believe that such expanded clinical audit can significantly advance public interest by improving the quality of healthcare services provided. Steps have been taken in these countries to effectively allow the use of personal information for clinical audit, notably under the UK HSC Act, although subject to credible safeguards. This removes any concern that such application of personal information will be in violation of medical confidentiality and provides assurance to the public that privacy and confidentiality interests in personal information will be safeguarded. We recommend that the relevant authorities consider taking similar legal steps to provide public assurance that privacy and confidentiality interests in personal information will be safeguarded.

Recommendation 5: We recommend that the relevant authorities consider legal provisions necessary to ensure that the potentially increased scope of clinical audit does not violate medical confidentiality and to assure the public that privacy and confidentiality interests in personal information will be safeguarded.

Section D: Additional Considerations about Consent

Vulnerable persons

4.44 Vulnerability may be thought to occur if an individual's ability to give informed and voluntary consent is compromised or if he or she would be at heightened risk for adverse consequences of the research. In our Genetic Testing and Genetic Research Report[23] we identified three common categories of vulnerable persons, namely:

(a) children and adolescents;

(b) the mentally impaired; and

(c) persons in dependent relationships: such persons include but are not limited to students, junior research assistants, medical or paramedical staff, personnel under military discipline, or prisoners.

[23] BAC (2005) *Genetic Testing and Genetic Research*, paragraphs 4.8 – 4.18, pages 25-28.

4.45 Vulnerable persons raise particular ethical issues in research, especially where consent is concerned. This is because their interests must be considered, if necessary by proxy, and their participation sought only when other research participants are unavailable or unsuitable.

4.46 Where personal information is concerned, it is our view that individuals in these categories are entitled, as a general rule, to the same considerations of privacy and protection as any other research participants.

4.47 In the case of children and adolescents, and still more in the case of infants, much of their personal information is naturally known to parents or guardians. It is the responsibility of researchers to ensure on the one hand that parents or guardians are appropriately informed when consent for their children to participate in research is sought, and on the other that children or adolescents are also informed and their consent sought, in a manner appropriate to their level of maturity. We reiterate that persons responsible for the care of children and adolescents should only act in the best interest of the latter. This "best interest" principle also applies when such a person is to provide informed consent on behalf of a child or an adolescent for the use of his or her personal information in research. In any case, personal information relating to children should be accorded the same privacy protection by researchers, as would be granted to information from any consenting adult.

4.48 In the case of mentally impaired persons, a similar principle applies. Consent to participate in research may be managed by persons in a position of legal guardianship, who are obligated to consider the best interest of such persons in their care. In any event the research participant should be involved as far as possible in the decision process, and enjoy the same privacy rights with respect to personal information as any consenting adult of sound mind.

4.49 In the case of dependent persons, it is important to avoid situations where a potential research participant might feel obligated to participate. For example, serving National Servicemen may feel obliged to give consent to those with authority over them. Similarly, it might be wise for researchers not to rely on their own research staff or students to serve as participants. Notwithstanding considerations of consent, however, we again stress that personal information from dependent participants should enjoy the same protection as that of any other participant.

4.50 We are therefore of the view that IRBs when reviewing research proposals should take note of cases where participants might appear to be vulnerable, and satisfy themselves that any concerns are appropriately addressed.

Recommendation 6: We recommend that IRBs, when reviewing research, ensure that any concerns in regard to vulnerable persons are appropriately addressed.

Withdrawal of Consent

4.51 Regardless of how a research participant is involved (whether in the provision of tissue, personal information or other forms of involvement), he or she should be able to withdraw consent to participate at any point. Researchers should assure potential participants that no reason need to be given for withdrawing consent and that such decisions will not compromise the quality of any care or entitlements that might be given to them or their families, where applicable.

4.52 When consent is being obtained, a research participant should be informed that, in the event he or she withdraws consent, the personal information and/or tissue samples provided will either be destroyed or irreversibly de-identified, so that it will not be possible to identify him or her. Such withdrawal does not affect completed research or tissue that has been used.

Recommendation 7: Research participants should be allowed to withdraw their consent to participate in a research at any time without explanation and without prejudice. They should be assured that upon withdrawal their personal information and/or tissue samples will either be destroyed or irreversibly de-identified.

V. Privacy and Confidentiality

5.1 Personal information that is used in biomedical research is often held in databases. Most researchers will have a database, in the sense of having a system to store and access the data collected in the research, including any personal information. When a database is large, accessed by many researchers, contains particularly sensitive information, or is to be linked with other databases, ethical considerations of data protection become more pressing.

5.2 It is not our intention to specify particular means by which such databases may be established or managed. Indeed, we recognise the importance of diversity in research databases, and such diversity necessitates different approaches to their creation and operation. However, we suggest that IRBs note and approve data management arrangements, taking into account these principles as applicable:

(a) A procedure should be available for research participants to obtain information, make inquiries and withdraw their consent to participate in the research;

(b) Safeguards should be in place to ensure that there is no inappropriate or unauthorised access to information in the database, and to ensure authenticity of the information;

(c) Depending on the sensitivity of the information or research concerned, a record may need to be kept of who has accessed information in the database and when;

(d) Procedures should be stated for re-contacting research participants or others such as relatives, if necessary;

(e) Procedures should be stated for obtaining consent related to deceased or incompetent participants, or for obtaining any information for which consent is not required, if appropriate;

(f) Research results using information or material from the database should not be published in a form that permits identification of individuals without consent;

(g) There should be proper limits established to any family contact, and the role of the participant's attending physician, if any, should also be clearly established if relevant; and

(h) Research participants should understand, when consenting to participate, the extent and nature of any feedback that they might expect to get on the results of the research as it progresses, and that they can refuse such feedback.

5.3 Insurance companies and employers should not have access to personal information in a research database. Research data is not obtained with the aim of providing research participants with specific information about their health status. Research data is of little value to insurance companies and employers, and may be misleading when used outside the research context. In addition, other sensitive information may be derived from research data, such as information about paternity or about the presence of heritable conditions. Researchers have an obligation to protect the privacy of research participants and other third parties such as the close genetic relatives of the participants, and to ensure the confidentiality of all information derived from the research. Issues concerning access to medical information by insurers and employers are further discussed in Part VI below.

5.4 When it is necessary for identifiable personal information to be disclosed due to compulsion by law or other public interest requirements, the research participant should be informed as soon as possible so that he or she may have the opportunity to challenge such compulsion.

5.5 It is the responsibility of researchers to prevent breaches of privacy in respect of personal information in their control or possession. A researcher will normally have access to personal information when it is collected from individuals who have agreed to participate in the research. Even though it is ethically proper for

the researcher to hold personal information for purposes covered by the consent, personal information should be de-identified as far and as early as possible in the information management process. In particular, the storage and transfer of personal information should be effected as de-identified information whenever possible.

Recommendation 8: Personal information should be de-identified as far and as early as possible and should be stored or transferred as de-identified information.

5.6 Researchers should ensure that personal information is protected by security safeguards appropriate to the sensitivity of the information and the risk of harm, actual or perceived. These safeguards should protect against loss or theft, as well as unauthorised access, disclosure, copying, use and modification. The degree and extent of safeguards should generally be proportionate to the sensitivity of the information held and the potential consequences that may arise from any inadvertent disclosure. Security safeguards should be comprehensive in proportion to the scale of the research when sensitive personal information is involved.

5.7 All researchers should respect the privacy of individuals concerned and not attempt to identify an individual from the de-identified information. A researcher accessing a de-identified database has no direct contact with and is unaware of the identity of the individuals contributing to the database. In the event that the researcher becomes aware of the identities of these individuals, whether through having access to a code by which information can be re-identified or through other means, the researcher is obliged to safeguard the confidentiality of the information.

Recommendation 9: Researchers should not attempt to identify an individual from de-identified information as it is a serious breach of ethics to do so.

5.8 Biomedical research that uses personal information (other than information that is irreversibly de-identified), or information that is not already in the public domain, must be approved by an IRB. If a personal information protection regime is established in Singapore (as per Recommendation 1), this requirement should be included.

5.9 There appears to be a consensus that irreversibly de-identified information should not fall within the purview of personal information protection regimes in countries that have such a regime. Since the information has been irrecoverably de-identified, the risks of privacy and confidentiality violations have been removed.

5.10 However, legal scholars and ethicists have both indicated that even if de-identification is usually adequate to safeguard the privacy interest of research participants, there may be circumstances when it fails to do so. For instance, de-

identification may not sufficiently protect the privacy interest of those affected by diseases that are typically found in only identifiable groups of people, such as Tay-Sachs disease in Ashkenazi Jews or sickle cell anaemia in people of African descent. The effectiveness of de-identification may also be limited in small and close knit populations, if extensive information is collected. If it proves possible to identify an individual from irreversibly de-identified data, researchers should comply with the spirit of this Consultation Paper, and take all possible measures to protect the privacy of the individual in such cases.

5.11 In general, however, we agree with the position that irreversibly de-identified personal information should not be subject to privacy and confidentiality requirements. In most cases, such information may be treated in the same manner as information in the public domain.

Recommendation 10: Irreversibly de-identified personal information generally need not be subject to privacy and confidentiality requirements.

5.12 For reversibly de-identified information, it is far less clear if such information should still be regarded as personal information. Leading scientific jurisdictions are still working towards a resolution. One of the key ethical issues is the extent of de-identification that is required before research information is considered to fall outside of privacy and confidentiality requirements. For some biomedical research, follow up data from the same individual is needed. Hence, reversibly de-identified information is required.

5.13 Research information that is reversibly de-identified should not attract the same legal and ethical obligations that attach to identifiable information. As technology advances, it may be harder to ensure confidentiality in reversibly de-identified information, short of irreversibly de-identifying the information. The extent of de-identification needed is a matter of proportion, so that effectiveness of de-identification should be balanced against the level of sensitivity of the information and the likely harm that would follow in the event that an individual is identified. Since research involving reversibly de-identified information must be subject to IRB approval, it is the responsibility of the IRB to consider the proportionality of de-identification proposed.

Recommendation 11: When reversibly de-identified information is used for research, IRBs should consider the adequacy of the extent and means of the de-identification in proportion to the risk. Should a person be identified from de-identified information, the person should still enjoy confidentiality and privacy entitlements.

5.14 Once identifiable information is procured, it is the responsibility of researchers to ensure its confidentiality. We have discussed various confidentiality considerations above. These considerations include the storage of personal information as reversibly de-identified information and only de-identified

information should be transmitted whenever possible. Accordingly, even if a researcher has obtained the informed consent from a research participant to hold personal information about him or her, it would be prudent for the researcher to store the information in such a manner that the complete personal profile of the research participant is not readily accessible. For instance, the researcher may want to maintain a system of de-identification through separate storage of medical information and identifying information of the research participants or by having the link between the codes held by an independent third party. We emphasise that the level of confidentiality safeguards, whether in the extent of de-identification or otherwise, should be commensurate with the potential risk to research participants. In addition, researchers must comply with all regulatory requirements governing the confidentiality of information received from medical or public registries.[24]

5.15 Generally, the confidentiality obligation of research institutions involved in large-scale research initiatives will be more wide-ranging than research performed by a single researcher. For example, certain large-scale research initiatives involve a system of de-identification to secure the confidentiality interest of research participants. This system ensures that separate custody arrangements are made for different aspects of medical information, tissue samples and other personal information collected from research participants.

5.16 When such a scheme is properly operated, it is possible to link various items of personal data for research purposes, but there is no linkage to specific individuals. The latter would require the approval of an IRB and an oversight committee, which should be independent of the sponsoring institution, to override the system. Researchers would of course have to comply with all regulatory requirements governing the confidentiality of information received from medical or public registries pursuant to such schemes.

Recommendation 12: The ethical principle of confidentiality should apply to the use of personal information from medical or public registries. Confidentiality safeguards should be commensurate with the potential risk of harm from inadvertent disclosure.

VI. Access to Medical Information by Employers and Insurers

6.1 Personal information should not be disclosed to a third party without the individual's consent. However, there are circumstances where a person may be required to make available his or her personal information in order to obtain access to certain economic, political or social goods. The possibility and extent of access to personal information by third parties is very relevant to public

[24] Medical registries and public registries have been discussed in Section B of Part V above.

confidence in the capability of existing institutions to safeguard the interest and welfare of individuals. In this Consultation Paper, we focus on access for two main non-therapeutic and non-research purposes: obtaining employment and obtaining insurance coverage.

Employment

6.2 An employer is reasonably entitled to ensure that a prospective employee is able to meet the requirements of the job by virtue of good health, either before or during employment. Many employers in Singapore do take into account the health status of job applicants, particularly if they provide employees with some measure of health insurance.

6.3 Employers will often arrange for prospective employees to undergo a medical examination with the understanding that acceptance to employment is subject to satisfactory medical examination. Pre-employment medical examination is considered acceptable so long as the information derived from the examination is relevant to the nature of the job that the prospective employee is expected to undertake. However, the usual ethical obligations attending medical information apply even though such information is not held by an employer for the purposes of health care provision or biomedical research. Once an employee leaves the employment, or if an employer declines to employ an applicant, the relevant medical reports should be carefully disposed of by the employer within a reasonable time.

6.4 Employers may also carry out more specific types of medical test on applicants or employees. For instance, employers may seek to conduct tests to reduce workers' compensation claims, to meet occupational health and safety obligations, or to increase productivity, by screening out employees who are most likely to be absent from work due to illness. In addition, the testing could potentially take the form of predictive genetic testing in an attempt to identify if an individual who is currently asymptomatic has a genetic profile that increases the likelihood that he or she will develop a disorder as a result of the workplace environment.

6.5 Predictive health testing of any kind, whether genetic or not, depends heavily on the validity of the tests as predictors, the level of probability associated with any prediction, and the nature of the effects of the disease or disorder. As gene technology is still very much in its infancy, there is often a high level of uncertainty in the predictive value of genetic information. We are concerned that potential employers may discriminate on this basis. Even for monogenic diseases, it is usually not possible to predict the severity or time of onset of the disease in question and there is the possibility that the disease may not even manifest itself during the working life of the individual.

6.6 An employer may not arbitrarily discriminate against a prospective employee on irrelevant grounds without ethical compromise. This issue can arise if employers discriminate on grounds of age, gender, race or religion, for example. In general we take the view that merit in the form of ability to do the job is the important criterion. In a similar way, discrimination based on the possibility of developing late-onset health problems, or on relatively irrelevant or minor health grounds, would be difficult to defend. However, a measurable and real impairment of ability, at the time of application or soon thereafter, incurs a cost on an employer, and may entail a risk to the employee or to the public.

6.7 We are of the view that genetic testing should not be part of pre-employment medical examination. However, we agree that the use of valid genetic or other health testing by employers is appropriate to address imminent health and safety concerns, or where the detected or predicted condition is incompatible with the requirements of the job, especially insofar as these affect third parties.

Insurance

6.8 In order to obtain life and health insurance, a person may be asked to provide detailed information about his or her health, the health of his or her parents and siblings, and certain lifestyle information such as smoking and drinking habits. A person may also be required to undergo a medical examination. The possibility of including predictive genetic test results as part of this information has surfaced as a concern in several jurisdictions.

6.9 There are costs to an insurance company if it is denied relevant health or medical information, genetic or otherwise. These costs are born by other policy holders. A system of national insurance can absorb this cost in the public interest of avoiding an uninsured population, but private insurers are not obviously under any obligation of this nature.

6.10 Concealing relevant information to which an insurance company is entitled may void a policy. If the insurance company is not entitled to the information but the policy applicant has it, an 'adverse selection' situation is created. On the other hand, it is not in the public interest, that individuals become reluctant to undergo necessary genetic or other health testing for fear of having to disclose the results. If this were to occur, both the ability of physicians to provide the best health care to patients and the potential benefits of biomedical research could be reduced.

6.11 There is no clear solution to the question of whether the insurance industry should have access to predictive genetic test results, because the interests of insurance companies and the interests of insured parties do not coincide, and because the predictive and actuarial value of genetic tests is often unclear. It may be the case that the actual risk of real loss to companies is quite small and

difficult to predict. There is however general consensus that no one should be compelled to undergo genetic testing in order to obtain insurance coverage.

6.12 We recognise the potential adverse selection problem that may arise as a result of inequality of information and that risk evaluation for the purposes of determining insurance coverage involves discriminating between applicants. However, we empathise with the public's concern of possible discrimination in the availability of insurance coverage.

6.13 A detailed review was undertaken by the UK House of Commons' Select Committee on Science and Technology in 2001. The Select Committee recommended that the Genetics and Insurance Committee (GAIC), a non-statutory advisory public body, closely monitor the situation to ensure that the insurance industry only made use of genetic test results approved by the GAIC.

6.14 Following the recommendations of the Select Committee, a moratorium was implemented by agreement between the UK Government and the Association of British Insurers from 2001. Under the moratorium, a person will not be required to disclose the result of a predictive genetic test unless approved by the GAIC (to date, only Huntington's Disease has been approved) and is for coverage of more than £500,000 of life insurance or £300,000 for critical illness insurance or income protection insurance with annual benefits of £30,000. The initial duration of the moratorium was 5 years and was later extended for another 5 years, to 2011.

6.15 We are of the view that a similar moratorium on the use of predictive genetic information could be considered in Singapore. This will allow both the insurance industry and relevant government authorities time to look into the substantive issues. Both parties should ensure that only relevant and reliable information is used in assessing insurance applications, and that the outcomes of the conditions considered are both serious and predictable, before considering lifting any such moratorium.

Recommendation 13: We recommend that the government consider implementing a moratorium on the use of predictive genetic information for insurance purposes and appoint an authority to consider long-term implications of the accessibility of predictive genetic test results by employers and the insurance industry and to monitor developments in this area.