FINAL REPORT

SCOPING A GENE BANK INVENTORY

INDUSTRY CANADA CONTRACT 5002843

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EXECUTIVE SUMMARY

BACKGROUND AND METHODOLOGY

This scoping study for a possible national inventory of DNA banks arose from the Government's investigation of whether it should take special actions in the general area of genetic privacy. The work was done between the signing the contract on January 7 2002, and delivering the final report by the end of February.

This study considers DNA banks only in the context of research and development. It defines a DNA bank as *"A collection of samples which can be used for sequence analysis of human DNA, and the information derived from analysis of these samples, and which can be linked by reasonable means with the individuals from which they were obtained".*

This study was carried out primarily through face-to-face interviews in Vancouver, Toronto, Montréal, Québec and St John's, the Canadian cities judged to contain the leading research programs in human genetics; these cities also offer good geographic and linguistic representation. Potential interviewees were identified mainly through personal knowledge of the community, and through referrals from those initial contacts. With the agreement of Industry Canada, I offered interviewees the option of confidentiality; very few requested anonymity.

FINDINGS

Banks

Of the 91 individuals identified or suggested as being involved in this area, 77 were contacted and responses were received from 70, some of whom stated that they were not involved but referred me to others. I met with 77 people (some were brought to meetings by the primary contact), 69 of them face-to-face and the rest by telephone or email.

47 individuals or groups were identified as collecting, or intending to collect, blood or tissue samples primarily for the purpose of research. It is not possible to determine the completeness of this list with respect to the cities visited. These banks included tissues obtained at surgery, or blood samples; the samples are usually stored frozen, or as immortalized cell lines, or as extracted DNA. All samples are collected by or in very close collaboration with clinicians. Health care organizations, or organizations mandated by governments, are increasingly establishing tissue or DNA banks for research and clinical care.

6 hospital or regional DNA or genetic analysis laboratories were identified that usually store DNA samples that are surplus to their immediate clinical analysis requirements, and also extract and store DNA from samples at the request of clinicians.

Identification of banks held by companies is the weakest part of this study.

Arising from their clinical responsibilities, hospital pathology laboratories hold enormous numbers of samples that can be used for DNA analysis. Pathologists are increasingly working closely with other researchers to assemble tissue banks for genetic analysis.

Ethical Context

An explosion of new knowledge about genetic influences on disease will occur in the next decade. Canada has very great opportunities in this area because of factors such as its multiethnic population, founder families, and excellent quality of health care and research. These Canadian resources are being mined by researchers and industries from other countries. Though individual Canadian researchers and teams are seeking to contribute to this area, by not addressing the question, Canada as a nation is deciding by default not to give priority to this very great opportunity, with its major implications for the national agendas in innovation and health.

Researchers involved in DNA banking are very aware of and concerned about ethical issues and concerns. The interactions between responsible research and health care are very close. Knowledge arising from research is immediately and directly applicable to patient care. However, the international history of research in this area contains examples of actions that have caused harm to patients, either because of well meaning but mistaken actions, or because of egregious lack of concern for the privacy and rights of patients.

Researchers and Research Ethics Boards are struggling with very complex issues arising from the legislated and policy requirements and burgeoning ethics literature related to the use of genetic information. Researchers and clinicians express frustration about the effects on the performance of research of uncertainties of the ethical framework for research in this area, and the variability within and between REBs in handling research protocols involving DNA banks. The present balances being achieved may not accord with the wishes or best interests of the patients involved, nor of Canadians as a whole. A national effort to establish Canadian best practices in this area is needed.

The following conclusions were reached:

1 Governance of DNA banks

The privacy issues raised by genetics do not differ significantly enough from those of other aspects of research involving human subjects to warrant a separate regulatory regime (Section 3.1).

Controls that are already in place for governance of the standards of clinical care are sufficient for governance of issues related to genetic privacy (Section 3.2).

Controls that are developing, building on those that have been growing since the 1970s primarily with the leadership of the Medical Research Council, can

confidently be expected to reach publicly acceptable standards of accountability in the near future (Section 3.3).

Therefore, no special federal regulatory initiatives are needed for genetic privacy in research and development.

2 Research ethics functions

The rapid evolution of research and ethics related to DNA banks is causing considerable uncertainty and variability within and between REBs, with perhaps unnecessary and destructive inhibition of health research (Section 2.4).

National best practices are needed for the standards and operational procedures for research ethics in this area, including considerations such as consent, ownership, custodianship, security, coding, transfer of samples between laboratories. This work should involve patients and Aboriginal peoples, as well as researchers, clinicians, ethicists, lawyers etc. CIHR should lead this work

3 Canada's opportunities in human genetics research

The next decade will see enormous advances in our understanding of genetics and human health, an area with great implications for innovation, for health care, and for the economy (Section 2.3.2). Canada's excellent resources in this broad area are being mined by researchers and industries from other countries. Canada is making a decision by default not to give priority to this very important area.

CIHR should immediately address the question of whether and how Canada should give priority to participating in this world-wide explosion of research and development opportunity. Together, CIHR and Genome Canada have the financial resources and mandates to bring Canada to the forefront of this area.

4 Is a national inventory needed?

Conclusion 4.1 leads to the conclusion that the need to regulate does not justify a national inventory.

The need to demonstrate that government has the area under surveillance has some merit as a rationale for a national inventory.

Facilitation of research may offer a valid rationale to identify tissue or DNA banks.

5 Is a national inventory feasible?

The value of an inventory will be limited by its completeness. The personal approach in this study offers the potential for high compliance in DNA banks in public institutions. Without a carrot or a stick, low compliance is likely in the commercial world.

1. BACKGROUND

1.1 INTRODUCTION

The purpose of this document is to fulfil the requirements set out in Contract 5002843, signed January 7, 2002, entitled "Scoping a Gene Bank Inventory". The contract describes this deliverable as :

> *Conducting a pilot study involving select representative organisations such as private sector research laboratories and clinical trials facilities, in order to test data gathering methodologies. The sites for the pilot study will be made in consultation and agreement with Industry Canada.*
>
> *Deliverable*
> *The second report will follow the completion of the pilot study, and will provide description and analysis on methodologies and experiences from the "field".*

Industry Canada also requested comments on governance.

1.1.1 The author

I was trained in biochemistry, did research and teaching in a Canadian faculty of medicine (1968-75) and then worked with the Medical Research Council of Canada (1975-2000) in a variety of senior positions in research administration and in policies for research ethics (see brief CV attached to Appendix 1). I therefore brought to this study an extensive understanding of and commitment to health research in Canada, and the conviction that excellence in health research can only be achieved in parallel with excellence in ethics, which must include a very high degree of public accountability.

1.2 DEFINITION

In the Phase 1 report, I discussed the term "gene bank" that was used in the contract, and concluded that this term was misleading because it implies a collection of genes rather than of the DNA of individuals. I proposed the term "tissue/DNA/gene banks" as being more inclusive. Use of this term in the field proved unwieldy, so I found myself shortening it to "DNA bank". With only this change, the following is the definition proposed in the Phase 1 report:

Definition of "DNA bank" for the purposes of a national inventory.

> **A collection of samples which can be used for sequence analysis of human DNA, and the information derived from analysis of these samples, and which can be linked by reasonable means with the individuals from which they were obtained.**

1.2.1 Exclusions

This definition excludes:

Written records of personal information that have not involved the analysis of DNA sequences, e.g., physicians' records, hospital charts;

Collections of human source materials from which information that allows the individual to be identified have been removed (or never existed), and which do not have coded links to other databases that will allow identification of the individual, i.e., unidentified or unlinked (anonymized) samples.

Samples that are collected for immediate specific analysis, after which they are discarded. This exclusion could erode with greater use of DNA micro-arrays (chips) which have the potential to provide a great deal of personal information that could affect the individual.

1.2.2 Inclusions

The essential components of this definition are: collection of samples; sequence analysis of human DNA; and linkage by reasonable means with individuals

1.2.2.1 Collection of samples

The banks of human biological samples of interest to this study will mostly have been collected within health care or health research environments, though some banks may be established for other purposes, such as anthropological research. Clinical purposes include diagnosis, treatment, and long-term follow-up. Such samples can also be used for genetic or other research. Samples can also be collected within research projects, or in the expectation that they will be valuable to study questions that cannot now be identified or addressed. Samples will also be collected for research that is carried out by commercial interests, including in academic environments.

1.2.2.2 Sequence analysis of human DNA

DNA in samples that have been professionally collected and stored can be expected to be stable indefinitely.

The ability to extract useable DNA from samples not collected for this purpose (e.g., pathological specimens preserved for microscopy) will vary according to the processes used for preservation. However, the stability of DNA frozen in solution, or dry at room temperature means that routine pathological samples can be used for DNA analysis.

1.2.2.3 Linkage by reasonable means with individuals

Because of concerns of personal privacy, the identifiability of banked samples pervades legislation and the ethics literature. For example:

> Canada's *Personal Information Protection and Electronic Documents Act* (PIPEDA, 2000) defines personal information as "*information about an identifiable individual ....*"

> Canada's *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS, 1998) states (Article 10.3(b) "*When collected tissue has been provided by persons who are not individually identifiable (anonymous and anonymized tissue), and when there are no potential harms to them, there is no need to seek donors' permission to use their tissue for research purposes, unless applicable law so requires.*"

> In the USA, *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*, published by the National Bioethics Advisory Commission (NBAC, 1999) recommends (Rec 1(a), "*Research conducted with unidentified samples is not human subjects research and is not regulated by the Common Rule.*"

1.2.2.4 Identifiability

There is broad international agreement on descriptors of the various levels of identifiability for personal information (NBAC, 1999, MRC, 2001, Australia, 2001). For example, TCPS (1998) identifies four categories:

> *Identifiable tissue can immediately be linked to a specific individual (e.g., by way of an identifying tag or patient number)*

> *Traceable tissue is potentially traceable to a specific donor provided there is access to further information such as a patient record or database.*

> *Anonymous tissue is anonymous due either to the absence of tags and records or the passage of time (e.g., tissue recovered from archaeological sites).*

Anomymized tissue was originally identified but has been permanently stripped of identifiers.

For the purposes of the above definition, identifiable tissue includes traceable tissue because the individual can be identified by reasonable means.

Some authors have expressed concern that no DNA sample can ever be truly anonymous because a DNA sample is unique to the individual (or an identical twin) and can be linked to the individual donor through comparison with DNA samples in identifiable or traceable banks. Indeed, this is the basis for forensic DNA analysis and remains identification. The word "reasonable" in the definition proposed for this study is intended to allow for this concern, while recognizing a certain elasticity.

1.2.3 DNA, RNA, Proteins

DNA banks can take many forms. DNA can be obtained from almost any stored pathological tissue, or any human source material or waste product that has not decomposed too far. Analyzable DNA has been recovered from long buried bones.

Modern collection of DNA usually starts with taking samples of tissue at surgery, or blood in the clinic, or using samples from skin or inner cheek scrapings or saliva. Blood samples (the most common source of DNA for banking) are usually centrifuged to separate the white blood cells from the red blood cells (which do not contain DNA) and serum. If a need is seen for a continuous source of the DNA, blood or tissue cells can be immortalized in cell culture so that they will reproduce themselves indefinitely in culture; samples from these cultures can be frozen indefinitely and the cultures re-started, to provide an endless source of the donor's DNA. DNA can be extracted from any of these sources and stored frozen in solution, or absorbed onto blotting paper and stored at room temperature. All these processes are routine, though preparation of immortalized cell lines is too costly for use in all banks.

DNA is the central code of life. Primarily, it carries the code for the synthesis of proteins which carry out all the functions of the cell and which comprise the bulk of its dry weight. Each cell with a nucleus (all non-gamete cells of the body except red blood cells) contains a copy of the body's complete DNA genome. The information coded in DNA is transmitted to the protein synthesizing machinery by one form of RNA (messenger RNA). The differences between different cell types arise because, in addition to the many proteins that are common to all cells, each cell type also makes specific proteins; they therefore contain different sequences of messenger RNA. A certain cell type will make different proteins at different stages in its life cycle, and in response to different stimuli. Researchers are therefore increasingly studying human RNA and protein

in specific tissues in relation to disease. RNA is very easily destroyed, and proteins and also less stable than DNA; changes in either can occur within seconds of removal of a tissue from its natural state. Samples for RNA and protein analysis therefore are increasingly being flash frozen. Some interviewees expressed the view that the growing abilities to analyze RNA and protein sequences have potentials for invasion of privacy that are comparable to those raised by DNA.

1.3 OTHER INVENTORIES OF REPOSITORIES

I and others have attempted to search the literature, using both normal literature search mechanisms (e.g.,MEDLINE) and website mechanisms (e.g., Google) for headings such as gene banks, tissue banks, DNA banks. Also, I asked relevant experts in Canada and abroad (details in the Phase 1 report) whether they knew of any other inventories of DNA banks, but received only few responses.

Findings are:

Canada: Verhoef, Lewkonia and Kinsella (1996) were interested in the policies surrounding formation of banks and the use of banked materials. They constructed a list of researchers and others involved in human DNA research in Canada by searching the mailing lists of agencies funding such research. Grantees were identified from the Medical Research Council, the Fonds de recherché en Santé de Québec, the Canadian Genetic Diseases Network, the Canadian Genome Analysis and Technology Program, the National Centres of Excellence, and the Canadian based members of the American Society of Human Genetics. 473 suitable people were identified and sent questionnaires; they included people involved in human DNA work, in research ethics boards, and senior administrators. Of the 230 identified as being involved in human DNA work, the 132 respondents included people who were "bankers" or contributors to banks (approximately equal numbers).

USA: The National Bioethics Advisory Commission (NBAC) engaged the RAND Corporation to study human tissue banks. The study was published by the RAND Corporation (RAND 1999) and is summarized in the NBAC report (NBAC, 1999). The report states that no other such study had been carried out in the USA, and made no reference to any other such study worldwide. The purpose of the study was described as follows:

> *"We intend this handbook to serve the research community as a comprehensive reference source of tissue banks in the United States and to facilitate the distribution of tissues for individual research projects."*

The summary provided in the Phase 1 report is in Appendix 2.

UK: MRC UK carried out an "audit" of all the tissue collections (including banks) held in MRC's units and major program grant holders. This "audit" has not been published (Evans, pers comm.).

1.5 METHODOLOGY

The Phase 1 report set out the approaches to be used in the study. The following approaches are broadly consistent with those commitments:

Focus on Vancouver, Toronto, Montreal, Québec and St John's

> The cities outside Ottawa are those most strongly associated with human genetic research in Canada; 6 of Canada's 16 medical schools are in these cities, including many of the most research intensive ones; these cities also represent good geographic and linguistic distribution. I also interviewed two people in Ottawa

2-3 working day visits to each city outside Ottawa

> Previous attempts to collect such information (Belle-Isle, 2001 and pers comm; Verhoef, Lewkonia and Kinsella, 1996) indicated poor response rates to questionnaire approaches.
>
> This study provides information only on the personal interview approach that was used.

Focus on research and development in academic health science centres.

> It rapidly became apparent that research in this area is very closely linked to clinical care.

Contacts for requests for interviews were built primarily on personal contacts from my time at MRC, and the referrals made by them and those who they identified.

> The intent stated in the Phase 1 report to identify people using banks from grantee lists in major funding agencies was attempted by asking people in CIHR and HSFC to search their databases. Both produced spreadsheets containing 300+ entries. I reviewed the key words on these and identified a total of 12 names of which 8 were in the universities on which I was focusing; I met with 2 of these people, and heard independently of 2 others from this group while "on the road".

For reasons of confidentiality, Health Canada was unable to provide the list of laboratories that they identified in 2000 for their survey of 47 laboratories that conduct genetic testing for late onset diseases (identified from 106 genetic testing laboratories) (Belle-Isle, 2001 and pers comm).

Contacts with commercial interests were the weakest part of this study.

For "big pharma", one company representative explored with colleagues whether they could accede to my request for information, reaching a negative decision for reasons of confidentiality and the time required to collect information. A person from another company, which I had not approached, called to discuss a possible national information meeting to address the interests of industry in collecting samples through clinical trials.

Contacts with companies other than big pharma arose from personal contacts in academe, reinforced by the Canadian Genomics Company Directory (Genome Canada, 2001).

Interviews sought information on banks held or used, the purposes for which they are held or used, numbers of samples, consents obtained, ethics approval mechanisms, and views on governance issues.

Interviews usually covered the areas outlined in the Phase 1 report, but did not follow the formal structure implicit in the list of questions in Appendix 3.

As agreed with Industry Canada, all interviewees were offered the option of maintenance of confidentiality of their identity and location

Industry Canada provided a "To Whom It May Concern" letter which included a statement to this effect (Appendix 1).

3 FINDINGS

3.1 RESPONSE RATES

I knew of or was referred to 91 individuals who were thought to be involved in the broad area of DNA banking (see Table 1 for numbers in each city). I contacted 77 people (mainly by email) of whom 70 replied. I interviewed 79 people (Table 2), almost all in face-to-face interviews.

Identification of potential interviewees was greatly assisted by personal knowledge on a first name basis of many leading scientists across Canada.

Almost all phone calls and emails were returned, and interview requests accepted. A senior research administrator in one university wrote to all department heads to inform them of this study and to seek their help in identifying potential interviewees. A department head in another university who is directly involved in this area arranged my complete agenda for a 3 day visit, ensuring that I saw all the relevant people.

The very high response rates in this study might be compared with the relatively low response rates obtained by questionnaire approaches (e.g., Belle-Isle, 2001, Verhoef, Lewkonia, Kinsella, 1996).. A number of explanations are possible, for example:

The sample of those identified favoured those who would respond;

The personal approach by someone well known in the community is favoured by potential interviewees. A number of interviewees stated that they would have given very low priority to replying to a questionnaire.

Since assessing the completeness of this study in identifying DNA banks in the cities visited would require knowing the answer sought, it is not possible to assess the true success rate of this approach.

3.2 BANKS IDENTIFIED

It seems appropriate to group the banks identified in this study into 4 categories:

Banks assembled and/or used by clinicians and researchers within academe or the health care system (Table 3);

Banks held by genetic analysis centres within the health care system (Table 4);

Banks assembled or held by companies (Table 5);

Banks held by pathology laboratories in hospitals.

2.2.1 Banks held and/or used by clinicians and researchers (Table 3)

This pilot study identified 47 individuals or groups collecting, or intending to collect, blood or tissue samples primarily for the purpose of DNA or RNA analysis. Some people or groups in Table 3 hold or work with more than one specific collection; also the wide extent of collaboration means that this list may contain some duplicates. As indicated above, it is not possible to measure the completeness of this list of collections.

The broad definition of "DNA bank" allows the inclusion of a wide range of activities centred on the collection of tissues in any of a number of forms, and by

a range of individuals. For example, samples obtained at surgery may be frozen immediately, converted into immortalized cell lines, or treated to extract DNA; blood samples can be treated to produce immortalized cell lines or have their DNA extracted. All the banks in this study involved samples collected in the context of clinical care, and therefore by, or under the direction of, a physician. The one exception in this study (Schreiber, Fong and Jamani, 1994) was when members of a geographically widely distributed family sent hair samples (5 hairs with roots) for analysis in a hospital clinical diagnostic laboratory to determine whether they carried the disease causing mutation known to be in the family.

Many of the collections identified in Table 3 are assembled and used by clinicians who treat the patients involved; these clinicians either lead the research laboratories in which the samples are analysed, or collaborate with molecular biologists and geneticists. Such examples appear to be most evident in surgical environments in which tissue samples are collected as part of the surgery, and the surgeon/researcher can ensure proper preservation. These examples tend to be mainly in cancer research, and to focus on research around the mutations that occur during life (somatic mutations) and appear only in the tumour. (Research involving inherited mutations can be carried out with blood samples since these mutations are present in every cell nucleus.)

In some cases, the collections are developed by researchers who are not directly involved in patient care, but who are in contact with the clinicians who treat the people involved; such examples tended to predominate when members of a family are approached to provide samples to allow research on a possible inherited disease.

A number of clinicians collect samples from patients whose condition they cannot explain or that appear especially interesting, for future analysis as knowledge advances or similar cases arise. When the clinician does not have appropriate laboratory resources, such samples are often stored within hospital or regional facilities (e.g., Table 4).

Health care organizations, or organizations mandated by governments, are now starting tissue or DNA banks for research and clinical care. Examples are the Tumour Tissue Repository of the British Columbia Cancer Agency and the intention of the Ontario Cancer Research Network to establish a repository; both of these propose to collect tissues from all cancer surgery patients (with individual consent), and to have the capacity to link the information obtained with the clinical records at the Department of Health (cancer is a reportable disease in some jurisdictions) and the treating institution. Cart@gène, an ambitious and innovative project to map the health status, including using DNA samples, of the population of Québec through a random sample of 1% of the population, is now attracting attention in the popular press (L'Actualité, 2002)

2.2.1.1 Ethics awareness and practices

All the people identified in Table 3 were fully aware of the ethical context of their work. All referred, usually without prompting, to the need to ensure free and informed consent, to the consent forms that they use, to the REB approvals for their work, and to their responsibilities as custodians of the samples. These issues are discussed more fully below (Section 2.4.4). As indicated in Section 2.4, a number of interviewees expressed concern about the uncertainties and variability of REB processes.

2.2.2 Genetic analysis centres (Table 4)

I met 6 people who lead hospital DNA or regional genetic analysis laboratories situated in teaching hospitals. These laboratories receive blood or tissue samples, extract the DNA and carry out the requested analyses. Five of these laboratories store the materials remaining after the clinical diagnoses have been completed; the sixth discards them after 6 months. Since all these samples are collected for clinical care purposes, they are all identifiable, either by name on the sample, or through a coding system. The requests for analysis, the performance of the tests, and the handling of the resulting information are under the controls of the relevant clinical standards.

All the genetic analysis centres use some of their stored samples, after anonymization, for routine testing to maintain and increase standards of service. These purposes include quality control, repeat testing to maintain technical standards and testing of new assays before they are incorporated into routine use.

All these laboratories will, on request from researchers, and with the appropriate REB approvals, extract DNA and store it for research purposes, often for a fee to cover costs.

2.2.2.1 Ethics awareness and practices

As for DNA banks collected by researchers and clinicians, all the people identified in Table 4 fully understood their responsibilities as custodians of samples derived from patients and used in clinical analyses. They were very much aware that the samples had been collected in the clinical context for purposes of genetic analysis as requested by the clinician. They recognized the sensitivity of the need to use some such samples, after anonymization, in order to ensure the continuing high quality of the procedures used in the laboratory. They also recognized the needs for research involving this very precious resource, and generally insisted that any such use could only be done with anonymized samples.

The holders of these banks also often provided a service to clinical researchers to extract and store DNA for future research purposes. They generally sought assurance that REB approval (which includes approval of the required consent processes) had been obtained for such storage, and had in place mechanisms to assure REB approval for research projects using the samples.

2.2.3 Banks held by companies (Table 5)

The review of banks held by companies is the weakest part of this study. The people with whom I interacted were focused on research in academic and health care institutions, and mentioned companies only rarely. Names of companies involved in this area were searched for in Genome Canada (2001) and Industry Canada (2001, a and b) yielding some potential names (see footnote to Table 5).

A request to Health Canada for access to their list of 106 genetic testing laboratories (Belle-Isle, 2001) was refused for understandable reasons of confidentiality (Belle-Isle, pers comm.). Mme Belle-Isle also informed me that a web site is being developed of all genetic laboratories; this is expected to be on-line by the end of March 2002. In addition, at the request of the Ontario Minister of Health and Long Term Care (September 2000), the Ontario Medical Association has initiated the Quality Management Program - Laboratory Services (QMPLS, 2002), which is expected to address all areas of laboratory services in Ontario; links with other provinces are expected. Parallel activities in other provinces were not followed up in this study.

As indicated above (Section 1.4), from my service on a teaching hospital REB, I was aware that companies sponsoring clinical trials are now seeking REB approval to ask patients to provide a blood sample for research; this was confirmed by interviews with a number of clinicians and REB members. Some of these requests are for research projects that are well defined at the time of the request, whereas others are for research in the future that is not clearly set out. In addition, the extent of patient information that goes along with the sample can include complete identifiability, knowledge of the clinical history and follow-up but without the name of the patient, or complete anonymization apart simply from the knowledge that the patient was in the trial. It can be generally assumed that these blood samples will be stored and used in research at a central facility, since the complexities of carrying out the research at each of the many sites in a multi-centred clinical trial would be prohibitive. An attempt to obtain the views of a major pharmaceutical company was not successful for reasons of the difficulty of collecting the detailed knowledge of their collections and concerns over confidentiality (I informed them that I believed that my records could fall under the requirements of Access to Information legislation).

2.2.4 Pathology Laboratories

Hospital pathology laboratories have been collecting tissue samples for many decades, as required for clinical care, and, at least in some jurisdictions, required by law. Because their purpose is clinical, the samples are identifiable. Historically, most such samples were preserved as paraffin blocks, for histology. These samples can easily be used for DNA analysis. A few 5 micron sections from such blocks can yield enough DNA for 10-20 mutation site analyses in known genes, though searching for a new gene will require much more DNA.

Though I interviewed 8 hospital pathologists, I feel that it is not valuable to list them as DNA banks due to the enormous numbers and varieties of such collections in Canada. The samples were generally collected within the clinical context, to which their consents (if any in older samples) were generally applied. Historically, such collections may have been accessed for research purposes with varying degrees of REB authorization and anonymization.

2.3 THE ETHICAL CONTEXT FOR DNA BANKS

Concerns over invasion of personal privacy led to the Government's interest in genetic privacy, and hence to this study. As agreed in the discussions leading to this contract (see Phase 1 report), this study focuses on human health because it considers only human DNA banks that are involved in research and development. Issues of governance arising in this study are therefore very closely related to ethical considerations founded on the potentials for harms and benefits.

Broadly speaking, the potential benefits from collection and use of DNA banks in health research will arise from their use in health care, from the development of new knowledge (primarily of significance to human health), and from development by industry of goods and services. The potential harms will arise from the use or release of information derived from banks that compromises or otherwise invades the privacy of the individual from whom the tissue was obtained, or that individual's family or community.

Throughout this study, I found a uniformly high awareness of ethical issues and concerns, and responsible approaches to trying to address them. I believe that this evidence of awareness is because those interviewed are at or very close to the front line of patient care, as physicians, surgeons, clinical geneticists, genetic counsellors, leaders of genetic service laboratories, or molecular biologists.

2.3.1 Potential benefits from DNA banks

Blood and tissue samples have been obtained from individuals and stored in various forms for many decades. Historically, such samples were pathological specimens used for clinical and teaching purposes. Starting in the 1980s, and

now increasing explosively, tissue samples are being collected for research and development, principally because of the enormous growth of our abilities to gain information relevant to health of individuals from their DNA, and the expectation that RNA and proteins will offer even more opportunities. The sequencing of the human genome and its associated chemical, molecular biological and informational technologies have further stimulated an already fast growing sector which is revolutionizing our understanding of human health. Tissue and DNA banks will increasingly be central feed-stocks for this development.

As outlined in Section 2.3, the interviews emphasized the very close links between research and clinical care in the use of DNA collected in the clinical context. The inter-relationships between the various aspects of clinical care and research are illustrated in Appendix 4, which was developed by the Coalition on Cancer Surveillance of the Canadian Association of Provincial Cancer Agencies (Paulse, pers comm) The very close interaction that is required for responsible family based research is indicated in Appendix 5, which outlines a possible sequence of events once an alert family physician has noticed an unusual frequency of a specific disease in a family, and Appendix 6, which illustrates the kind of family information that is needed, the size of the family that is needed to allow such analyses, and the complexities of the interactions between some inherited diseases.

The feedback between research and patient care is evident, for example, in a family with inherited breast cancer, where the information can be used to guide women as to whether they should consider a double mastectomy before cancer appears; only those in the family who carry the mutation need to consider this, and growing evidence suggests that they should also consider an ovariectomy. In Newfoundland, I was told by clinicians (e.g. J Green, Parfrey), that their research funds are used directly for the care of their patients, since the requirements for clinical care and research are the same, and the research information feeds back directly to the patients. Of greatest importance is the immediate effects on their health care, and the savings to personal anxiety arising from such knowledge. Also, great savings result to the health care system and to the economy because prevention and treatment can be focused, and because valuable productive lives are saved.

2.3.2 Opportunities for Canada

Throughout the interviews, there was a sense of excitement over the opportunities for new knowledge about genetic causes of disease and their interrelationships with other factors. The sequencing of the human genome and the vastly increased technical abilities to work with DNA and RNA that it engendered have initiated a wave of opportunity for discovery that is well recognized internationally. The next decade or so will witness enormous advances in our understanding of questions such as: how genes cause disease, alone or in interaction with other genes; how environmental factors trigger or

prevent genetic influences on disease, and how the individual's genetic inheritance determines their response to pharmaceutical interventions in disease.

These opportunities are recognized worldwide, by researchers, governments and industry. Countries (Iceland, Estonia) are taking steps to ensure that their unique genetic heritages are used for the benefit of their peoples. High priority is being given by organisations such as the National Institutes of Health, USA, to facilitating such research; in 1996, the NIH established the Center for Inherited Disease Research which is supported by 12 of NIH's Institutes ".....to provide genotyping and statistical genetics services for investigators seeking to identify genes that contribute to human disease." (CIDR, 2002). Health care agencies are initiating specific actions towards collecting tissue and DNA banks for research to take advantage of these opportunities. Companies are being formed (see Section 2.2.3) to develop new health care products and services. In Québec, a project is being started under the name of Cart@gène to collect health and DNA information on a randomly selected sample of 1% of the population to provide fundamental data for health services planning. Pharmaceutical companies are collecting blood samples from patients in clinical trials for future research into areas such as correlating disease and treatment outcomes with genetic factors. Clinicians are collecting blood or tissue samples to assist in the care of their patients, and to allow research into the diseases that they treat. Clinical and fundamental researchers are working, often together, with such materials to investigate the bases of disease and seek more effective means of prediction, prevention, diagnosis and treatment.

Identification of relatively rare genetic conditions that cause disease in most or all of the people who carry them (high penetrance monogenic conditions) is likely to remain very productive. New technologies are also opening up the possibility for population based studies of frequently found genetic characteristics that cause disease in only a few individuals who carry the mutation (low penetrance multigenic conditions); because of the numbers of carriers, such conditions are likely to have a higher impact on the health of the population.

Canada has enormous opportunities in this broad area, arising from our:

Multiethnic population;

Founder populations, for example in Newfoundland, Québec, among the Aboriginal peoples, and in some long-standing religious communities; some of these are supported by extensive genealogical records;

Publicly funded international quality health care with extensive health care records;

International quality research institutions across Canada

International standards of research, including in clinical research, genetics, molecular biology, genomics, ethics, the law, health services and policy research, and population health;

National and provincial funding sources with mandates that are consistent with the objectives of linking genetics research with health care.

These Canadian opportunities are being recognized and mined by researchers and industries in other countries, notably our friends and competitors to the south. Canadians often find it preferable to share their DNA resources with researchers or industries in other countries because the needed personnel, fiscal and other resources are much harder to assemble in Canada.

These Canadian resources and opportunities are unevenly distributed across the country. Some regions are rich in founder populations and the clinical care opportunities to define them, but lack the financial resources to assemble the family and clinical lineages, and/or the molecular biological and genomic technology needed to use them to optimal advantage to the individual patients involved, or to the region. Others have very strong molecular biology but not founder families. Other regions have all the required resources, and some are using them effectively. Canadian teams are competing with each other and with well-supported international teams for the limited Canadian expertise and resources.

There is no evidence of a coordinated Canadian effort to build on the opportunities that appear so abundant, and that are recognized by individual Canadians, and by industry and researchers in other countries. By not addressing the question of whether Canada should be considering a national approach in this area, Canada is taking a negative decision by default. This lack of consideration in an area as important as the new genomics is inconsistent with the high priority accorded by Government to the innovation agenda and to health.

2.3.3 Potential harms from DNA banks

The potential for harms from DNA banks arises from misuse of the information that is derived from them. Personal privacy is only one component of such harms. An extensive literature documents the potential for such harms and the unfortunately all too frequent instances when patients have suffered. Some such instances arose in the early stages of the development of this area because, despite careful thought, researchers and clinicians had no experience with the issues involved, and had to develop the needed understanding and knowledge. Such cases should now be rare because the growing literature, experience and standards mean that professionals have very little excuse for lack of awareness of the issues, and non-professionals should not be involved in this area. However, instances of mistreatment of patients have arisen for reasons such as

ambition, competition, negligence or worse. The following outline examples are offered to illustrate issues and occurrences:

After much thought, clinician researchers studying a family with a serious inherited disease decided that the best way to inform the members of the family (whose DNA they had collected and analysed with full consent) about the results of their studies would be to invite them all to the hospital on the same day and inform them individually of whether they carried the genetic mutation. They provided consultation but were dismayed at the inadequacy of their emotional support and care for some of the affected people and their immediate family members.

Clinicians who had been collecting DNA samples from patients with a disease suspected of having a genetic cause, learned of a test for a newly discovered genetic mutation. They tested stored samples from affected patients for the new mutation without anonymizing them. They then realised that they knew who among the patients carried the new mutation, and who did not, and decided that they had to inform each patient of his or her status on the principle that the patient had a right to know. Most welcomed the information, but a few resented being told something that they did not want to know.

REBs that review multi-centred and multinational clinical trials that are sponsored by pharmaceutical companies are now increasingly being asked to approve the taking of additional blood samples, with consent, for future genetic studies, which may be only vaguely described. There is often considerable uncertainty about issues such as the ability to link the samples to individuals (will they be identifiable, traceable, anonymized?), where the samples will be stored or analysed, or the REB approval system(s) under which future studies would be controlled.

Researchers from far away identified a large family with a serious disease, took blood samples and then disappeared. The family learned later that their samples had resulted in the discovery of a gene, but they received no feedback or clinical care.

Many members in a community consented to provide blood samples to study a disease. The community found out from the public press that the samples had been used for an anthropological study that identified the community and challenged ancestral and cultural values.

Members of a large family with an inherited condition causing sudden premature death were being called from across the continent after the death of relatives. No feedback was provided to the family members.

A research team identified strong clinical evidence that a 30-40 year old research subject was highly at risk for sudden death from the inherited disease that they were investigating, but did not inform the patient or his physician. The patient died suddenly of this condition a few months later. The information would have allowed an intervention that is known to prevent death from that cause.

2.3.4 Ethical considerations in DNA banks

The following outline of the ethical issues reflects those expressed in a number of articles in a recent issue of ISUMA (2001), which provides an excellent overview of the area.

2.3.4.1 Collection of samples

The requirements for collection of samples for clinical or research purposes are outlined in documents such as TCPS (1998), NBAC (1999) and MRC (2001). These establish the need for REB review and approval to take samples for research projects; such approvals require appropriate consent. Collection of samples in the context of health care is addressed through the relevant processes for consent. The effectiveness and public accountability of REB processes are discussed in Section 3.3.

Ethical, legal and other such issues aside, the gathering of a collection of DNA is very easy. DNA is very stable. It can be obtained from sources such as hair roots, saliva, bodily wastes, skin scrapings, or handkerchiefs. Such materials can be preserved indefinitely in a freezer, or at room temperature with appropriate preservatives (Birnboim, pers comm.; Frégeau et al, 2001). DNA can be extracted from such samples "...with meat tenderizer, detergent and rubbing alcohol" (Younghusband, pers comm., and GSLC, 2002), and stored on blotting paper in a family photo-album.

2.3.4.2 Consent

A fundamental principle of law and of ethics is that no person shall be touched or involved in any way without that person's free and informed consent. This concept is at the heart of policies for research (e.g., TCPS, 1998, WMA, 2000) and for health care. Free and informed consent to being touched is interpreted to include consent to the uses of the results of being touched, i.e., the uses of information about the person, or of tissues or samples that have been obtained.

In Canada, the most recent statement of this principle in the law is in the *Personal Information Protection and Electronic Documents Act* (PIPEDA, 2000), which sets out the legal requirements for collection of personal information by commercial interests in electronic form, and also its use and disclosure. The

applications of this Act to personal health information and to health research are under intensive discussion, which is likely to become more intense in the next two years, when the provinces are expected to consider developing substantially equivalent legislation. A compendium of current and draft Canadian federal and provincial legislation relating to privacy (CIHR, 2000) and a summary of provisions in other countries (CIHR, 2001) have been prepared by Me Patricia Kosseim.

The application of the principles of informed consent to the collection and use in research of samples from which DNA can be extracted and analysed is the most contentious of the areas of ethics, and underlies all the other areas outlined in this Section. The central issues identified in the interviews appeared to be secondary uses of established collections and consents for unspecified future uses.

2.3.4.2.1 Secondary uses of established collections

This heading indicates a broad range of potential uses of already existing collections that were established under conditions of consent, for example, that were in the clinical context alone, that did not include the possibility of research, or that did not describe the specific proposed research.

Given the dangers of invasion of privacy that might result for the use and dissemination of the information inherent in DNA samples, the principle of free and informed consent outlined above would, in a strict sense, require that no use in research of materials obtained from an individual is ethically acceptable unless that individual has explicitly given a free and informed consent to such use. A different view widely held by health researchers is expressed by the Association of Australian Medical Research Institutes, as quoted in the Issues Paper of the Australia Law Reform Commission (Australia, 2001):

> *"The donors were aware that these samples were collected and would be used in research to prevent disease in future, and welcomed this in a fitting spirit of altruism at a time before detailed forms were filled in to meet any possible contingency.*
>
> *It would be disastrous for research, as well as disrespectful to the donors to prevent research on such collections of samples or to insist on consent from relatives, many of whom may not even be aware of the circumstances of the donor or even that the donation occurred. In some cases, it would cause serious distress to living individuals, and bring no benefit to those who are deceased."*

Many clinician researchers with whom I spoke noted that, when asked whether they would consent to the use of their tissue or blood samples in

research, the large majority of their patients and family members (estimated at more than 90%) responded to the effect that they would be very happy if their research samples could contribute in any way to learning more about their disease. However, not all patients or their family members responded in this way.

2.3.4.2.2 Consents for unspecified future uses

The ethical acceptability of seeking a consent for future uses that are not known precisely at the time of obtaining the samples from the individual also has caused much debate.

Some of the clinicians, researchers or banks identified in Tables 3 and 4 store tissues or DNA in the expectation that they will be valuable for future research projects that can not now be designed or carried out, or because the physicians cannot define the patient's illness at the time of collection. Similarly, samples are collected by clinicians, researchers and industry, from patients (and their family members) whose medical conditions are well-characterized, but for whom current treatment options may be less than optimal. Such samples are banked to provide sources of research materials for use when new knowledge has accumulated and new projects, as yet undefined, become timely or possible. Pharmacogenomic research, which is based on the possibility that genetics might determine an individual's response to pharmaceutical treatment or the occurrence or side effects, is a major rationale for such collections.

The ethical principle of free and informed consent is being interpreted by some to mean that consent can only be valid when the research subject is fully informed of the precise uses to which the sample will be put. However, the principle of autonomy might well be interpreted to include the view that research subjects be permitted to consent to unspecified uses of their tissues or DNA, perhaps within certain restrictions.

2.3.4.3 Ownership

A subject's right to withdraw from research is a central principle of the ethics of research involving humans (TCPS, 1998). Consent to participate in research is not an irrevocable commitment; consent can always be withdrawn. However, It may not be possible to implement a withdrawal of consent in all cases, e.g., when treatment has caused an irreversible change in the patient, or when the patent's data have been pooled so that an individual's data can no longer be separated, or the sample has been anonymized and hence can no longer be identified with the subject. I was told that some argue that anonymization is unethical because it prevents exercise of the right to withdraw the sample from research.

Extending this concept to DNA banks implies that a person has the right to withdraw their DNA or genetic information at any time, though this will not be possible once the sample has been anonymized. In terms of ethics, this implies that the person from whose body the DNA was derived should be regarded as retaining ownership of that DNA. The same would be true of any information that is derived from that DNA sample. (Note, this conclusion of ethics may have limited validity in law.)

The concept of ownership in ethical terms (again the legal implications require professional analysis) may need also to be extended to anonymized tissues. Consistent with international standards, current policies in Canada (TCPS, 1998) require that a person give free and informed consent for any use in research of samples obtained from them, and that this consent include instructions as to the purposes for which the sample is to be used. The provisions of this consent should become binding on any use of the sample, even after anonymization.

2.3.4.4 Custodianship

If the ownership of the DNA is as above, the person who holds the bank must be regarded as the custodian / steward / trustee of the property of the DNA donors, or the executor of their wishes. The custodian's use of the samples, or release to others, must be subject to the wishes of the owners of each sample (usually expressed in consent forms) and, as relevant, by restrictions placed on such access or use by the health care standards or authorities, by research ethics standards or processes (focused on REBs) and by legislation. The ability to link samples and/or information to individuals, the security of samples and of the means by which they can be linked to individuals, and the expressed wishes of the donor of the sample are among the central responsibilities of the custodian.

Some interviews revealed the difficulties of maintaining control over samples once they have been sent to another laboratory. Some custodians have been trying to get the samples back without success, occasionally because the commercial interest involved has changed hands, or the individual to whom they were sent will not release them. The need for best practices to ensure responsible custodianship of samples that have been transferred to other sites is clear.

A further component of the responsibilities of the custodian is the management of the DNA banked resource. Even if the donor has consented to use of the banked DNA for a number of purposes, the custodian should regard the sample as a precious resource, to be accessed or conserved in a manner that would be consistent with the primary wishes of the patient and family, especially if the patient is no longer alive.

2.3.4.6 Privacy

As stated above, concern over privacy and discrimination led to the Government's consideration of genetic privacy and hence this study. Privacy is highly prized by Canadians, and was the focus of PIPEDA (2000) and much other federal and provincial legislation (CIHR, 2000). Concerns over privacy are also significant drivers of TCPS (1998), NBAC (1999), Australia (2001) and MRC (2000 and 2001).

Maintaining the privacy of individuals through scrupulous care that their personal information is not released is a golden rule of health care and of research. Consent is required if confidentiality is to be broken. Of central concern to the research environment is whether information obtained about a patient or family as a result of consenting to participate as a research subject will be considered as health information for purposes of insurance.

2.4 INTERACTIONS BETWEEN RESEARCH AND REBS

Throughout the interviews, I repeatedly heard expressions of frustration by researchers and clinicians about the effects on the performance of research due to uncertainties of the ethical framework for research in this area, and the variability within and between REBs with respect to their treatment of research protocols involving DNA banks. Researchers and clinicians recognized that this is in a sense understandable because the area is both new and fast moving, and because they fully recognise the roles that REBs must play in the governance of research involving human subjects. However, researchers and clinicians also recognise the resulting inhibition of the ability to do research in this very fast moving and competitive area. Of the issues summarized above, those of consent driven by the needs for privacy appear to be the major causes of these uncertainties.

REBs operate under legislated requirements (e.g., PIPEDA 2000, the Civil Code of Québec, legislation summarized in CIHR 2000), under guidelines or policy statements (e.g., TCPS, 1998), and under the influence of a prolific academic literature in law and ethics (e.g., articles in ISUMA, 2001). REB members must interpret all these influences as they feel appropriate to each protocol that they consider. They need to take into account concerns about the possibility of error while the research is being performed, and the possibilities of eventual legal actions arising from perceived or actual harms or injustices. All of these factors, and others, are pressures towards a very cautious approach to their assessments of protocols. The question for society is whether this caution is consistent with the standards of Canadians, and in particular with the expectations of the patients and their families who donate their tissues and blood samples for research.

Researchers and REB members are struggling with very complex issues such as those outlined in various parts of this report. My interviews indicated that few are satisfied that the balances now being achieved are in the best interests of the patients involved, or of Canadians as a whole. A national effort to establish Canadian best practices in this area is needed if Canadians are to achieve the optimal balances.

3. GOVERNANCE OF DNA BANKS

The preceding discussion of the ethical context of DNA banks and their use necessarily leads to the question of whether special governance mechanisms are required for their governance.

3.3 IS GENETIC INFORMATION SIGNIFICANTLY DIFFERENT FROM OTHER HEALTH INFORMATION?

Genetic information is necessarily health information. A question for this study is whether genetic information is sufficiently different from other health information to warrant special governance in the context of research and development. In their discussion of the full range of genetic information and its use, Lemmens and Austin (2001) point out why genetic information might be considered to be significantly different (prediction of disease, familial implications, concerns over discrimination and stigmatization, the lack of control over one's genetic heritage, etc.) but conclude:

> *"....that genetics does not raise inherently new ethical and legal questions. However, that does not mean that there is no need for increased scrutiny of existing regimes of the development of new regulatory responses."*

Though this study focuses on collection and use of DNA banks in research and development, it is clear that, once obtained, genetic information can be used for many purposes. However, this is true for any personal information. The issue therefore focuses on the conditions under which DNA banks are managed.

3.4 USE OF BANKS IN HEALTH CARE

The outline above of the benefits of DNA banks indicates the very close relationship between DNA banks and health care. Families are identified and banks collected in the context primarily of health care. (Banks may also be collected for other purposes such as insurance, the military, the police etc, that are outside the scope of this study.) Hence, the ethical principles of health care must be at the foundation of the collection and use of any such bank. Standards of clinical care are under the regulation of professional bodies and health care systems.

These principles demand that the interests of the patient be at the forefront of all activities involving DNA banks in this context. The patient must be given the optimal available health care. Because DNA information implicates the family, patient care implicates family health care, and even that of the community, especially in cases when the community relationships have significant social components that are similar to those in families. Any health information that could affect the health of the individuals must be made available to them, through health professionals, as soon as it is known, qualified by the right of the individual or the family to refuse to be given or to know of such information, a right that is exercised by some individuals.

These considerations of the responsibilities of health care professionals to their patients form the foundation of professional standards, procedures and disciplinary actions. The processes for achieving and maintaining these standards are well established in Canadian health care. Further actions in this regard by the federal government with respect to genetic research seem unnecessary.

3.4 USE OF BANKS IN RESEARCH AND DEVELOPMENT

The Nuremberg Code (1947) and the Declaration of Helsinki (1964, 7th revision 2000), are the seminal international documents on the ethics of research involving humans. The *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS, 1998), Canada's leading document in this area, sets out the ethical principles and the processes required to implement them. TCPS (1998) is consistent with international standards. Central to the ethics of research involving humans is the requirement that, before it is allowed to proceed, any research project that involves human subjects or identifiable materials derived from human subjects, must have been reviewed and approved by a duly constituted and functioning research ethics board (REB).

In its consideration of a research project, the REB must first address the scientific aspects of the proposed research. Is the involvement of humans in the research appropriate? Can the project as designed yield the answers sought? The REB must then address the ethical aspects of the proposed research. Are the harms to which the research subjects are to be exposed as low as possible given the nature of the research? Is the maximal benefit being obtained from the research? Do the benefits anticipated from the research outweigh the harms foreseen? The REB must finally ask whether the mechanisms by which potential subjects will be approached to seek their consent to participate in the research will allow them to exercise a free and informed consent, without coercion or other pressures; the REB must also address issues such as conflict of interest by those involved in the research.

In effect, approval of a research project by the REB is a statement, on behalf of the Canadian people that, if the research is carried out as described and approved, it will meet the ethical standards and expectations of Canadians.

McDonald et al (2000) have analysed the overall governance of research involving human subjects. NCEHR (2000) has also analysed the need for an accreditation system for research ethics functions in Canada. These reports effectively describe the current situation, and reach conclusions and make recommendations that have received wide-spread support in health research:

> REBs in academic institutions function to generally high standards, due primarily to the work of dedicated and caring people, and based on national policies that are consistent with international standards.
>
> REBs in academic institutions operate in a manner that has little demonstrable accountability or transparency to Canadians. There is no registry of academic REBs, nor any knowledge of REBs that serve researchers outside academic centres, such as those that are involved with health research that is carried out in physicians' practices. Neither Health Canada nor the research funding agencies verify that their policies are being followed, though both are taking steps in this direction.
>
> The requirement in the TCPS for continuing review and monitoring of research as it is carried out is rarely met in practice.
>
> The *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS, 1998), is published by the three federal research funding agencies, which have authority only over the research that they fund. Health Canada has adopted the International Conference on Harmonization's document on Good Clinical Practices (ICH GCP).
>
> REBs work essentially alone in addressing issues that are common to all. Despite some efforts by MRC and the National Council on Ethics in Human Research to bring REBs together to discuss common issues and develop common approaches, there has been little collaboration between REBs in developing policies or educational approaches, addressing common concerns, or considering issues of the effectiveness and efficiency with which REBs do their work. The newly formed Canadian Association of Research Ethics Boards (CAREB) is expected to play a significant role in this area.

The differing views of DNA banks by different cultural groups became very evident during the development of the TCPS, and was re-stated in interviews with people who work with Aboriginal peoples.

> Aboriginal peoples have views and cultural values that very strongly influence the attitudes to ownership and disposal of blood or tissue samples and materials derived from them, They have also many poor experiences of research practices. Any effort to develop guidelines or policies for DNA banking must include meaningful representation from Aboriginal peoples, not only because their views must be respected in research that involves them, but also because they give expression to views that may be held by individuals in other cultures.

Significant efforts were already being started in the 1990s to address issues such as these, but these have greatly accelerated since 2000. Indeed such concerns in 1992-3 caused me to initiate the work that led to TCPS (1998). The steps now underway include:

> Health Canada is working towards establishing a national governance system for research ethics processes for all research that the federal government carries out, that it funds, and that it uses in carrying out its regulatory responsibilities, for example in licensing of pharmaceuticals;
>
> Health Canada's revised regulations for clinical trials (Health Canada, 2001) refer to REB review and auditing of research carried out to meet Health Canada's regulatory requirements;
>
> Newfoundland is developing legislation to create a Provincial Health Research Ethics Board to be the sole legal site for ethics approval of all health research carried out in the province (Clarke, pers comm)
>
> The College of Physicians in Alberta requires all physicians who's research is not under the REBs in the health science centres to seek ethics review by the College's REB;
>
> Québec is authorizing a limited number of REBs to review health research protocols carried out in that province;
>
> The federal research funding agencies have established a joint Panel and Secretariat to ensure that the TCPS is brought to, and maintained at, international standards. They are also initiating a system of Memoranda of Understanding (NSERC, 2001) with institutions in which they fund research to govern the conditions under which those funds are to be used. These MOUs include very explicit requirements for research ethics;
>
> The Canadian Association of Research Ethics Boards (CAREB), which will involve REB members and staff, is now developing as a grass roots organisation designed to provide a forum for joint work towards the highest standards of research ethics;

The National Council on Ethics in Human Research (NCEHR) is initiating workshops designed to provide education and training for REB members and staffs in their functions. This continues their work since 1989 in organising national meetings and in visiting institutions to learn about and advise on their REB operations;

Researchers are working with Aboriginal leaders and peoples to develop mutual understandings of how to meld the opportunities for health care that result from research with the traditional and present cultural values of the communities. CIHR's Institute for Aboriginal Health is participating in this essential work.

These actions indicate that the need for research ethics approval functions to be brought to a high standard of public accountability are now being recognized at the federal and provincial levels, and that concrete actions are being taken or can be confidently anticipated in the near future.

4 CONCLUSIONS

4.1 Governance of DNA banks

The privacy issues raised by genetics do not differ significantly enough from those of other aspects of research involving human subjects to warrant a separate regulatory regime (Section 3.1).

Controls that are already in place for governance of the standards of clinical care are sufficient for governance of issues related to genetic privacy (Section 3.2).

Controls that are developing, building on those that have been growing since the 1970s primarily with the leadership of the Medical Research Council, can confidently be expected to reach publicly acceptable standards of accountability in the near future (Section 3.3).

Therefore, no special federal regulatory initiatives are needed for genetic privacy in research and development.

4.2 Research ethics functions

The rapid evolution of research and ethics related to DNA banks is causing considerable uncertainty and variability within and between REBs, with perhaps unnecessary and destructive inhibition of health research (Section 2.4).

National best practices are needed for the standards and operational procedures for research ethics in this area, including considerations such as consent, ownership, custodianship, security, coding, transfer of samples between

laboratories. This work should involve patients and Aboriginal peoples, as well as researchers, clinicians, ethicists, lawyers etc. CIHR should lead this work

4.3 Canada's opportunities in human genetics research

The next decade will see enormous advances in our understanding of genetics and human health, an area with great implications for innovation, for health care, and for the economy (Section 2.3.2). Canada's excellent resources in this broad area are being mined by researchers and industries from other countries. Canada is making a decision by default not to give priority to this very important area.

CIHR should immediately address the question of whether and how Canada should give priority to participating in this world-wide explosion of research and development opportunity. Together, CIHR and Genome Canada have the financial resources and mandates to bring Canada to the forefront of this area.

4.4. Is a national inventory needed?

Conclusion 4.1 leads to the conclusion that the need to regulate does not justify a national inventory.

The need to demonstrate that government has the area under surveillance has some merit as a rationale for a national inventory.

Facilitation of research may offer a valid rationale to identify tissue or DNA banks.

4.5 Is a national inventory feasible?

The value of an inventory will be limited by its completeness. The personal approach in this study offers the potential for high compliance in DNA banks in public institutions. Without a carrot or a stick, low compliance is likely in the commercial world.

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Younghusband, Ban. Interim Chair, Discipline of Genetics, Memorial University of Newfoundland.

APPENDICES

TABLES

Table 1

NUMBERS OF PEOPLE CONTACTED AND INTERVIEWED

	Vancouver	St John's	Toronto	Montréal	Québec	Totals
Identified	26	6	29	17	13	91
Contacted	23	6	24	12	12	77
Replied	20	6	23	11	10	70
Interviewed	22	20	17	9	9	77
Meeting	19	20	16	6	9	70
Email	-			1		1
Phone	3		1	2		6

Notes:
"Identified" is the numbers of people who I or others identified or suggested as being involved in various ways with DNA banks

"Contacted" is the numbers of people who I contacted, mainly by e-mail.

"Replied" is the numbers who responded to my contact

"Interviewed" is the numbers of people with whom I met,
The means of the meetings are also indicated

The larger number of people interviewed than identified or contacted in Newfoundland is because most contacts and meetings in St John's were arranged by Dr.Ban Younghusband.

INTERVIEWS / MEETINGS HELD **Table 2**

Met face-to-face unless indicated with (t) for telephone interview or (e) for email correspondence only

Name	Location	Notes
Abraham, Samuel	British Columbia Cancer Agency	Director, Technology Development With Sarah Lee
Alman, Ben	Hospital for Sick Children, Toronto	Paediatric orthopaedic surgeon, oncology researcher
Andrulis, Irene	Samuel Lunenfeld Research Foundation, Mount Sinai Hospital, Toronto	Cancer researcher
Arbour, Laura	Vancouver, Women's and Children's Hospital	Paediatrician, Clinical geneticist, working with First Nations peoples to address opportunities and concerns
Asa, Sylvia	University Health Network, Toronto	Director, Pathology, researcher
Banerjee, Diponkar	British Columbia Cancer Agency	Pathologist
Barden, Nicholas	Centre Hospitalier, Université Laval	Genes involved with bipolar disorder and depression
Barer, Morris	University of British Columbia	Centre for Health Policy Research Scientific Director, CIHR Institute for Health Services and Policy Research
Birnboim, Chaim	Ottawa, Regional Cancer Centre	Physician, Molecular biologist
Brisson, Jacques	Hopital Saint Sacrement	Clinical epidemiologist, collaborating with molecular biologists
Carson, Nancy	Ottawa, Children's Hospital	Head, Regional Molecular Genetics Diagnostic laboratory
Clarke, Beverley	Government of Newfoundland and Labrador. Health and Community Services	Assistant Deputy Minister, Policy and Program Services. With Morgan Pond
Cole, David E C	University Health Network, Toronto	Clinical geneticist,
Comité de direction, Reseau de medecine génétique appliquée	Province of Québec	Claude Laberge Président Invitation of Me Bartha Maria Knoppers.
Compton, Carolyn (t)	McGill University Health Centre	Pathologist in Chief, MUHC, Chair, McGill Department of Pathology
Cournoyer, Denis	Montreal General Hospital	Chair, REB

Cullen, Jim	Vancouver General Hospital,	Pathologist
Cynader, Max (t)	Vancouver General Hospital	Director, Centre for Neurosciences
Eaves, Connie	British Columbia Cancer Agency	Associate Director, NCE for Stem Cell Research
Eisen, Andrew	Vancouver General Hospital	Neurologist, collecting and working with DNA banks
Fernandez, Bridget	Memorial University of Newfoundland	Director, Provincial Genetics Service
Gallinger, Steven	Mount Sinai Hospital, Toronto	Surgeon, cancer researcher
Gavsie, Ronnie	Ontario Genomics Institute	President and CEO
Gleave, Martin	Vancouver General Hospital	Oncologist, bank, clinical research
Green, Jane	Memorial University of Newfoundland	Geneticist, working with a range of familial diseases
Green, Roger	Memorial University of Newfoundland	Geneticist, molecular biologist, working with a range of familial diseases
Guha, Abhijit	University Health Network, Toronto, Western Hospital	Neurosurgeon, Co-Director, Labatts Brain Tumour Centre
Gulliver, Wayne	Newlab Clinical Research Inc	Chairman/Medical Director. Physician working with familial skin diseases. Original founder of Newfound Genomics. With Debbie Reynolds, President and CEO
Hall, Judith (t)	Vancouver, Women's and Children's Hospital	Past Chair, Paediatrics, Clinical Geneticist.
Hamet, Pavel	Centre Hospitalier, Université de Montréal	Director of Research.
Harnett, John	Memorial University of Newfoundland	Chair, Discipline of Medicine; Former chair, REB.
Hayden, Michael	Vancouver, Centre for Molecular Medicine and Therapeutics	Physician, clinical researcher, Head, CMMT, Scientific Director, Xenon
Hudson, Tom (e)	McGill University	Professor, genomics researcher
Huntsman, David	Vancouver General Hospital	Physician, bank, molecular
Hyslop, Peter St. George	Tanz Centre for Neurodegenerative Diseases	Director, Molecular biologist, researcher
Kamel-Reid, Suzanne	University Health Network, Toronto	Director, Genetic Diagnosis Laboratory

Kennedy, James	Centre for Addiction and Mental Health	Professor, psychiatry, molecular biologist
Khandjian, Edouard	Centre Hospitalier Universitaire de Québec, Pavillon Saint François D'Assise	Directeur, Banque Lymphoblastique, Réseau de medicine Génétique appliqué du FRSQ
Khraishi, Majed	NCE in Arthritis, St John's	Rheumatologist
Knoppers, Bartha Maria	Faculté de droit, Université de Montréal	Chair, International ethics cttee, Human Genome Organisation
Laberge, Claude	Centre Hospitalier, Université Laval,	Director, Réseau de medicine Génétique appliqué du FRSQ
Labrie, Fernand	Centre Hospitalier, Université Laval	Directeur scientifique, Institut de recherche
Langlois, Sylvie	Vancouver, Women's and Children's Hospital	Past Director, Molecular Genetics Diagnostic Laboratory
Levy, Julia	QLT Inc	President and CEO
Ling, Victor	British Columbia Cancer Agency	Vice President, Research Vice President, CIHR With Stephen Herst
Loomis, Chris	Memorial University of Newfoundland	Vice President, Research
Maziade, Michel	Centre Hospitalier Robert Giffard	Director, Research
McDonald, Lucinda	Centre for Health Information, Newfoundland and Labrador	Director of Communications
McGillivray, Barbara (t)	Vancouver, Women's and Children's Hospital	Paediatrician, Clinical geneticist, Former Chair, UBC REB (medical)
McInnes, Rod	Hospital for Sick Children, Toronto	Scientific Director, CIHR Institute of Genetics
McMaster, Robert	Vancouver General Hospital, UBC	Chair, Medical Genetics, UBC
Minden, Mark	Princess Margaret Hospital	Oncologist, researcher
Ouellette, Francis	Vancouver, Centre for Molecular Medicine and Therapeutics	Bio-informatics, Data security
Parfrey, Patrick	Memorial University of Newfoundland	Clinical epidemiologist, working with a range of familial diseases
Paulse, Bertha	Dr. H Bliss Murphy Cancer Centre, St John's	CEO
Phillips, Robert	Ontario Cancer Research Network	CEO
Pritzker, Kenneth	Mount Sinai Hospital, Toronto	Pathologist in Chief

Pullman, Daryl	Memorial University of Newfoundland	Ethicist
Rahman, Proton	Memorial University of Newfoundland	Rheumatologist, Scientific Director, Newfound Genomics
Ray, Peter	Hospital for Sick Children	Director, Genetic Diagnostic Laboratory
Robb, Desmond	Memorial University of Newfoundland	Pathologist
Rouleau, Guy	Montreal General Hospital	Physician, DNA bank leader, molecular biologist
Sadovnick, Dessa	Vancouver, Women's and Children's Hospital	Clinical Geneticist
Scherer, Stephen	Hospital for Sick Children, Toronto	Associate Director, Centre for Applied Genomics
Schreiber, Wes	Vancouver General Hospital	Clinician, working with inherited disease
Shaw, Patricia (t)	Sunnybrook and Women's Hospital, Toronto	Pathologist, Ovarian cancer researcher
Simard, Jacques	Centre Hospitalier, Université Laval	Chaire de recherche du Canada en oncogénétique
Skamene, Emil (t)	McGill University Health Centre	Director of Research
Spratley, Richard	Vancouver General Hospital	Former Director, Research Services, UBC
Tetu, Bernard	Hotel Dieu, Québec	Pathologist, researcher
Thomas, David	McGill University	Chair, Department of Biochemistry
Tremblay, Michel	McGill University, Cancer Research Centre	Director
Tsao, Ming	University Health Network, Toronto	Pathologist, researcher
Vohl,		
Wherrett, John	University Health Network, Toronto Western Hospital	Director, CIHR funded Brain Bank
Xie, Yagang	Memorial University of Newfoundland	Director, Molecular genetics Laboratory
Younghusband, Ban	Memorial University of Newfoundland	Interim Director, Discipline of Genetics; Researcher working with inherited diseases. Former Chair, REB
Confidential 1		Physician
Confidential 2		CEO, gene banking company
Confidential 3		President and CEO, genetic analysis laboratory

COLLECTIONS / BANKS CLINICIANS / RESEARCHERS Table 3

NAME	Location	PURPOSE	Samples	NOTES
Alman, Ben	Hospital for Sick Children, Toronto	Cartilage and fibrous tissue tumours	6-800 over 10 years	Patient samples from orthopaedic surgery Applying for CIHR IHRT group
Andrulis, Irene	Samuel Lunenfeld Foundation	Osteo- and soft tissue sarcomas Breast cancer tissue	Part of NCIC bank held in Winnipeg	Also CIHR funded IHRT colon cancer study with Newfoundland
Arbour, Laura	British Columbia Women's and Children's Hospital	Spina Bifida and birth defects Autoimmune liver disease		Research projects on hold while discussions with First Nations peoples are being held
Asa, Sylvia	Princess Margaret Hospital	Flash frozen tumour tissue bank	Starting	Linked directly to careful pathological analysis
Barden, Nicholas	Centre Hospitalier, Université Laval	Bipolar illness and depression	1K over 16 years	Family based bank
British Columbia Cancer Agency	Vancouver	Cancer care and research. Gene/marker discovery. Somatic and mendelian mutations	Starting BC-wide tumour and DNA banks	Intend to collect tissue from all BC Cancers, with links to BC Cancer registry (reportable disease).
Birnboim, Chaim	Ottawa Regional Cancer Centre	Colorectal cancer Research related to disease and feedback to patients	350 since 1993	Research and clinical care. Uses Genofix and paraffin blocks for room temp storage.
Cart@gène	Province of Québec	1% of Québec population for screening research	Starting	Link genetic and health information to assess regional needs for health services planning
Cole, David	Toronto General Hospital Genetic Repository	Tissues and DNA from many disease areas seen in clinic or referred by other clinicians	8K	Provides service for many clinicians and researchers

Compton, Carolyn	McGill University Health Centre	Tissue and blood samples from patients in MUHC	Developing	Research and clinical service resource based on top quality samples.
Eisen, Andrew	Vancouver General Hospital	ALS Clinical and research	200+ plus relatives	Close collaboration with Umaa University, Sweden. Identifiable/traceable
Fernandez, Bridget	Provincial Genetics Service, Nfdland	Samples in a range of diseases	10-12K files, 1-1.2K pts/year	Consider immortalizing when patient seriously ill
Gallinger, Stephen	Mount Sinai Hospital	Gastro-intestinal cancers	50-75/year x 5yr	Population based and familial studies
Gleave, Martin	Vancouver General Hospital	Prostate cancer Clinical and research	Hundreds	Started many years ago. Working with Huntsman in collection and storage
Green, Jane	Memorial University, St John's	Familial colorectal and other cancers Insulin dependent diabetes	40-60 families Since 1980s.	Newfoundland families and genetic heritages. Sees all cancer genetics patients in province.
Green, Roger	Memorial University, St John's	Glaucoma, Hereditary sensory neuropathy, Colon cancer, other areas	Variety of start dates, sample numbers per disease	Works with other St John's research projects. Started the gene banking and analysis service now provided by Xie.
Guha, Abhijit	University Health Network, Toronto Western	Brain tumour tissue samples, flash frozen	1700 patients 5.2K samples collected, approx half used	Samples available for research purposes, since 1993
Gulliver, Wayne	St John's Nfld	Familial dermatological diseases	10K patients in computer database	Initiated Newfound Genomics. Now working with New Lab Clinical Research Inc.
Hamet, Pavel	Centre Hospitalier, Université de Montréal	CHUM involved in numerous research initiatives within university, provincially and with international collaboration	Banks held in Chicoutimi, Saguenay – Lac St Jean region	Close links to Cart@gène, with major roles in phenotyping and genetic counseling ,
Hayden	Centre Molecular Medicine & Therapeutics	Huntington's Disease, Atherosclerosis	6K 150 brains Since 1984	Samples obtained from patients world-wide.

Hudson, Tom	Centre Génomique de Montréal	Asthma, early onset heart disease, type 2 diabetes	1K for each disease, mix of families and case controls	Repository kept at Chicoutimi Hospital, Saguenay/Lac St. Jean region
Huntsman	Vancouver General Hospital	Clinical and research CV and pulmonary Ovarian cancer Various others (res)	Hundreds	Collaborative and personal research. Also collects for potential future uses.
Hyslop, Peter St George	Centre for Neuro-degenerative Diseases, Toronto	Neurodegenerative diseases	Hundreds	Cell lines developed only when funds permit. International collaborations
Kamel-Reid, Suzanne	University Health Network, Toronto	Tumour tissue samples	Hundreds	Samples from genetic analysis regional center. Links to UHN bank at Princess Margaret Hospital
Kennedy, James	Centre for Adiction and Mental Health, Toronto	Every major psychiatric disorder	8.7K 70% Canadian, 10% Australian, 20% American	Molecular genetics of psychosis
Khandjian, Edouard	Hopital St François d'Assise	Banking immortalized cell lines for clinical research needs	980 individuals since 1989	Immortalize and bank cell lines at request of 12 researchers in Montréal and Québec. FRSQ funded.
Laberge, Claude	Centre Hospitalier, Université Laval	Numerous collections with many collaborators	Thousands	Directeur, Réseau de médecine génétique appliquée
McGillivray	BC Women's & Children's	Clinical and research Patients seen in clinical work. Also hereditary cancers. Study of CV stent patency starting	15-20 families 500	Store samples (consent and REB; was REB chair; research ethics leader).
Minden, Mark	Princess Margaret Hospital	Leukemia	2000 patients over 15 years	Oncologist, treating physician
Ontario Cancer Research Network	Across Ontario	Tumour tissue bank	Starting	Seeking to establish a province wide tumour tissue registry

Parfrey	Memorial University, St John's	Range of diseases, mainly metabolic. Arrhythmic right ventricular disease	Numerous families	Research and clinical. Clinical care directly related to and assisted by research
Rahman	Memorial University, St John's	Ankylosing Spondomyelitis Rheumatoid and other Arthritis		Research purposes arising from clinical responsibilities
Ray, Peter	Hospital for Sick Children, Toronto	Prepare and collect samples at request of researchers	30K DNA samples	Started in 1987 with focus on Duchenne
Robb	Memorial University, St John's	Tumour tissue banks	5-600 tissue samples	Collecting from pathology responsibilities in surgery
Rouleau, Guy	McGill University Health Centre,	Wide range of projects through Québec Genetic Diseases Network and his own projects	20K samples, 50 diseases	Getting into multi-genic diseases Linked to Cart@gène
Sadovnick	BC Women's & Children's	Alzheimers, multiple sclerosis, bipolar, schizophrenia, other neurological		Since 1984. Linked across country and internationally Stored at U West Ont. Clinical care, research
Shaw, Patricia	Sunnybrook and Women's Hospital, Toronto	Ovarian tumour banks, within Ontario and in collaboration with USA (NIH funds).		Seeking inter-provincial collaboration
Simard, Jacques	Centre Hospitalier, Université Laval	Families with inherited cancers	Thousands	Gene discovery for familial cancers
Tetu, Bernard	Hotel Dieu Hospital, Québec	Ovarian cancer		Collaborations with Jacques Brisson and others
Tremblay, Michel	McGill Cancer Centre	Needs tumour banks for cancer research		Works with clinicians collecting and using banks
Tsao, Ming	Princess Margaret Hospital, Toronto	Lung cancer		Samples arising from NCIC lung cancer treatment trials

Vohl, Marie-Claude	Centre Hospitalier, Université Laval	Obesity, metabolic lipid disorders		Works with Réseau de mérdecine génétique appliquée
Wherrett, John	University Health Network, Toronto Western	Brain bank	1900 brains	CIHR funded since 1980s
Xie	Memorial University, St John's	Haemophilias Clinical and research		Collaborates with physicians caring for patients
Younghusband, Ban	Memorial University, St John's.	Congenital insensitivity to pain		Collaborates with physicians caring for patients
Confidential 1		Clinical and research	100-200	Range of diseases, some familial, some community based.
Confidential 2		Clinical and research	80-90	Families across N America. Mutations v rare and family specific

Table 4

DNA SAMPLES HELD BY GENETIC ANALYSIS SERVICE LABORATORIES

Name	Location	Samples	Notes
Carson	Children's Hospital of Eastern Ontario,	1,000	Analyze 2,400 samples /yr. Most discarded at 6 mo. Bank samples for REB approved research uses
Kamel-Reid, Suzanne	University Health Network, Toronto	Thousands	DNA remaining after genetic analysis of clinical samples
Langlois, Sylvie	Vancouver, Childrens	20-25K 1-1.5K	Laboratory service established 1989 3,000 samples analyzed /yr, all stored, identifiable. Samples collected by researchers stored at their request, mostly in neurological areas.
Ray, Peter	Hospital for Sick Children	30K	DNA remaining after genetic analysis of clinical samples
Rouleau, Guy	McGill University Health Centre	20K	DNA remaining after genetic analysis of clinical samples
Xie	St John's, MUN	2-3K 1K	Lab service established 1998-9. Previously offered by a researcher at MUN. 1,800 samples tested /yr, expected to grow to 3K. Now store all, but space may require selective disposal in a few years Provide extraction and storage for cancer and clinical genetics groups on request, with proper REB approvals

Table 5

COMPANIES INVOLVED IN DNA BANKING

Name	Location	Purpose	Samples	Notes
Newfound Genomics	St John's	Gene/mutation discovery Originally psoriasis Now obesity, Type 2 diabetes, Inflammatory bowel disease. Osteoarthritis proposed	1,200 Expect 2,500	Collecting samples from patients and families who respond to disease related advertisements. State that no DNA will leave Newfoundland, and that research will be done here.
Confidential		Cardiovascular Specific central nervous system disorders Specific metabolic diseases Obesity,	20-30K from around the world, up to 10% from Canada	Traceable with codes held by physicians, not company. No secondary users.
Confidential		Service DNA analysis		Analyses samples on request, individual or government, mostly in paternity cases (e.g., family support requirements) (samples identifiable). Stores samples in case of need for verification, response to challenges. No samples released

Genome Canada's Draft *Canadian Genomics Company Directory* (March 2001) lists 54 companies, with outlines of their areas of interest. Those that appear to me to work with DNA banks are AEgera Therapeutics Inc, Chronogen Inc, Ellipsis Biotherapeutics Corporation Inc, Gallileo Genomics Inc, Hemax Genome Inc, Newfound Genomics and Xenon Genetics Inc. Procrea and Signalgène were also mentioned by interviewees.

Pharmaceutical companies are now often requesting REB approval for their projects to collect blood samples from patients in clinical trials.

Dr. Guy Rouleau informed me that his genomics analysis and DNA banking facility has a contract with Pharmacia for storage of samples obtained by them through research that they sponsor.

Industry Canada Industrie Canada

Appendix 1

TO WHOM IT MAY CONCERN:

This letter is written to inform you that Dr Francis Rolleston is working under contract with the Life Sciences Branch of Industry Canada in January and February 2002.

The Government of Canada is now studying the broad area of genetic privacy. As one component of this initiative, we are exploring the possibility of identifying the collections (banks) of human tissues in Canada, or collected in Canada, that could be used for genetic analysis. This overview should also include collections of information derived from genetic analyses. Dr. Rolleston has been asked to carry out a pilot study to determine the feasibility of such an inventory, and to set out its parameters if it were to be carried out.

Dr. Rolleston plans to work with a representative sample of institutions and organisations across Canada to identify the kinds of genetic banks that they hold or plan, and related information such as the conditions under which the tissue samples were collected, including the consents involved, and the plans for their use. Recognizing the potentially sensitive nature of the information that he will seek, Dr Rolleston has agreed to prepare his report in a generic manner that will not identify any particular institution or organisation involved in his study. I attach a copy of Dr. Rolleston's curriculum vitae.

Please contact me should you require any clarification or additional information about this important research project.

Sincerely,

Dean Barry
Policy Research & Development Officer
Life Sciences Branch, Industry Canada
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Birth

Montreal, 1 June 1940

Education

Queen's University, Hons BSc, Biochemistry, 1962
Oxford University, DPhil, Biochemistry, 1966
University of Chicago, Physiology, Post-doctoral, 1966-1968

Employment

University of Toronto, Faculty of Medicine, Assistant Professor, 1968-1975
Medical Research Council of Canada
Assistant Director, Grants Program, 1975-1977
Director, Special Programs, 1977-1983; Public Affairs, 1983-1986; Scientific Evaluation, 1986-1993; Innovation Teams, 1993-1997; Ethics and International Relations, 1997-2000
Canadian Institutes of Health Research
Director, Ethics, 2000

Contractual as Francis Rolleston Consulting January 2001-

Genome Canada. Industry Canada
Institute for Environmental Research, on patenting in biotechnology, recreational therapy, nuclear waste management.
Senator Yves Morin

Volunteer

Research Ethics Boards, Ottawa Hospital, National Research Council, 2001-
Ottawa Science and Technology Ethics Roundtable (founded and run), 2001-
Canadian Association of Research Ethics Boards
Canadian Blood Services, Ethics Review Board, 2001-

Publications

Biochemistry. Control of intermediary metabolism, protein synthesis:
Peer reviewed papers and reviews, 1967-1974
Ethics and peer review:
Articles, book chapters, 1977-2000

Textbook: Mitchell L. Halperin and Francis S. Rolleston. *Clinical Detective Stories: A Problem-Based Approach to Clinical Cases in Energy and Acid-Base Metabolism*, Portland Press, 1993.

Appendix 2.

RAND Corporation study

Summary

The RAND Corporation Handbook of Human Tissue Sources (RAND 1999) surveyed the whole USA. It was commissioned by NBAC background research for its paper (NBAC 1999). The RAND corporation publication states:

> *"We intend this handbook to serve the research community as a comprehensive reference source of tissue banks in the United States and to facilitate the distribution of tissues for individual research projects."*

The report states that it represents the first time that this information has been assembled in a single document and the first time that the magnitude of archives of stored tissues has been assessed.

The 200+ page report contains chapters entitled:

Large tissue banks, repositories and core facilities
Tumor registries
Tissue collections created from longitudinal and individual research studies
Pathology specimens
State screening laboratories and forensic DNA banks
Cryopreservation facilities / storage banks
Organ banks / blood banks

The RAND report "*...attempts to provide information about several aspects of stored tissue samples by addressing the following questions:*

1. *Where are the tissues stored?*
2. *How many tissue samples are stored at each institution?*
3. *Who are the sources of stored tissue samples?*
4. *Why were the tissue samples originally collected?*
5. *For what purposes have the stored tissues been used?*
6. *Who has access to the samples?*
7. *How are the tissue samples stored?*
8. *What identifying information is kept with the tissues?*

The authors of this report identified collections of stored samples through:

A literature review of papers about tissue banks and DNA banks
Searches of the internet (the relevant sites are listed)
Searcher of RAND's RaDIUS database and NIH's CRISP database to identify federally funded sources of stored tissue
Personal communication and consultation with experts.

The overall conclusions of the report can be summarized as follows (from Chapter 10, RAND 1999):

- Collections range from formal repositories to informal stores of specimens in a researcher's freezer
- Sizes range from less than 200 samples to more than 92 million (National Pathology Repository and DNA Specimen Repository for Remains Identification, the world's largest repositories;
- A total of more than 307 million specimens from more than 178 million individuals existed in 1998, and the numbers are growing at more than 20 million per year.
- The National Institutes of Health is the probably the largest funder of extramural (outside government) tissue repositories;
- Pathology departments at teaching institutions collectively constitute the largest and oldest stores of tissue samples in the USA. The vast majority of these samples were collected for diagnostic or clinical reasons
- Newborn screening laboratories contain approx 13.5 million Guthrie cards
- More than 2.3 million specimens are in repositories established for research, including some very longitudinal studies, yielding many research publications.
- Blood banks collect many samples, but keep them only for short periods, though some samples are kept for research and quality control.
- Tissue and organ banks keep few samples, and generally not for research
- Forensic and remains identification banks are used for the purposes that are implicit in their titles
- Many valuable specimens and data resources exist from a variety of sources, but no centralized database allows researchers to obtain access to and information about them.
  NCI is developing a national information database of breast cancer resources for research and clinical purposes in connection with the National Action Plan on Breast Cancer

Appendix 3

Identification of tissue/DNA/gene banks used in research in Canada
A pilot study.
Francis Rolleston
January-February, 2002

I am working with Industry Canada on this pilot study for identification of tissue/DNA/gene banks used in research. The report is due at the end of February 2002.

CONTEXT

This project is part of the Federal Government's study of genetic privacy. A number of departments and agencies have formed a Genetic Privacy and Information Working Group to develop recommendations on policies that the government should be considering in this broad area. A perceived need to understand the range of repositories of samples that could provide genetic information about individuals led to this project.

FOCUS ON RESEARCH

This project will focus on banks that are used, or could be used, for research purposes, and will look only at those that are outside government. I will be interested in banks collected in health care settings only to the extent that they are intended to be used in research. Others will be looking at areas such as insurance, employment and governmental functions (e.g., military, police).

SAMPLING APPROACH

In this pilot study, I intend to focus on Vancouver, Toronto, Ottawa, Montréal, Québec and St John's. Building on my own knowledge of leaders in this broad area, and advice from them and from sources in Industry Canada, the literature and elsewhere, I am visiting each of these cities to speak with as many people as I can, and to interview others by phone.

CONFIDENTIALITY

Given the sensitivity of the issues, I have sought from Industry Canada the assurance that I can prepare the report in a generic manner that will not identify any particular institution of organization involved in this study.

INFORMATION SOUGHT

Questions for each organisation/individual

Type(s) of organisation or function
Number of tissue/DNA/gene banks
General nature of banks

Questions on each bank

Collection of the bank

Why were the samples collected?
What were the criteria for selection of individuals providing samples?
Who collected the samples?
How many samples are in the collection?
How many individuals are represented in the collection?
If derived from another collection, from where did the samples come?

What consent was given to collect the samples?
To place the samples into this collection?

To what extent can the samples be linked to the individuals who provided them?

When was the collection established?
Is accrual continuing?

What REB approval was given to make this collection?

Storage of the bank

Where is the collection stored?

In what forms are the samples stored?

To what extent can the samples be linked to the individuals who provided them?

What security arrangements are in place to protect the samples and their identifiability to the individuals who provided them?

Is there a planned date for destruction of the samples? When?

What consents were given to store the samples?

Uses of the bank

Has the reason for which the collection was established been satisfied?
What was it?
When was it completed or when is it expected to be completed?

What further or secondary uses are envisaged for the collection?

What is the expected need for identifiability for these further uses?

What decision-making authorities or processes are in place for further or secondary uses?

What consent has already been obtained or is envisaged for secondary uses?

What REB approval systems are/will be required for further or secondary uses?

Your views on the role that government should or should not play in governance of tissue/DNA/gene banks

I have been asked to report on views about the government's role(s), if any, in national governance of genetic privacy.
Your views on this question would be very important.

I look forward to working with you

Francis Rolleston
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January 12th, 2002

Appendix 4

COMPONENTS FOR CANCER SURVEILLANCE

IN CANADA

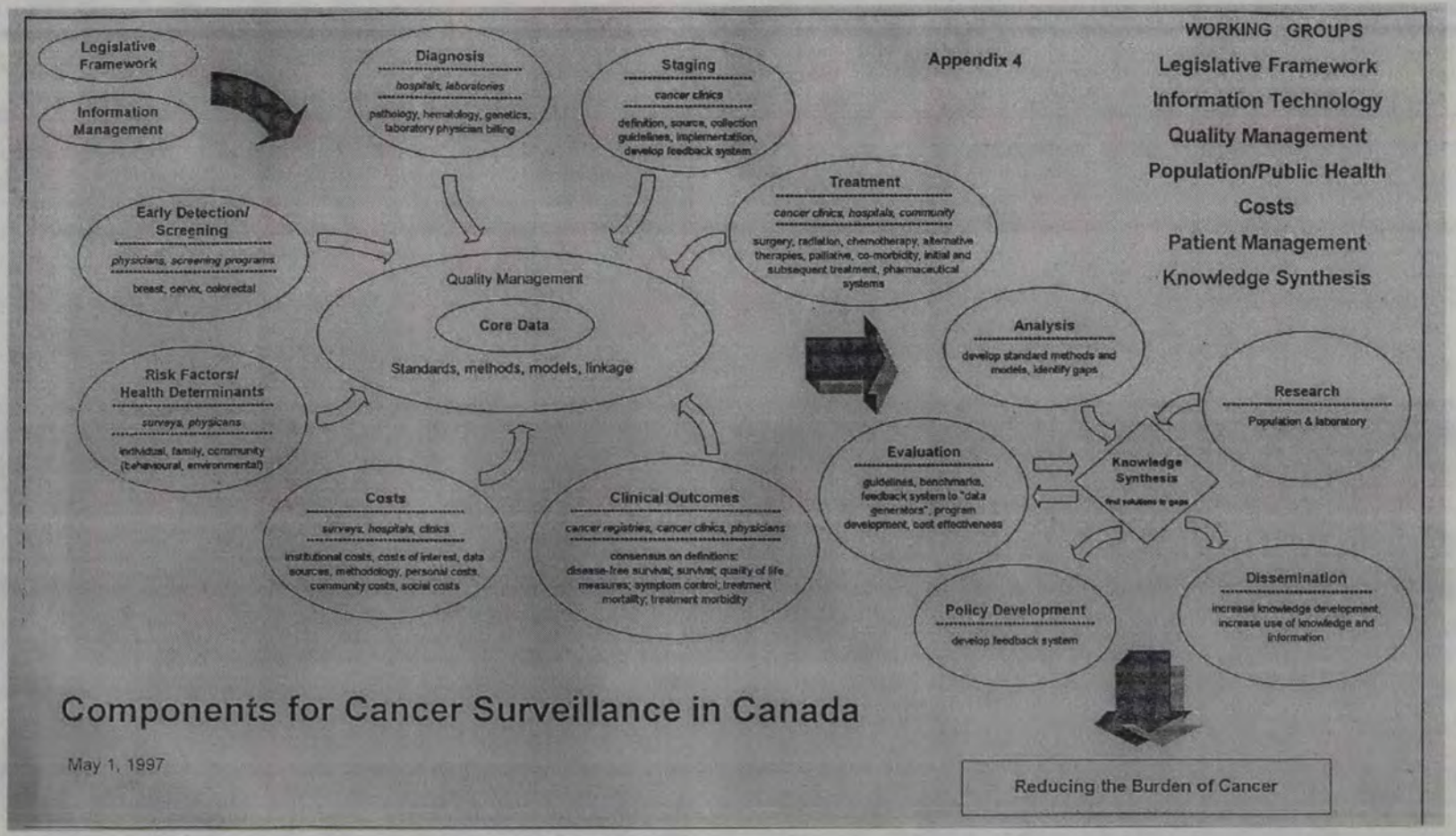
Prepared

by the

Coalition on Cancer Surveillance

of the

Canadian Association of Provincial Cancer Agencies


Appendix 4
WORKING GROUPS
Legislative Framework
Information Technology
Quality Management
Population/Public Health
Costs
Patient Management
Knowledge Synthesis
Legislative Framework
Information Management
Diagnosis
hospitals, laboratories
pathology, hematology, genetics, laboratory physician billing
Staging
cancer clinics
definition, source, collection guidelines, implementation, develop feedback system
Treatment
cancer clinics, hospitals, community
surgery, radiation, chemotherapy, alternative therapies, palliative, co-morbidity, initial and subsequent treatment, pharmaceutical systems
Early Detection/ Screening
physicians, screening programs
breast, cervix, colorectal
Quality Management
Core Data
Standards, methods, models, linkage
Risk Factors/ Health Determinants
surveys, physicans
individual, family, community (behavioural, environmental)
Costs
surveys, hospitals, clinics
institutional costs, costs of interest, data sources, methodology, personal costs, community costs, social costs
Clinical Outcomes
cancer registries, cancer clinics, physicians
consensus on definitions: disease-free survival; survival; quality of life measures; symptom control; treatment mortality; treatment morbidity
Analysis
develop standard methods and models, identify gaps
Research
Population & laboratory
Evaluation
guidelines, benchmarks, feedback system to "data generators", program development, cost effectiveness
Knowledge Synthesis
find solutions to gaps
Dissemination
increase knowledge development, increase use of knowledge and information
Policy Development
develop feedback system
Components for Cancer Surveillance in Canada
May 1, 1997
Reducing the Burden of Cancer

Appendix 5

Summary outline of a possible sequence of events in gene discovery in families.

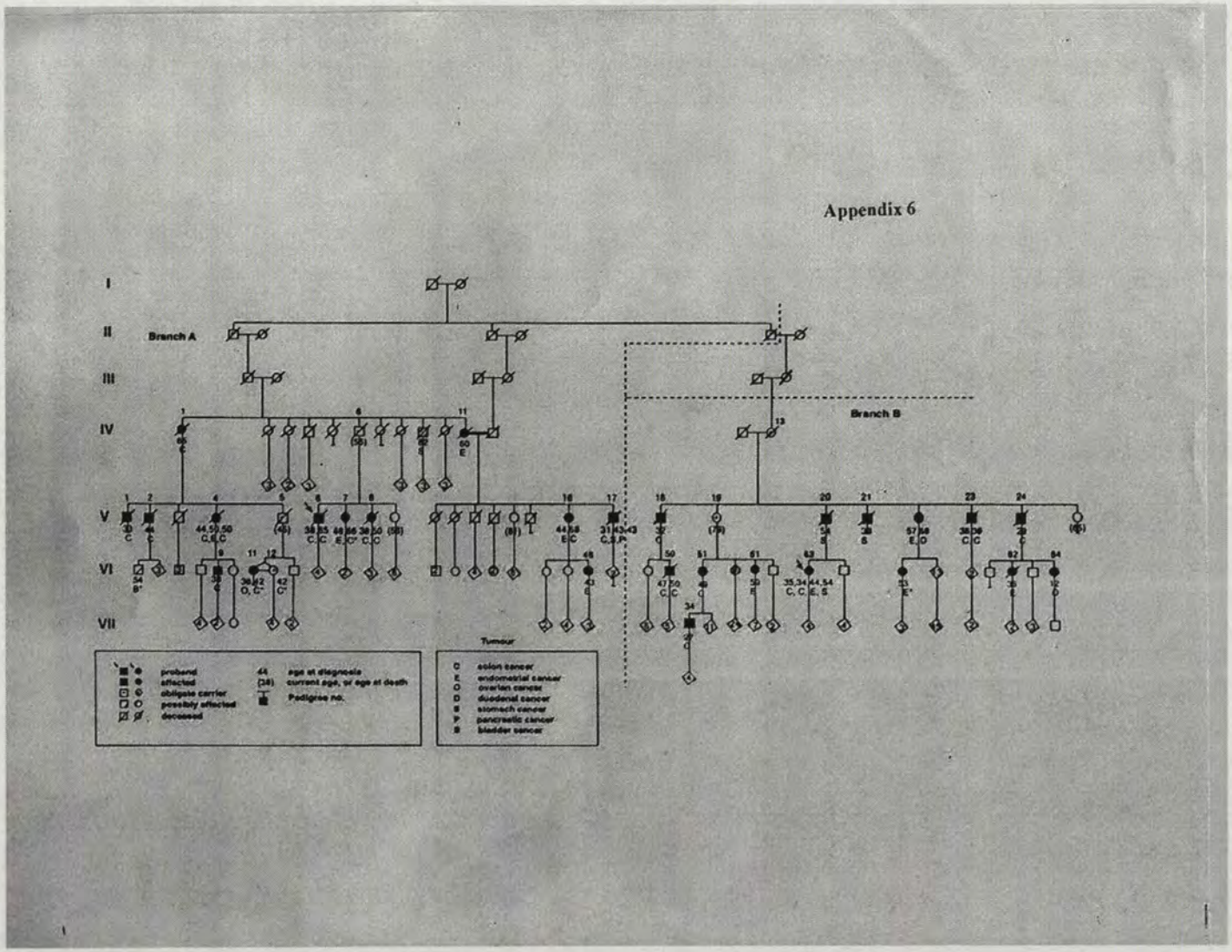
Activity	**Patient/family involvement**	**Regulatory environment**
Identify possible familial disease	Observation by health care professionals	Clinical care
Inform researchers of possible family for research purposes.	Mutual awareness of opportunity and interest	Clinical care / confidentiality
Consent to participate in the research	Clinician seeks patient consent and patient seeks family consent to be approached by researchers. Researchers must not approach patient/family without their consent. Researchers seek consent of each individual to be involved.	Research ethics governance mechanisms for research project, to include means of researcher contact and consent processes
Collect family information (See Table 7)	Clinicians and other researchers collect family and medical history and blood/tissue samples	Clinical care, including genetic counselling, Research ethics governance for research interactions
Molecular research	Clinical care and feedback, with counselling, as information accumulates on patients and families	Clinical care and research ethics governance
Identify gene and mutation(s) affecting family	Feedback to patients and family. Offering of genetic testing information. Counselling as to treatment/prevention etc options.	Clinical care standards
Extend new information to application to general population	Application of research results to general population as appropriate, funded by health care systems etc	Clinical care.

Appendix 6

Pedigree of a family involved in gene discovery for colon cancer

Provided by Dr. Jane Green.

Appendix 6


I
II
III
IV
V
VI
VII
Branch A
Branch B
proband
affected
obligate carrier
possibly affected
deceased
age at diagnosis
current age, or age at death
Pedigree no.
Tumour
C colon cancer
E endometrial cancer
O ovarian cancer
D duodenal cancer
S stomach cancer
P pancreatic cancer
B bladder cancer