Policy Implications of Commercial Human Genetic Research in Newfoundland and Labrador

A Report for the Newfoundland and Labrador Department of Health and Community Services

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Table of Contents

Executive Summary

This report considers the policy implications of commercial human genetic research conducted in Newfoundland and Labrador. For purposes of this executive summary, "commercial research" should be understood as referring to any human genetic research that might result in a commercial product. Hence it refers both to research that is initiated and sponsored by private companies or organisations, as well as that which originates in the public sector but which might lead eventually to marketable products.

Commercial genetic research concerns issues that arise at the interface of health and economics. Although still in its infancy genetic research promises many significant health benefits including new screening techniques, diagnostic tests, and various new therapies and products. Those who patent and market the genetic discoveries that lead to these new products and services stand to reap substantial economic rewards. At the same time it is anticipated that health care costs will increase as these new products and services become available.

Commercial genetic research is of especial significance to Newfoundland and Labrador. The province's relatively homogeneous founder population is thought by many to make this province an excellent place to conduct genetic research. A number of significant genetic disorders appear to be more prevalent within this population. While local academic researchers have been working on various disorders for many years, there is simply too much work for the small number of researchers located here. Furthermore the province lacks the technical infrastructure necessary to carry out much of this work. If this important research is to be conducted in a timely manner collaboration with the private sector will be necessary.

The central challenge in this regard is to present a model for regulating commercially sponsored genetic research that ensures that both the health and economic burdens and benefits that accrue as a result of this work are fairly distributed among all relevant stakeholders. An acceptable model for regulating commercial human genetic research must pass the test of ethical, legal, and social-political acceptability without sacrificing the commercial viability of the research.

This document examines a variety of possible models for governing commercial human genetic research in Newfoundland and Labrador. These models are critiqued systematically with a view to identifying one that best meets the ethical, legal, social-political and economic demands. Two key considerations inform the discussion of the various models and the eventual recommended choice: (1) the unique status of human DNA, and (2) health as a public good.

First, inasmuch as human DNA is the necessary raw material that will lead to various genetic discoveries and associated health products and services, it is important to determine its legal nature and status. This is still a much debated issue in international law but there appears to be an emerging consensus that human DNA is an unique (*sui generis*) kind of entity that combines elements of private property, public resource, and the common heritage of humanity. The recommended model presented here incorporates this hybrid view of the nature of human DNA. Second, inasmuch as health and health care are treated as public goods in Canada, the economic burdens associated with genetic illness will generally be shared by all. It seems reasonable then that any economic benefits that might accrue as the result of participation in genetic research should be directed in the first instance toward the public. Again the recommended model supports this view.

The key recommendation of this report is that the province should adopt a **Provincial Approval Model** for commercial human genetic research. This model requires that as a condition of conducting human genetic research in Newfoundland and Labrador, *all sponsors of genetic research with commercial potential must submit a benefit-sharing proposal along with supporting rationale*. Thus in addition to granting the standard ethics approval required prior to engaging in any human subjects research, the province must be satisfied that the proposed benefit-sharing arrangement is appropriate.

Two supporting recommendations are necessary in order to facilitate the implementation of the Provincial Approval Model:

- The province should move expeditiously to implement the **Provincial Health Research Ethics Board (PHREB)**. The proposed Provincial Approval Model will operate at arms length but as an adjunct to standard research ethics approval. Hence it is essential that the PHREB be in place before the Provincial Approval Model can be instituted.

- The province should establish a **Standing Committee on Human Genetic Research (SCHGR)**. The mandate of the standing committee

> will be to advise the province on current developments in the field of human genetics in general, and to serve as the body that reviews proposed benefit-sharing agreements under the Provincial Approval Model.

The main body of the report proceeds in a systematic manner to provide the substantive argument that leads to the above recommendations. A brief review of the historical-economic-political context presented by Newfoundland and Labrador is provided (Sec. 3). A variety of ethical problems presented by commercial human genetic research is presented (Sec. 4), and a number of models that might be implemented in order to address these issues are surveyed (Sec. 5). Discussion of the main substantive arguments that support the Provincial Approval Model is then provided (Sec. 6) including an extensive treatment of the unique status of human DNA (Sec. 7). The case for the Provincial Approval Model is summarized (Sec. 8), and a proposed method of implementation is provided (Sec. 9). The latter sections of the report include some additional recommendations (Sec. 10) and concluding thoughts (Sec. 11).

In closing it should be noted that Newfoundland and Labrador is the first jurisdiction in Canada and one of the few internationally to move forward with specific recommendations in this regard. This document has been reviewed by a number of experts and some of the ideas contained herein have been presented at various national and international conferences. There is much interest both nationally and internationally in our progress. We thus urge the province to move quickly to implement the key recommendations presented here.

Section 1: Introduction

Biotechnology has become big business in recent years. It has been projected that the worldwide market for biotechnology-based products will grow to $38 billion in 2005 (from $15 billion in 1995) (Knoppers, 1999, 1). This world wide growth is reflected in the Canadian biotech industry. The federal and provincial governments of Canada have placed a special focus on developing this sector.[1] There has also been substantial growth in private investment in biotechnology. Between 1997 and 2001, annual venture-capital investments in biotechnology grew 11% per year from $372 million to $617 million (Industry Canada, 2002b). Canada also boasts the second largest number of biotechnology companies in the world – more than 400 in 2001, up from 121 in 1994 (Caulfield, 1999, 149; Industry Canada, 2002b).

Genetic research constitutes a significant portion of all this activity.[2] Approximately 9% of the biotechnology companies presently operating in Canada work specifically in the area of genomics (Industry Canada, 2002b). Furthermore, genetic research plays an increasing role in many other sectors of the biotechnology industry.

1.1 Newfoundland & Labrador's Potential as a Site for Human Genetic Research—It is genetic research that is the focus of this report, specifically *commercially sponsored* research into the genetics of human beings, or human genetic research that may begin without commercial intent but which nonetheless results in a commercial product. This is a topic of special importance for the province of Newfoundland and Labrador because the province is viewed by many to be a particularly good place to carry out human genetic research. There are four main reasons behind this claim:

[1] For example, in 2000 the federal government created Genome Canada, a not-for-profit corporation charged with developing and implementing a national genomics strategy. To date, Genome Canada has received $300 million in funding from the federal government (www.genomecanada.ca).

[2] Throughout this report, the phrase 'genetic research' is used very broadly. While it is fairly common to distinguish between genetic research, genomics research, proteomics research and so on, these distinctions do not matter for the purpose of this report. As such, the phrase 'genetic research' is used to cover all these areas.

- Almost 90% of the current inhabitants of Newfoundland and Labrador are descended from immigrants, mostly English and Irish, who settled here before the mid-19th century (Mannion, 1977, 5; Taubes, 2001; Industry Canada, 2002a, 103).

- Many of the province's present inhabitants belong to large, close knit families about whom good genealogical and medical records now exist, or can be readily assembled.

- A number of disorders occur or are suspected to occur among the current provincial population at unusually high frequencies, with cases often localized to particular regions.[3] Examples include cardiovascular disease, diabetes, obesity and psoriasis (Atkinson, 2000; Taubes, 2001).

- Residents of the province are generally willing to take part in scientific research. (Atkinson, 2000; Greenwood, 2000; Industry Canada, 2002a, 104).

Some believe that a well documented, 'homogeneous' gene pool like this will make it "easier for researchers to identify the genes associated with specific diseases"[4] (Industry Canada, 2002a, 103). As a result, substantial interest now exists in Newfoundland and Labrador's potential as a place to do human genetic research. Indeed, one commentator describes Newfoundland as ". . . something of a motherlode to the drug development industry" (Greenwood, 2000).

The degree to which this interest is warranted is controversial. It is quite well accepted that a population like that found in Newfoundland and Labrador is valuable for attempting to discover connections between single genes and particular medical conditions. However many conditions result from the interaction of multiple genes along with a variety of other factors, such as diet, environment, and stress. In such cases whether a genetically 'homogeneous'

[3] Although this point is noted separately, it is actually a result of the already noted fact that such a large proportion of the present-day population can trace their ancestry back to 19th century settlement (or earlier).

[4] Whether or not the province's population can properly be described as "homogenous" is also debatable. (Atkinson, 2000) Similar controversies exist about other areas (in particular, Iceland) in which the gene pool is claimed to be homogeneous (Greely, 2000, 160; Arnason et al, 2000, 373-4).

Jane Green, a local geneticist, has suggested in conversation that it might be better to think of the province as containing a number of different homogeneous populations.

population like Newfoundland and Labrador's offers any particular advantage for research is questionable.[5]

It should be noted, however, that not all human genetic research aims at gene discovery. Other possibilities include:

- pharmacogenomics research projects that attempt to determine the influence of a person's genetic makeup on the efficacy and/or safety of a particular drug;
- validation studies that attempt to confirm supposed gene discoveries made elsewhere;
- baseline genetic epidemological studies; and,
- post-patent studies designed to identify a particular niche for a new product.

Thus, even if the value of this province's population with regard to gene discovery turns out to be exaggerated, there may be other sorts of human genetic research for which this province's population is particularly useful. Regarding all these possibilities what must not be forgotten is that, despite all the 'geno-hype' regarding the huge commercial potential of human genetic research in general, the industry is still in its infancy. Any predictions about its economic potential are largely speculative (Caulfield, 2002, A15).

Interest in conducting human genetic research in this province provides both opportunities and challenges. The potential economic opportunities, though speculative, are clear. Newfoundland and Labrador could benefit significantly from having this research conducted here: infrastructure could be developed, the province's research capacity enhanced, and the provincial economy stimulated.

[5] Consider the case of Iceland, whose population has also been claimed to be genetically homogeneous. The following comment about using its population in genetic research might also apply to Newfoundland and Labrador:

> "It is not yet clear whether drugs based on errant genes found in Icelanders will work elsewhere. Icelanders may not possess the full spectrum of human genetic weaknesses, or they may have them with different frequency." (Wade, 2002)

There are potential health benefits for the province's residents as well.[6] As this work proceeds it is anticipated that tests to identify those at risk for various genetic disorders will be developed. Eventually it is expected that products to treat or prevent these disorders will be produced. A challenge is presented, however, by the differing natures of the two kinds of opportunity just mentioned. That is, human DNA is significant both as an economic good and as a health related good. Given the variety of perspectives on the nature of these goods, human DNA can be valued in quite different ways. This report acknowledges this value tension at the outset. The position taken here is that these value spheres are not necessarily incompatible. The challenge is to strike an appropriate balance between them.

In addition to the general concerns just mentioned, a 'technical' issue is raised by the fact that human DNA is both an economic and health related good. Since human genetic research raises issues that arise at the interface of health care and commerce, recommendations about policies to govern it must be sensitive to the manner in which they might be interpreted in light of proposed protections under the North American Free Trade Agreement (NAFTA) that aim to preserve Canada's public health care system.[7] These provisions are already under pressure given recent developments in Alberta and elsewhere that are moving toward greater privatization in health care (CUPE, 2002). Inasmuch as the distinction between commercial benefits and health benefits is often obscured in human genetic research, our concern is not to contribute to further erosion of the principles of the *Canada Health Act* by proposing a policy approach that might be interpreted to privatize health benefits in some way.

1.2 Ethical Issues—Human genetic research raises a host of ethical issues. Primary in this regard is the status of human DNA. Should it be treated as a commodity that is the property of the individual donor? Is it better thought of as a kind of common, public good? Or, is there some other way of conceiving of the status of DNA that would be more appropriate? The economic and health perspectives just mentioned might provide different responses to such questions.

A second set of issues stem from the fact that a person's DNA carries a great deal of information about that individual and his or her relations. Thus privacy issues

[6] Economic and health benefits do not exhaust the potential benefits of human genetic research, although they are the sorts of benefit that matter most for the purposes of this report. Other benefits might include increased intellectual activity in the province and an elevation of external opinion of the province (due to recognition of the province as a centre for genetic research).

[7] See the North American Free Trade Agreement Annex II.

are often at the core of discussions of the ethics of human genetic research. This second set of issues also raises a point that needs addressing before proceeding any further. Discussions of the status of human DNA run the risk of being ambiguous regarding whether what is being referred to is the physical substance or the information it contains. As might be expected given the set of issues just identified, the issues raised in this report primarily concern the information contained in human DNA and concern the physical substance only insofar as it provides access to that information. Unless specifically noted, it should be assumed that it is the information contained in human DNA that is of primary interest when DNA is discussed in this report.

A third set of concerns stems from the fact that one's genetic makeup is thought by many to be intimately tied up with one's personal identity (Nelkin and Lindee, 1995, 2). Hence some believe that certain kinds of genetic research are incompatible with human dignity. Finally, the *methods* used to carry out human genetic research raise issues that seldom arise in other human health research. For example, inasmuch as geneticists aim to study families as opposed to individuals, the usual procedures for acquiring informed consent to research may need to be modified. Yet another novel issue stems from the fact that while most human subjects research involves a single defined experiment, genetic researchers often develop 'gene banks' that could be used in the future for an unpredictable variety of research programs. It is at present a matter of some debate whether the standards for ethical research developed for 'single run' experiments are adequate for 'open ended' human genetic research projects (Greely, 1999).

Some of these ethical challenges have already been addressed in Newfoundland and Labrador. In the fall of 2000 the provincial government set in motion a process to establish in legislation, a Provincial Health Research Ethics Board (PHREB)[8]. The mandate of the board will be to oversee all health related human research in Newfoundland and Labrador. The terms of reference for the proposed board will ensure that all health related human research conducted in the province—including all human genetic research—is reviewed and monitored by the PHREB. However, in drafting specific guidelines for human genetic research no attempt was made to address the substantive issues that arise with regard to commercial genetics.[9]

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[8] See Appendix B for the terms of reference for the PHREB and Appendix C for the proposed guidelines for genetic research. The process to establish the PHREB continues to move forward. At present it is anticipated the proposed legislation will be considered by the provincial legislature in 2003.

[9] As it now stands, the PHREB proposal suggests that the issues raised by commercial genetics research are essentially the same as those raised by other forms of commercial research (See

Addressing the issues raised by commercial human genetic research is particularly important because the present state of funding for academic research in general, coupled with the significant costs associated with genetic research in particular, ensures that only a fraction of human genetic research will be done in the near future unless this research receives substantial commercial funding (Caulfield, 1999, 152). The expectation that the research agenda will be dominated by commercial interests raises a distinctive set of ethical questions all its own. Again, this is because two competing (though not necessarily incompatible) sets of values, namely economic and health related, are at stake.

1.3 The Goal of this Report—This document addresses the challenges posed by commercial human genetic research by outlining a variety of models for governing commercial human genetic research in Newfoundland and Labrador. The aim is to identify a model that passes the tests of ethical, legal, and social-political acceptability, without sacrificing the commercial viability of the research. Social-political acceptability is mentioned specifically in this regard because it is the citizens of this province who must be convinced ultimately of the merits of the proposal. The conclusion is optimistic. Governed properly, commercial human genetic research can be conducted in a manner that ensures both that the health and economic interests of the citizens of Newfoundland and Labrador are protected, even as the commercial interests of the sponsors of this research are advanced.

1.4 Organization of this Report—Sections 2 through 4 provide the background for this report. Section 2 describes the process that led to the writing of this report. Section 3 explains the historical, political and economic context in Newfoundland and Labrador as it is relevant to commercial human genetic research. Section 4 describes the ethical challenges posed by this research.

Sections 5-7 present some possible models for the governance of commercial human genomics research in Newfoundland and Labrador and provide a basis for choosing amongst those models. Section 5 describes the possible models. Section 6 explains some basic assumptions this report relies upon in assessing the relative merits of the various models. Section 7 then presents an extended discussion of the most controversial issue that must be addressed in considering the merits of the models – the ethical status of human genetic material

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Appendix C, Section 4). It maintains, however, that those who serve as research subjects must be informed that the research is being carried out as part of a commercial enterprise. The position outlined in this document agrees with the second statement, but not the first.

Sections 8-9 respectively make the case in favour of what we call the Provincial Approval Model and consider how that model should be implemented.

Section 10 presents the main recommendations made by this report.

Section 11 offers a brief conclusion.

Section 2: Background and Methodology

This report is the result of a project funded by the Newfoundland and Labrador Department of Health and Community Services via the Newfoundland and Labrador Centre for Applied Health Research. Additional funding was provided by the Newfoundland and Labrador Department of Industry, Trade and Rural Development. Research and writing of the report took place between September, 2001 and August, 2002. A project advisory group was struck at the outset consisting of local experts in genetics, law, health policy, business, and bioethics. Both sponsoring government departments were represented by observers who attended the regularly scheduled advisory group meetings. A complete list of the research/writing team and advisory group members is provided in Appendix A.

The initial stage of this project consisted of a literature search in order to identify key issues in commercial human genetic research as well as approaches that have been taken to govern such research in various parts of the world. Following this stage experts in health law and health policy were consulted, as were representatives of private industry and government. This was accomplished through meetings held in St. John's with local experts, as well as trips to national and international meetings on genetic research. Various aspects of the project were discussed with national and international experts at meetings of Genome Canada (Vancouver, January 2002), the Annual Congress of the Social Sciences and Humanities (Toronto, May 2002), and a pre-conference workshop for BIO 2002 (Toronto, June 2002). Aspects of the work were presented at national and international conferences in Toronto (May 2002) and Montreal (September 2002).

In March, 2002 a symposium on the Commercialization of Human Genetic Research was held at Memorial University of Newfoundland. Featured speakers were Timothy Caulfield (Faculty of Law, University of Alberta) and Henry Greely (Faculty of Law, Stanford University). Both Caulfield and Greely are leading experts in the area of commercial genetic research. In preparation for this symposium an early version of this document was prepared. Portions of it were presented in a public meeting held as part of the symposium. Copies of the draft were also circulated to Greely and Caulfield, along with local representatives of government, academia and industry. An afternoon-long discussion of the draft was held involving many of these people along with members of the project team.

From April through August of 2002 the draft report was revised in response to comments on the earlier version. Literature review and additional consultation with key informants continued throughout this time. In June and July of 2002,

two sessions were organized by Bioeast, a biotechnology industry association in Newfoundland and Labrador. At these sessions representatives of industry, government and academia came together with the express purpose of gaining further insight from industry regarding the proposals outlined in this report. Various concerns and recommendations presented in the June session were incorporated into the version presented for the July meeting. A final draft was produced after this meeting and reviewed by Richard Gold (Faculty of Law, McGill University), Eric Jeungst (Biomedical Ethics, Case Western Reserve University) and Timothy Caulfield (Faculty of Law, University of Alberta).

A detailed list of those consulted over the course of the project is included as Appendix E.

Section 3: The Historical-Political-Economic Context

Although Newfoundland and Labrador has a strong record of economic growth in recent years, it also has a well known history of economic hardship. Part of this history involves cases of perceived economic mismanagement and promises of economic opportunity that failed to materialize. Some examples include: dissatisfaction with returns from the Churchill Falls hydro-electric project; the perception that the province does not retain an adequate share of the royalties arising from off-shore oil developments and, most importantly, the collapse of the North Atlantic cod fishery. Such experiences of perceived economic mismanagement in both the public and private domains, have contributed to a level of scepticism (some might say cynicism) regarding future economic prospects. Any proposal regarding commercially sponsored genetic research must be sensitive to the recent history of economic disappointment in this province.

Economic disappointments notwithstanding, the people of Newfoundland and Labrador have demonstrated a strong communal ethic in dealing with such hardships. The people of this province have displayed tremendous resilience, ingenuity and will power in their efforts to preserve local communities and a traditional way of life in the absence of economically viable enterprises. While it is now evident that cod stocks will not recover any time soon, other economic opportunities might present themselves. Human genetic research with its potential economic windfall could be characterised as one such opportunity.

Human genetic research has been conducted in Newfoundland and Labrador for more than thirty years. Researchers located at Memorial University have carried out the vast majority of this work. A variety of genetically related diseases have been investigated including colon cancer, psoriasis, Bardet-Beidl Syndrome, polycystic kidney disease, von Hippl-Lindau disease, a variety of neuropathies, Alderdice Syndrome, hereditary breast cancer, multiple endocrine neoplasia, retinal degenerative diseases, hereditary ataxia and arrhythmogenic right ventricular cardiomyopathy (ARVC). Significant progress has been made in a number of areas. However, the relatively small pool of local researchers and limited resources has necessitated collaborative efforts with researchers and research facilities elsewhere in Canada and abroad. For example, researchers at Johns Hopkins University identified the MSH2 gene (a gene linked with a form of colon cancer), in part as a result of research into a Newfoundland family identified by Dr. Jane Green, a professor at Memorial. Likewise, a gene linked with a form of hereditary ataxia was identified by a group of researchers at

McGill University using a Newfoundland family. In this case the collaborating researcher at Memorial was Dr. Elizabeth Ives. In general such collaborative efforts have worked well and local researchers continue to participate in these arrangements.

There have been instances in recent years, however, in which outside researchers have conducted studies in this province with neither the knowledge nor collaboration of the local research and clinical communities. Two recent examples will serve to illustrate the kinds of problems that can arise when such research is conducted inappropriately. Neither example deals with commercially sponsored research *per se*. Nevertheless, it is worth noting at the outset that even projects that are ostensibly motivated primarily by concern for human health, and not out of economic self-interest, can have such deleterious effects. Such negative outcomes could well be exacerbated in an unregulated or poorly regulated market environment. A third case discussed below is an example of a commercially sponsored project that has led to some problems in terms of control of genetic samples.

The first case involved researchers from the University of Western Ontario. This team conducted their work in a small community in western Newfoundland beginning in 1995. Researchers and clinical staff at Memorial were unaware of this activity until April of 1999 when a front-page headline in a national newspaper announced: "'Doomed' Newfoundlanders opt to eat, drink and be merry" (Gillis, 1999, A1-2). The story reported that the researchers had been studying a certain cardiac defect that was prevalent in this community. The research team had worked closely with local physicians in identifying family members, and had taken steps to ensure appropriate consent had been obtained and that follow-up care was provided. Apparently, however, the research team's efforts to convince the locals of the need to change their diets had been resisted. The implication of the newspaper headline was that this somewhat hedonistic lot was largely fatalistic in their attitudes. If they were to die early in any case they would rather enjoy their high fat diets in the time they had left.

It appears that the researcher who granted the interview had identified the small community by name. The industrious reporter had subsequently visited the community and managed to extract quotations from a number of the local residents. Several of these residents were identified by name in the article. This instance raises issues regarding the invasion of privacy and the further stigmatisation of both this community and the province. In addition there were concerns regarding appropriate genetic counselling and the clinical management of the cases identified. The potential negative effects such a report might have on

the local resident's future attempts to acquire life insurance or to secure bank loans should also be considered.

The second, more troubling case of genetic misadventure involved researchers from Baylor University in Texas. Although it is difficult to pin down when exactly this team started to visit the province, it appears they were here off and on throughout the 1990s. Most of their work focused on a particular heart condition (arrhythmogenic right ventricular dysplasia). This condition generally strikes affected males in the prime of life. In effect their hearts simply stop beating.

These 'helicopter geneticists', as they came to be known, had a propensity to descend upon remote communities. They would take family histories, bleed local residents, and conduct EKG's and Echo-cardiograms. Residents recall signing something, but were often unsure of what it was. No copies of consent documents were left with the participants. Genetic samples and test results disappeared with the researchers who were dubbed the 'Texas Vampires'. In some cases these researchers arranged with local hospitals to use equipment for testing, but again patient records went with them when they left. Efforts by clinicians from the Provincial Genetics Program to retrieve information from the Baylor team generally went unheeded. Given the vital importance of this information for appropriate patient follow-up and care, this lack of co-operation was particularly vexing. Although researchers at Memorial were never formally involved in the Baylor study, local researchers, clinicians and ethicists became centrally involved in seeking a resolution. Overtures to the Institutional Review Board (IRB)[10] at Baylor eventually resulted in a joint investigation by Baylor and Memorial. The investigation took place throughout much of 1999. Some steps have since been taken toward retrieving relevant patient records, although at the time of this writing many records are yet unaccounted for. It should be noted that Dr. Bob Roberts, the cardiologist who led the Baylor team, was subsequently censured by that institution for similar unacceptable practices in other studies. As of November 2001 his research funding was revoked and he is forbidden to conduct clinical research for five years (Wood, 2001).

It should be emphasised once again that the Baylor team was supposedly driven primarily by health related concerns as opposed to economic incentives. Nevertheless, there were disturbing developments in terms of the inappropriate acquisition, transfer, and use of genetic materials and patient records. When commercial interests are introduced with the associated problems of proprietary

[10] The IRB is the U.S. equivalent to the Canadian Research Ethics Board (REB).

rights, the potential abuses could well be magnified. Our final case illustrates how such problems might arise.

This case involves efforts to retrieve DNA samples from Celltech, a California based biopharmaceutical company. The company has been involved in research on psoriasis in Newfoundland and Labrador (Baird, 2001, A5). Between 1992 and 1998, 2000 vials of blood were collected from residents of this province. In some instances the samples represent four or five generations of the same family, a real advantage in terms of isolating the gene or genes that may trigger the condition. According to Dr. Wayne Gulliver, a local dermatologist who was centrally involved in collecting the samples, the original agreement was for the samples to be stored at the Psoriasis Research Institute in California. Celltech would get 25 micrograms (about 20%) of each sample for their research purposes. The rest would be stored at the Institute until an adequate facility to store the samples and to conduct further research could be developed here in Newfoundland. Those facilities are now available, but Celltech has threatened the Psoriasis Research Institute with legal action if they return the samples to Newfoundland. Celltech's apparent concern is that the samples could get into the hands of a competitor who is also looking for the 'psoriasis gene'. Gulliver insists there is no interest in giving the samples to competitors. Rather, the interest is in using these valuable samples to do other related research. However, it does not appear that the samples will be returned any time soon.

It is in part as a response to situations like those described above that the province began the process of implementing the PHREB. A section of the PHREB proposal provides guidelines for human genetic research (see Appendix C below). Many of the issues addressed there are relevant to human genetic research whether commercially sponsored or otherwise. However, the sub-committee that drafted those guidelines viewed the substantive issues associated with commercial genetic research as beyond its mandate at that point. Hence the need for the present project.

As a final step in the process of setting the stage in present day Newfoundland and Labrador, we present a brief description of the activities of three commercial human genetic ventures presently operating in the province.

3.1 Newfound Genomics: Newfound Genomics is a research-based clinical genomics company. Founded in 2000, the company was originally jointly owned by Gemini Holdings plc of England and local Newfoundland investors. In 2001, Sequenom, a California based genetics company, acquired Gemini and with it, Newfound Genomics. Newfound Genomics continues to operate,

however, as a stand-alone company based in Newfoundland and Labrador. At present, the company has 11 employees and operates offices in both St. John's and Stephenville. Its main research facilities are in St. John's.

By gathering and analyzing clinical and medical information about individual research subjects, Newfound Genomics investigates relationships between genes, human health and disease. Where possible research is directed at common disease areas that offer substantial commercial potential for therapeutic and diagnostics applications. Current research projects focus on obesity, type 2 diabetes, inflammatory bowel disease and osteoarthritis. This research aims at contributing to earlier diagnosis of diseases, more accurate prediction of prognosis for the disease, and the development of more effective drugs. Of particular note for this report, Newfound Genomics has adopted a policy of engaging in benefit-sharing in the event of future commercialization of its research findings.[11,12]

3.2 NewLab Clinical Research Inc.: Newlab Clinical Research Inc. is a privately owned medical research organization based in St. John's, Newfoundland.[13] It was founded in 1997 and at present has more than 10 employees. The company focuses on pharmaceutical, holistic, cosmeceutical and genetic research trials. It has completed approximately 100 such trials. Through its founder, the company has a database of approximately 15,000 patients from Newfoundland and Labrador. Like Newfound Genomics, NewLab has a policy of engaging in benefit-sharing. It does so through such things as charitable donations and negotiated royalties on possible future commercialization of its research.[14]

3.3 Xenon Genetics and Memorial University of Newfoundland—A group of researchers at Memorial University of Newfoundland are presently carrying

[11] "a net royalty on revenues generated from any potential commercialization of discoveries by Newfound Genomics will be contributed directly to an appropriate independent Newfoundland and Labrador not-for-profit foundation for the benefit of the people of Newfoundland and Labrador" (Newfound Genomics and Gemini Research Press Release, 2000).

[12] The previous two paragraphs are based on information from www.newfound-genomics.com and personal communications with representatives of the company.

[13] Dr. Wayne Gulliver, NewLab's chairman and medical director was a founder of Newfound Genomics.

[14] This paragraph is based on information from www.newlab-cro.com and personal communications with representatives of the company.

> out research for Xenon Genetics, a privately-held, genomics based drug discovery company based in British Columbia and Quebec. This case is an excellent example of the crossover between academic and commercial research that is common in human genetic research. The university has negotiated a graduated benefit-sharing arrangement with Xenon that ties benefits to various milestones achieved as the project moves forward.

Having surveyed the present state of affairs in Newfoundland and Labrador, the next section presents a discussion of the ethical issues that must be confronted in deciding whether and how commercial human genetic research should be regulated in this province.

Section 4: Ethical Issues Raised by Commercial Human Genetic Research

This section discusses the issues raised by *commercial* human genetic research. What are they? In their investigation of debates about the commercialization of human genetic research, Lori Nelkin and Dorothy Andrews detect "a conviction that turning tissue, cell lines, and DNA into commodities violates body integrity, exploits powerless people, intrudes on community values, distorts research agendas, and weakens public trust in scientists and clinicians" (Andrews & Nelkin, 1998, 31). This statement summarises succinctly the ethical issues typically raised in discussions of commercial human genetic research. These issues are examined in more detail in this section.

When considering the potential ethical problems posed by commercial human genetic research, two distinct sets of issues need to be distinguished. First, there are those that apply to many or all forms of commercial health research. Second, there are issues that apply to commercial genetic research in particular. Before turning to these issues in more detail, however, it is worth emphasising once again why the prospect of commercial human genetic research raises distinctive ethical questions. It is because human DNA is often seen as having a status that is at odds with its use in a commercial enterprise. This, of course, makes it important to consider how the status of human DNA *should* be viewed. That matter is examined in some detail in Section 5 of this report.

4.1 Issues Raised by the Commercialization of Health Research in General

4.1.1—Skewing the Research Agenda: In recent years, universities have faced increasing pressure to find private support for their research projects. As a result a large and ever increasing amount of university research is supported to some degree by private investment. For example, in the year 2000 industry funding for research at Canadian universities and teaching hospitals exceeded the total research funding provided by all of Canada's provincial governments combined[15] (Lewis et al, 2001). This

[15] U.S. figures on funding for genomics research are available for the year 2000. That year, the U.S. government spent approximately 1.8 billion dollars on genomics research, while private industry (i.e., genomics and pharmaceutical firms) spent more than 2.9 billion dollars on genomics research (Stanford in Washington Program, 2002).

reliance on private funding has been the source of considerable controversy. How will the need to find private financing affect the research agenda? Pressure to do research that will receive private financial support may influence researchers to ignore projects that are not considered to be commercially viable (Lewis et al, 2001).

In the case of human genetic research this could mean that some rare genetic conditions will be unappealing to researchers, however important and beneficial that research might be to those who possess these conditions[16] (Burgess, 1998, 339-340). Just as there are 'orphan drugs' which, though effective, are not produced because the market for them is not considered profitable, so some 'orphan genes' may not be adequately researched due to their lack of commercial potential (Duffy, 2002, A10). This is a particular problem for Newfoundland and Labrador since, as mentioned in Section 1, some rare conditions occur at an elevated rate in this province.[17]

The problem of commercial pressure on the selection of research topics operates at an additional level to the one just outlined. Just as commercial pressures may shape the topics chosen 'within' genetic research, they may also affect the choice of research topics more broadly. The potential to make large profits by pursuing genetic causes and treatments to various conditions may bias researchers in favour of commercial genetic solutions even though other sorts of prevention or intervention might serve the public better. For example, research may focus on genetic causes of obesity rather than on causes stemming from diet or lifestyle.

4.1.2—Corrupting the Research Process: In addition to worries about the skewing of research by commercial forces, the possibility is often raised that commercial pressures may corrupt the research process itself. Two distinct sources of concern can be identified. One involves the effect commercial forces will have on the integrity of researchers' work. There may be pressure to interpret the results of research so as to favour the

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[16] In some instances, researchers may learn things by studying rare conditions that will have application beyond those conditions. This was, for instance, the reason behind the project described in section 3.3. However, it is not reasonable to assume this will be true of all rare conditions.

[17] An orphan disease may still affect a great many people. The 1982 U.S. Orphan-Drug Act operates conceives of an orphan disease as one affecting fewer than 200,000 Americans.

source of funding for the research. Alternately, there may be pressure to suppress results that do not suit the interests of the research funder. The well known case of Nancy Olivieri provides an example of this, although it also provides an example of a researcher going to considerable lengths to resist such pressure. In that case, Olivieri, a researcher at Toronto's Hospital for Sick Children, was demoted and threatened with firing after revealing information about a drug under study that the manufacturer of the drug wanted kept private[18] (Thompson et al, 2001).

A second source of concern centres on the question of whether the desire for profit will cause researchers to cut corners on the ethical research standards that protect research subjects. Do we need increased monitoring of the consent process for commercial research? Should the same standards of informed consent apply in the case of commercial research?[19] The previously noted research misconduct by investigators from Baylor University (see Sec. 3) provides an example of 'cutting corners' on research standards.[20]

4.1.3 The Blurred Line Between Commercial and Academic Research—Given that this report focuses specifically on the topic of commercial human genetic research, it might be assumed that there is a hard and fast distinction between commercial and academic research. In theory there is, but as the example of Xenon Genetic's arrangement with Memorial University of Newfoundland illustrates (see section 3.3), in practice the distinction is much less clear. While some projects clearly are commercial from the beginning, it is also quite possible that projects that start out as pure academic endeavours will develop into ventures with significant commercial value. Indeed, universities actively encourage their researchers to generate such results. For example, an analysis of DNA patents held in the U.S. as of 1999 revealed that 9% of those patents were assigned to public universities and an additional 14% were held by private universities (Stanford in Washington Project, 2002). Thus almost a quarter of the DNA patents issued at that time were held by universities.

[18] The demotion was later reversed.

[19] It is this issue that prompts the PHREB declaration that subjects must be informed if research has a commercial aim.

[20] Although, as noted in that section, it should be kept in mind that that this project is better viewed as academic rather than commercial.

[21] This illustrates how blurred the line between commercial and academic research can become. Any proposals this report makes about regulating commercial human genetic research must account for this.

4.2 Issues Raised by the Commercialization of Human Genetic Research in Particular

4.2.1—Patenting & Intellectual Property Rights: It is broadly, although not universally, accepted that some form of intellectual property protection is needed if commercial human genetic research is to be viable (Gold, 1998, 63-4). The principal form this has taken is in the patenting of genes or portions of them. Such patents afford the holder a limited term, monopoly right to benefit from the application of that gene or fragment. While this practice is now well established in much of the world, including Canada, it is still highly controversial. To some, allowing human genetic material to be treated as subject to intellectual property claims is inconsistent with proper recognition of its status. Patenting does not fit well, for example, with a view that sees the genome as the 'common heritage of humanity'. This issue of the proper status of human genetic material is discussed more fully in Section 7 of this report.

4.2.2—Commodification of Individual DNA: Just as the issue of patenting raises problems at the 'output' side of research, there are similar issues at the 'input' end. Should the individuals who provide their DNA to commercial research projects be compensated for providing this valuable raw material? Some argue the answer is yes. (Bear, 2001a). Others object that this would represent an unacceptable commodification of individual DNA (UNESCO, 1997; HUGO, 1996).[22] Again, this topic is taken up more fully in Section 7.

4.2.3—Personal Privacy and Private Companies: As was seen in considering the PHREB proposal, genetic research invariably raises

[21] In addition, 13% were held by non-profit research institutes and 6% by government. Thus, at least 42% of the DNA patents in the U.S. were not held by private businesses (assuming private universities are not counted as private businesses).

[22] While this issue is usually phrased in terms of payment to individuals, there is no clear reason why it could not be phrased in terms of payment to collectives. In fact, discussions of this issue are often vague about whether what is troubling is the mere idea of any kind of payment to any entity for participation in research, or whether it is payment to *individuals* that is objectionable.

concerns about privacy. Are these worries altered when the holder of genetic samples is a private company? Some argue they are worsened, claiming that a private company may be more likely to be lax regarding privacy concerns. Others argue that a private company will be more responsive to privacy concerns in order to protect its reputation (Gulcher and Stefansson, 2000).

4.2.4—Chilling Academic Research: Naturally, commercial research enterprises will seek to protect the features that make their research potentially valuable. One way of doing this is to ensure that no one else has access to the same data as the enterprise.[23] Commercial projects may therefore seek exclusive access to those people who donate genetic material to their projects. Celltech's efforts to prevent the return of DNA samples to Newfoundland is a case in point. Should this be allowed? Here the commercial enterprise's desire to protect the value of its research must be balanced with the need to carry on academic research.[24] If, for example, commercial projects pay subjects for their participation, will this create the expectation that academic projects should do likewise and so make it more difficult for such projects to operate?

4.2.5—Benefit-Sharing: An underlying assumption for many of the concerns raised so far, is that human genetic material has a special kind of status and significance. This is often what lies behind concerns about gene patenting, payment for participation in research, and related issues. A concomitant of this broad assumption regarding the unique nature of human DNA is that those who engage in commercial human genetic research incur special moral obligations to share the benefits of that research with research subjects, members of a particular community, or with society in general. Human genetic research is seen as unique in this regard in that these "benefit sharing" obligations are generally thought to be more stringent for this type of research than they are in other kinds of research. In particular, it is sometimes argued that commercial research entities should share a portion of their profits and/or products with those who most need them (e.g., the people of the developing world) and/or

[23] A recent news report suggests this phenomenon is already occurring (Everson, 2002, A3).

[24] This is not merely a hypothetical issue. A proposed commercial research project in Framingham, Massachusetts was recently abandoned due to the inability of academic and commercial researchers to accommodate one another's concerns. See appendix D for details.

those whose DNA was used to produce these products and profits (e.g., the people of Newfoundland and Labrador) (HUGO, 2000).[25]

[25] The idea of benefit-sharing was endorsed in a recent speech at BIO 2002 by Carl Feldbaum, the president of the Biotech Industry Organization (Feldbaum, 2002).

Section 5: A Survey of Possible Models

This section presents some possible models for governing commercial human genetic research. No attempt is made here to compare the relative strengths and weaknesses of one model to another. That task is left for subsequent sections.

Two points should be remembered when considering these models. First, although they are presented here as though they are mutually exclusive, it may be possible to combine aspects of various models in order to create the optimal arrangement for the local circumstances. Second, the various models presented either implicitly or explicitly take a stand on the nature and status of human DNA. Models that tend to favour market forces as the appropriate mechanism for managing research and development in human genetics tend to view DNA as a commodity. Those that favour a stronger role for state intervention tend to emphasise the intrinsic value of DNA as some kind of a common public good.

5.1 No Governance—This possibility is very simply stated: "Do Nothing". It may be that no governance is required beyond what the PHREB Proposal already contains (See Appendices B and C).

5.2 Forbidding Commercial Human Genetic Research—Another simple (one might say, "simplistic") response would be to completely reject the idea of commercial human genetic research. That is, the province might take the stand that the idea of generating a profit from human genetic material is morally otiose, and should thus be prohibited.

5.3 Licensing an Exclusive Private Gene Bank—An example of this model has already been proposed and partially implemented.[26] In 1998, Iceland's parliament passed the Act on a Health Sector Database (HSD Act). That act gave the government of Iceland the power to grant an exclusive licence to a private company for up to twelve years for the purpose of assembling a database of the medical records of the people of Iceland. In January of 2000 such a licence was granted to deCODE

[26] The word 'partially' might overstate things. While legislation enabling this project has been passed, the huge controversy the project has generated has slowed work on the project so that it has not yet proceeded beyond a very early stage. deCODE frequently announces discoveries made through its research, but these are not the result of the HSD project.

Genetics Ltd.[27] Also in 2000, Iceland's government passed the Act on Biobanks. This sets out the conditions under which a 'bank' of genetic material can be assembled. The intent of this act is to govern deCODE's overall project of assembling a database of genetic information on Icelanders that would be linked to the Health Sector Database and to a database of genealogical information deCODE has assembled. deCODE plans to use this database for its own research purposes and to sell access to the database to other researchers. deCODE's plan is enormously controversial, both within Iceland and beyond. A detailed explanation of the project and the controversy it has generated is presented in Appendix D.

The Icelandic situation presents a possible model for governing genetic research in this province, although the controversial nature of that situation should most certainly be kept in mind. The province might license a private company to assemble a health, genetic and genealogical database of its residents. The governance required in this scenario would be to oversee the operations of the database, ensuring, for instance, that only those with a legitimate interest would gain access to it.[28] As in Iceland, this would require legislation setting the conditions under which the database would operate. In addition, ongoing monitoring of the database's operations would be necessary. In Iceland this has been accomplished by means of a small permanent committee with the requisite expertise.[29] With these measures in place the private company would either use the database in its own research, or sell access to the database to other interested parties. The province would negotiate some form of payment in exchange for licensing the private company. [30]

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[27] Actually, the license was granted to deCODE's wholly owned Icelandic subsidiary. deCODE itself is incorporated in Delaware, USA.

[28] Settling who has a legitimate interest would, of course, require some serious discussion.

[29] Iceland's Act on a Health Sector Database requires a committee consisting of a lawyer (as chair), a health professional with expertise in epidemiology and an expert in information technology.

[30] deCODE has agreed to pay the Icelandic government a $1 million (US) annual licensing fee and to provide the Icelandic government with a share in deCODE's yearly profits, up to $1 million per year (Greely, 2000, 188).
deCODE also struck a deal with Hoffman La Roche under which drugs developed by Hoffman La Roche as a result of deCODE's research would be provided to Icelanders who need them free of charge (Rose, 2001, 26).

A variation on the Icelandic approach is also worth noting. deCODE's original proposal was for a database which could be used not only as a research tool, but also as a source of centralized information about patients. In the original proposal the identity of those about whom the database contained information was to be encoded in such a manner that, while identities would be protected, it would be possible for medical practitioners to decode those identities in order to recover information on particular patients. This caused an outcry over privacy concerns, however, and the HSD Act as it was eventually passed instead called for one-way (i.e., supposedly irreversible) encryption of individual identities. This makes the database useful only as a research tool. The province of Newfoundland and Labrador could decide to pursue a research only approach to a database or to pursue a combined treatment/research approach.

Sources of Controversy in Iceland: Without making any comment at this point on whether these constitute sufficient reasons for rejecting this sort of approach, it is worth noting the reasons why the deCODE project has been so controversial. If the province were to embark on a similar path it would either need to find a way to answer these concerns, or else should expect that similar controversies would arise.

(a) **Presumed Consent** – The HSD Act, along with other legislation connected with deCODE's project, allows for the collection of information and biological samples using the standard of presumed consent (i.e., where information and/or samples have been collected for another purpose, it is presumed that consent has been granted for that material's inclusion in deCODE's database unless an explicit denial of consent has been made).
(b) **Lack of Public Consultation** – In the eyes of many the arrangement was reached with deCODE without adequate public consultation.
(c) **Privacy Protection** – The concerns raised here are essentially those outlined in section 4.2.3.
(d) **Chilling Academic Research** – The concerns raised in this respect are essentially those outlined in section 4.2.4. In this case, however, these concerns are somewhat heightened given the size and exclusive nature of deCODE's project.
(e) **Commodification** – It has been charged that deCODE's arrangement with Iceland treats genetic and health information as

an economic commodity. The issues raised here are similar to those discussed in sections 4.2.1 and 4.2.2.

5.4 Creating a Public Gene Bank—As with the previous model, an example of this approach has already been proposed and partially implemented.[31] Estonia plans to set up a combined database of health records and genetic information about its individual citizens. Estonia's Human Genes Research Act (2000) allows for the establishment in early 2001 of the Estonian Genome Project Foundation (EGPF).[32] The EGPF's purpose over the next five years is to assemble and maintain a database containing health, genealogical and genetic information on about 1 million of Estonia's 1.4 million inhabitants. This is essentially a larger scale version of deCODE's proposed project with two significant differences:

(a) The database is to be set up and maintained by an arms length public agency (the EGPF), not a private company. Financing is to be accomplished through EGeen, a company set up by the EGPF.[33] Initially the EGPF will be 100% owner of EGeen, but this is to be watered down eventually. EGeen will have exclusive commercial access to the database, but will be in the business of reselling this access.

(b) While Iceland's/deCODE's database is intended solely as a tool for research, the Estonian database is intended to function both as a research tool and as a centralized resource for individual health care.[34]

Estonia's project provides another possible model for Newfoundland and Labrador to follow. A similar database could be set up for the province. Alternately, the province could pursue a 'pure research' version of this model.

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[31] As with deCODE's project, Estonia's venture is still in the very early phases. Relevant legislation has been adopted and a small pilot project has begun.

[32] Bartha Knoppers, a well known Canadian expert in health ethics and law, was a key consultant on the design of the law.

[33] EGeen is incorporated in Delaware, USA with a subsidiary set up in Estonia.

[34] As noted above, this was the original plan in Iceland. It was later abandoned in favour of a 'pure research' approach.

Estonia's project has not generated as much controversy as deCODE's. In part this is because the database is not to be held in private hands.[35] In addition Estonia's project deliberately rejects the idea of presumed consent. All the information in the database is to be assembled on the basis of informed consent. Further details of the Estonia project can be found in Appendix D.

5.5 A Provincial Advisory Agency—In contrast to the two 'mega-project' approaches just outlined, two smaller scale and as yet untried approaches should be considered. The first would place almost no restrictions on those wishing to carry out commercial human genetic research beyond those imposed by the PHREB. It would, however, put in place a provincial agency that would help Newfoundlanders and Labradorians negotiate terms with companies wishing to collect genetic material from them. The sole additional restriction on those seeking consent from individuals to participate in human genetic research would be a requirement that they advise prospective research subjects/DNA sources that the advisory agency exists and that they may consult with it before agreeing to participate.

A rationale for such an agency is as follows. By definition, commercial human genetic research aims to make a profit. Given that this research cannot be conducted without using particular individuals' DNA, it might be thought that those who provide the DNA also deserve compensation. The tradition in Canada is that individuals are not paid for participating in medical research, but it may be that this tradition must change where commercial human genetic research is concerned.[36] It might therefore be concluded that the necessary governance of commercial human genetic research in this province consists in a process whereby the government assists Newfoundlanders and Labradorians in getting fair compensation for their participation in research. The province could set up an agency competent to give advice as to what constitutes fair compensation for providing DNA in a particular case. This process might typically involve

[35] Although, as noted above, eventually Egeen (the company that will control access to the database) will be owned in part by private investors.

[36] In Quebec this is more than just a tradition. Under Quebec's Civil Code, individuals may not be paid for participating in experiments (other than as a compensation for inconvenience or expense) (section 25). The same section rules out payment for "a part or product" of one's body.

consulting with individuals, but could also involve groups. Families might seek payment as a group, as could patient support groups or hospitals with already existing sample collections.[37]

Such an agency would require at least three different sorts of expertise. It would need to make financial assessments of the value of particular research projects in order to provide advice on what constitutes fair compensation. It would need the competence to draft and negotiate contracts on behalf of clients. Finally, it would need to carry out a public relations campaign to make residents of the province aware that the agency exists. It might also conduct a public relations campaign on an international level in order to convince people around the world that they deserve compensation for participating in genetic research (since, among other things, adoption of this system in places other than this province would make the system more viable here).

5.6 Provincial Approval—The Advisory Agency approach just outlined deals with the challenges posed by commercial human genetic research primarily at the level of the individual. Another possibility is a Provincial Approval process that would deal with these challenges at the provincial level. This model is thus similar in form to the proposed PHREB that will deal with the challenges posed by health research in general at the provincial level.

The Approval Model could be implemented in two quite different ways. An 'active negotiation' version would involve a process of exchange between those wishing to carry out particular commercial human genetic research projects and representatives of the province in order to arrive at a mutually agreeable proposal for dealing with issues such as benefit-sharing. A 'submit for approval' version, on the other hand, would leave it to those wishing to conduct human genetic research to devise a benefit-sharing proposal. Representatives of the province would then either approve or reject the proposal. In the case of rejection, reasons for the rejection would be provided in order to give the researchers the option of revising and resubmitting the proposal. An appeals mechanism would also be provided in case a sponsor wished to contest a negative assessment. This latter model would resemble the approach presently taken to research ethics approval in general.

[37] In the case of sample collections, some contentious issues regarding ownership of the collection would need to be addressed.

Both of these approaches would require administrative support, although clearly the active approach would require more since it would require some group or individual who could act as the province's negotiator in these matters. The 'submit for approval' approach would not require a negotiator *per se*, although it would require a body capable of assessing the acceptability of individual proposals. Either approach would require a body with a broad variety of expertise from areas such as medicine, genetics, business, science, health policy and ethics.[38] For the most part it is anticipated that submission for approval will be the most effective and efficient approach for the vast majority of research projects. However, there may be cases where the unique features of a particular project require more direct negotiation between the province and the research sponsor. If and when such cases arise it should be possible to appoint qualified negotiators on an *ad hoc* basis.

Finally, assuming that the province will proceed with enabling legislation to establish the PHREB, no further legislation should be necessary for the purpose of implementing the provincial approval model. The general requirements for ethics review established by the PHREB should simply include a requirement that any human genetic research must go through the provincial approval process for benefit-sharing prior to receiving full ethics approval.

[38] There may be some concern as to whether or not the province will have the necessary expertise available to operate both the PHREB and the proposed Advisory Board. This point is addressed in Sec. 9.1.

Section 6: Basic Assumptions

The next three sections of this report develop a case for the Provincial Approval model as the most appropriate model for dealing with benefit-sharing agreements for the province of Newfoundland and Labrador. This section explains four assumptions that are relied upon in formulating this case. These assumptions set the context for the more controversial discussion to follow in section 7, namely that regarding the value of human DNA. Section 8 then draws on the previous two sections in order to make the case for the Provincial Approval model.

6.1 Ethical Adequacy—As noted in section 1, our starting point is an ethical one. Too often in projects of this sort ethical considerations are treated as a sort of 'add-on'. First, we figure out what we want to do and then we see whether or not what we have decided to do on other grounds can be made to look ethically acceptable. Our approach, on the other hand, is to treat ethical adequacy as a necessary condition for any model that is to be a serious contender for recommendation.

6.2 Health Care as a Common Good—We take as an underlying principle the idea that health care is thought of as a common good in Newfoundland and Labrador. Health care is viewed here as a shared enterprise that should be equally available to all (Romanow, 2002). Having said this, however, it must be recognized that the province cannot claim a perfect allegiance to this principle. Inconsistencies and gaps exist in the health care system. Nonetheless, this is a guiding principle of great importance to most Newfoundlanders and Labradorians.

It should also be remembered that this principle implies not only rights, but also responsibilities for Newfoundlanders and Labradorians. For example, if the burdens associated with particular medical conditions are shared, then a case can be made that any benefits associated with them should also be shared.

6.3 No 'Genohype'[39]**—**A model must be selected on the understanding that the commercial prospects of genetic research are still very uncertain. The rosy predictions of massive rewards may or may not be true. As was noted in the introduction to this report, it is quite well accepted that a

[39] We take the term 'genohype' from Timothy Caulfield (Caulfield, 2000, 441).

'homogeneous' population like that of Newfoundland and Labrador is useful in studying single gene disorders. However, some speculate that most such disorders, particularly ones that will lend themselves to substantial profit, may have already been discovered (Greely, 2002). Assuming this is true, if substantial commercial profits are to be made through human genetic research, they will be made through the study of medical conditions related to multiple genes or through activities other than gene discovery.[40] Here the prospects for the success of this research are far from certain. The shape that successful commercial research will take may or may not lend itself to much research being done in Newfoundland and Labrador. This does not mean that bold projects should not be pursued, but it does mean that they should be pursued only with a clear-eyed understanding of the uncertainty involved.[41]

6.4 Stability—It is important to recognize that commercial research enterprises need to conduct their activities under stable conditions. So far as the regulatory environment is concerned, commercial sponsors need to know at the outset what the costs of doing business in Newfoundland and Labrador will be. Furthermore, they have a right to expect that the rules that govern their research and business activities will not be subject to continual and arbitrary change. Hence it is important that the model adopted provide such stability.

[40] See section 1.1 for some examples.

[41] What must not be forgotten here is that human genetic research has two quite distinct types of value – commercial and health related. Even if it turns out to be true that this province is not a particularly useful place to do *commercial* human genetic research, it may nonetheless be true that there is valuable human genetic research to be done here. For example, it has recently been argued that a greater focus needs to be placed on incorporating genetic research into epidemiological studies (Willett, 2002). The province of Newfoundland and Labrador may be a useful place in which to take such an approach.

Section 7: The Status of Human DNA

This section takes up the controversial question of how we should conceive of human DNA. As noted earlier, many of the ethical issues surrounding commercial human genetic research stem from particular conceptions of the status of human DNA. Naturally this makes investigating the question of the status of human DNA a necessary precondition for choosing amongst the models outlined in section 5.

Before proceeding with this investigation, however, a point made in section 1 should be reiterated. As was noted there, discussions of the status of human DNA run the risk of being ambiguous regarding whether what is being referred to is the physical substance or the information it contains. In order to avoid this ambiguity, it should be kept in mind that the issues raised in this report primarily concern the *information* contained in human DNA and concern the physical substance only insofar as it provides access to that information.

7.1 The Legal Status of Human DNA—Our primary focus in this section is to investigate the ethical status of human DNA. As a starting point, however, it will be necessary to discuss briefly its legal status. In short, the legal status of human DNA, both in Canada and elsewhere, is uncertain (Caulfield, 1997, 64). Some legal scholars emphasize the idea of individual property in this regard, stressing the degree of control over one's genetic material that the idea of property carries with it (Roche, 1997). Others suggest control can be maintained without resorting to identifying human genetic material as a form of property[42] (Chadwick, 1997; Knoppers, 1996). Insofar as any sort of consensus exists, it is that human genetic material does not fall neatly into any of established legal categories (Litman and Robertson, 1996, 83). Hence some have argued that human DNA should be treated as *sui generis* (i.e., unique). While treating human DNA in this manner would allow us to draw upon already established legal categories such as property and person, it would avoid forcing human genetic material into either precise category. The *sui*

[42] A slightly more qualified view is expressed by Moe Litman: "in most circumstances the principles of the law of persons can adequately protect the fundamental interests of individuals implicated by their genetic material. In rare cases property principles might be needed to provide this protection" (Litman, 1997, 23-4).

generis approach is amenable to the one that informs this report with regard to the *ethical* status of human DNA.

7.2 DNA ≠ Identity—As a first step toward developing an account of the ethical status of human DNA, a common way of conceiving of the status of human DNA is considered. This view conceives of human DNA as intimately linked with a person's identity. While not entirely false, this conception needs substantial correction.

Dorothy Nelkin and M. Susan Lindee provide the following apt description of the connection between human DNA and identity as it is commonly presented in popular culture and the media:

> "DNA in popular culture functions, in many respects, as a secular equivalent of the Christian soul. Independent of the body, DNA appears to be immortal. Fundamental to identity, DNA seems to explain individual differences, moral order, and human fate. Incapable of deceiving, DNA seems to be the locus of the true self…" (Nelkin and Lindee, 1995, 2).

This is an elaborate claim, but accurate. The following quotation from one of the participants in the psoriasis study discussed in section 3 provides a typical example of someone taking this view:

> "Your DNA is the very thing that makes you you. It's the most personal, private part of you—that's what they have [that] belonged to me" (Baird, 2001, A5).

Three related ideas are suggested in the above passages, all of which need to be resisted.

> **Genetic Determinism** – the view that individual genes completely determine the properties a person will have.
>
> **Genetic Essentialism** – the view that a person's DNA is the key to his or her identity or essence (Nelkin & Lindee, 1995, 41-49).
>
> **Genetic Reductionism** – the view that most or all of the significant aspects of a person are ultimately reducible to his or her genetic makeup (Caulfield, 2000, 452).

None of these views are true. Genetic Determinism is false for two reasons. First, as already noted, most of the effects of our genes are the results of multiple genes. The 'one gene, one trait' idea is a considerable oversimplification. Second, where both the effects of single genes and combinations of genes are concerned, one's genetic makeup will generally not *guarantee* a particular outcome. Rather, it makes one more or less likely to develop in a particular way given particular environmental conditions.

Not only do the above facts show Genetic Determinism to be false as a general thesis, they point to the weakness of Genetic Essentialism and Genetic Reductionism. Because our genes do not clearly determine how we shall develop, it is not true that they constitute our essence or that our most significant aspects may be reduced to our genetic makeup.

This is not to say that our genes are not a significant aspect of who we are.[43] They are indeed significant. Not only do they provide considerable *information* about our life prospects, they play *a* causal role in determining those prospects. It is, however, only *a* role, and one whose significance is frequently exaggerated.

7.3 The Ethical Status of Human DNA— Having rejected the idea that human DNA is the key to human identity, it remains to consider how human DNA should actually be viewed. Should the DNA of Newfoundlanders and Labradorians be thought of as the property of the individuals in whose body the DNA is found? Is it a provincial resource? Should it be viewed as a sort of common good to be used for the benefit of all? Each view has its adherents and our own project group is divided on this question. In what follows, the most commonly held positions on this issue are outlined and the commonly advanced reasons for holding them are explained. The section concludes with a discussion of the merits and demerits of each view.

[43] There has been some academic discussion about whether human DNA is of special significance because of some unique feature it possesses. Holm (1999) argues there is nothing unique about DNA, while Hoedemaekers and Dekkers (2001) argue there is. Our approach is to set the issue of uniqueness aside. The important question, as Hoedemaekers and Dekkers note, is not whether human DNA possesses some *unique* feature but whether it has features, unique or not, that make it *significant* (Hoedemaekers and Dekkers, 2001, 377). As argued above, it does possess such features.

7.3.1 Human DNA as an Individual Possession—One way to view human DNA is as the property of the individual from whose body it is extracted. This position carries fairly clear implications for the regulation of human DNA. If human DNA is thought of as a possession then, within certain broad limits, individuals should be free to do with it as they please. The role of government would then be to ensure that the residents of Newfoundland and Labrador are not exploited by commercial research projects.

Discussion: A necessary first step in this discussion is to distinguish between the physical DNA molecule and the DNA sequence that contains the genetic information. Clearly it is the latter that is of most importance for research and commercial purposes.

To some extent this view of human DNA as personal property is at odds with typical ways of thinking about the body and its components. In general the human body and its component parts are not for sale in Canada. For example, the sale of organs and whole bodies is prohibited under Newfoundland and Labrador's *Human Tissues Act* (RSN 1990).[44] This suggests that they should not be considered as property. Furthermore, while the sale of blood is not illegal in Newfoundland and Labrador,[45] Canada's blood system runs on the basis of purely voluntary donations.

Nonetheless, DNA is significantly different from either organs or blood. Unlike organs, blood and the DNA it contains are replaceable. A person's body will, for example, replace the blood one might give up to a commercial enterprise.[46] Furthermore, while Canadians do not pay for blood they receive during medical treatment, the same will not always be true of the pharmaceutical products and tests drug companies may develop from DNA. But

[44] The same is true of every common law province and territory in Canada (Litman & Robertson, 1996, 52-53).

[45] An exemption for "blood or a blood constituent for therapeutic purposes, medical education or scientific research" is explicitly made in section 18 of the *Human Tissues Act*.

[46] It is because blood is "replaceable by natural processes of repair" that it is distinguished from bodily organs in Newfoundland's *Human Tissues Act*.

are these differences from blood and body parts sufficient to make a property view acceptable?[47]

In fact, there is a compelling reason to reject the property approach. The reason is that information about human DNA is not simply information about a particular individual, but also about those to whom that individual is biologically related. Geneticists are fond of pointing out that it is not individuals that they study, but families.[48] This is because it is in the nature of DNA that the information it contains is communal, not individual. This is one of the main reasons why the study of human DNA raises distinct ethical issues. Due to its communal nature it is not something that fits easily into our typical ethical and legal frameworks, since these usually look at matters from the perspective of the individual.[49, 50] The point, once again, is that the communal nature of human DNA

[47] One reason for being wary of a view of human DNA as property is that conceiving of it this way has a troubling implication with regard to the possible transferring of this property right. Naively, property seems the sort of thing that can be given or traded away so that the original owner no longer has any say in what might be done with the property. There are reasons, however, to conclude that this is an inappropriate way to view human DNA (Litman and Robertson, 1996, 60-61). Given the tremendous amount of information about an individual that is contained in his or her DNA and the personal significance with which human DNA is viewed, there is good reason to think that individuals should retain some degree of control over their DNA, at least so long as it is identifiable as *their* DNA. This is not, however, an insurmountable problem for the property view of DNA. One possible response would be to treat human DNA as a special sort of property that is to some extent inalienable from the individual in whom it is found (Litman and Robertson, 1997, 61-64). Nonetheless, the need to engage in such restriction might make us question the applicability of the property model to human DNA.

[48] "Since we inherit our genes from our parents, pass them on to our children, and share them with our close and distant relatives, every genetic diagnosis, test and procedure involves many people" (WHO, 1997).

[49] This is the source of the controversy over whether genetic researchers should seek 'community consent' to research in addition to the standardly sought individual consent to research (Annas, 2001, 2328).

[50] Canada's recent *Personal Information and Electronic Documents Act* could be interpreted to require that those seeking to gather human DNA and an accompanying family/medical history seek permission not only from the initial individual whose DNA and information they wish to collect, but also from all other 'identifiable individuals' about whom health information will be revealed. If interpreted this way it would require researchers to get informed consent from the proband's extended family before proceeding.

makes it inappropriate to view it as individual property.[51] As one Newfoundland resident who has participated in human genetic research puts it:

> "If someone said tomorrow, 'I'll give you $100,000 for a blood sample,' I'd have to think about it … All that I am has come from before. I don't think it's even totally mine to give -- this genetic material belongs to my whole family, for generations" (Staples, 2002).

The property view of human DNA fails. Nevertheless it carries an important lesson for the status of human DNA. While ultimately unconvincing, the property view's focus on the importance of individuals exerting control over what happens to their DNA is important. It is a concern that must be accommodated ultimately by any acceptable view of the status of human DNA

7.3.2 Human DNA as Resource—Another possibility is to view DNA as a natural resource, different in terms of its possible uses, but not in fundamental kind from other natural resources like oil or iron ore reserves. Again, this is a view with fairly clear policy implications. In fact, the only real differences between this and the 'individual possession' view are that (i) the owner of the property is a group not an individual, and (ii) there is a clear moral imperative to use the resource wisely. While it is not clear that an individual would do anything morally wrong if he were to trade his DNA to a drug company for a collection of old gum wrappers, on this view, the province (or federal government, depending on the resource) has a duty to be a wise steward of the resource, acting always in the best interest of the province's residents. That aside, however, this view is in principle the same as the individual property view. The practical difference is that the recipient of any benefits that may be negotiated is the province rather than an individual.

[51] This is not to say that individuals should have no control over their DNA. Again, keep in mind the comparison to bodily organs. Although these are not property, one does retain substantial control over what may be done with them.

Discussion: Arguments for this view are rarely given. Rather, the view is simply assumed in many cases, as in the following passages:

> "The Rock's Genetic Gold Mine" [Headline] (Abraham, 1998, A9).
>
> "…Newfoundlanders … [seek to] control a natural resource of vast potential value – their own genes" (Atkinson, 2000).
>
> "…Newfoundland [is] something of a motherlode to the drug development industry" (Greenwood, 2000).
>
> "Newfoundland and Labrador [is] … a *unique* resource in Human Genomics" (Gulliver, 2001).
>
> "The population of Newfoundland and Labrador is an important resource for genetic research" (Industry Canada, 2002a, 103).

It is not surprising that such talk emerges where Newfoundland and Labrador is concerned. Many sensitive issues in this province centre on the use of its resources, so it is perhaps natural to use that familiar framework when speaking about human genetic research. Nonetheless, it does not follow that it is accurate or useful to describe the province's gene pool in these terms. What reasons can be offered for conceiving of the province's genetic makeup this way? The most plausible seems to be that human DNA is rarely valuable in isolation. Rather, if the DNA of residents of this province is valuable at all, it is as part of a group. Moreover, much of this value is derived because of Newfoundland and Labrador's particular history and culture.[52] It might be argued that if the value of the DNA is traceable to the province itself, then it is the province itself that is the appropriate beneficiary of that value. This is, however, a somewhat suspect argument since it is not true that the DNA of the province's residents is only valuable if the province is considered as a whole. To the contrary, research tends

[52] E.g., without the province's geographic isolation and the close family bonds that bind people to the province, the genetic structure of the provincial population would be very different.

to focus on families or communities and not on the province as a whole.[53]

In addition to the just mentioned reason for scepticism about this way of viewing human DNA, it should be noted that there is a compelling reason for rejecting a view that takes the 'natural resource' interpretation as entirely right. If we were to adopt a view that said the DNA of individual Newfoundlanders and Labradorians should be thought of as *nothing but* a natural resource, this would have some clearly unacceptable implications. The most obvious would be that individual Newfoundlanders and Labradorians would have no say in how and when their individual DNA would be used. This is self-evidently unacceptable.

7.3.3 Human DNA as the Common Heritage of Humanity— Both the 'resource' and the 'individual property' view are, to a considerable extent, minority views in the literature on the commercialization of genetic research. There, human DNA is rarely described as being an individual or communally held property. Rather, it is typically presented as a common good to be used for the benefit of all humanity. For instance, UNESCO's 1997 *Universal Declaration on the Human Genome and Human Rights* declares: "In a symbolic sense, it [i.e., the human genome] is the heritage of humanity" (Article 1). Likewise, the Human Genome Organization's 1996 *Statement on the Principled Conduct of Genetic Research* asserts that "the human genome is part of the common heritage of humanity." Of particular importance in the present context is the fact that along with such a conception of the human genome generally comes the rejection of the idea of individual payment for access to human DNA. For example,

> "The human genome in its natural state shall not give rise to financial gains" (UNESCO, 1997, Article 4).
>
> "The actual or future benefits [of proposed research] discussed should not serve as an inducement to

[53] Granted, the value of the Newfoundland and Labrador genome might be enhanced by establishing an Icelandic or Estonian style 'gene bank'. This would not, however, change the fact that communities and families have a research value quite apart from the existence of any such gene bank.

> participation. Nor should there be any financial gain from participation in genetic research" (HUGO, 2000).
>
> "If one accepts that the human genome is part of our common heritage, demands for financial compensation to individual participants in research projects do not seem to have a strong foundation" (Berg, 2001, 242).
>
> "The principle that the genome is part of the common heritage of humanity implies that 'the Human Genome Project should benefit all humanity.' This would seem to preclude the provision of disproportionate benefit to any particular individual or community" (Weijer, 2000, 368).
>
> "The concept of common heritage can find some roots … in the old legal concept of 'res communis'. Indeed essential characteristics of the concept of 'res communis' are used in the concept of 'common heritage': that is, the principle of no ownership and the fact that the things concerned are to be devoted to a common utility" (Byk, 1998, 238).

Discussion: In one sense this view is trivially true. All of us by virtue of being human must have inherited the human genome. Clearly then the human genome is in one sense the common heritage of humanity. We argue, however, that the significance of this fact has been overstated. Given that the human genome is the common heritage of humanity, it is plausible to draw the conclusion that the possibility of owning the human genome outright should not be considered (since such a scenario would involve an ownership claim on each of us). Still, while this is a plausible claim it is also an uncontested claim. No one seriously endorses the view that it should be possible to own the human genome outright. Granted, gene patents do allow to some an exclusive, time limited right to derive profit from particular genes. However this is hardly to endorse outright ownership of the human genome. This does not mean that there are no good reasons for rejecting the patenting of genes and gene fragments, but it does

mean that the reasons do not stem from the fact that the human genome is the common heritage of humanity.[54]

In similar fashion, the significance of the idea of common heritage has been exaggerated regarding the issue of payment for providing one's DNA. As was already noted, it is often claimed that such payments are inappropriate because the human genome is our common heritage. However, basing this conclusion on the idea of common heritage reflects a confusion. After all, if individuals are paid for providing particular physical samples of their DNA, it does not follow that the researchers who pay them thereby acquire ownership of the information contained in those samples.[55] But it is precisely that information that is our common heritage. It appears then that the concept of common heritage cannot tell us anything about the acceptability of payment for providing DNA. As with the issue of patenting, however, this should not lead us to conclude that payments are acceptable. We argue, in fact, that the opposite conclusion is correct. However, our reasons for reaching this conclusion are not rooted in the idea of common heritage.

7.4 Conclusion Regarding the Status of Human DNA—As already noted, a rough consensus seems to be emerging in the law that human genetic material does not fall neatly into any traditional categories. Rather a *sui generis* approach is appropriate. "[G]enetic material is truly unique, and its legal status ought to reflect this" (Litman and Robertson, 1996, 83). While the legal consensus seems to be based on purely practical considerations, this is the correct theoretical view as well. As already noted, the human genome literally *is* the common heritage of humankind. This makes it the sort of thing that is not properly suited to outright ownership by anyone. At the same time, my DNA is in a very real sense mine. It is found in my body and almost nowhere else (except where 'lost' cells might end up). This points to a need for an individual to retain significant control over what happens to his or her DNA, although as noted above, it is questionable whether this control should ever be severed

[54] See Gold, 1996 for a discussion of the issues surrounding patenting.

[55] They acquire access to that information, but access and ownership are not the same. For example, when one buys a DVD of *Gone With the Wind*, one acquires access to the movie, but does not own the movie. To see that this is so consider what would happen if you set up a business that sold copies you had made of the DVD. The fact that you could end up in substantial legal trouble is a sign of the fact that you do not own the movie itself.

as it can be with property. Finally, although the claim is weaker here than in the other two cases, there are some, largely metaphorical, respects in which the collective gene pool of Newfoundland and Labrador resembles a natural resource. Human DNA thus fits neatly into none of our standard categories. To paraphrase Litman and Robertson, genetic material is truly unique and its ethical status reflects this.

Section 8: The Recommended Model

The last section concluded that human genetic material is an unique kind of entity; it is neither individual possession, nor natural resource, nor communal property. Rather it incorporates elements of all these. This section draws on that conclusion in order to identify which of the possible models presented in section 5 best accommodates this conception of human DNA.

8.1 Rejecting the Exclusive Private Gene Bank and Public Gene Bank Models

We proceed at the outset through a process of elimination. What might be described as the two 'mega-project' approaches (i.e. the Exclusive Private Gene Bank and the Public Gene Bank models) are unacceptable for a number of reasons.

First, Newfoundland and Labrador's history of failed mega-projects must not be forgotten.[56] Given this history it can be expected that any proposed genetic mega-project will be greeted with suspicion, if not hostility. While our principled rejection of these models would be the same even if this report had been prepared for another region of the country, this province's history provides a powerful additional reason for rejecting these approaches. Human genetic mega-projects have generated enormous controversy in places without this province's history.[57] Here the situation could be expected to be worse.

With regard to the Public Gene Bank Model, the main reason to reject it is that it fails to meet the 'no genohype' requirement. Setting up an Estonian-style public gene bank would be an enormously complicated and expensive process. Its public justification would require speculations about potential social and economic benefits that may never materialise. Given the already noted uncertainty of the commercial prospects of human genetic research, it would be nothing short of foolhardy to commit Newfoundland and Labrador to such a project at this point.

[56] See section 3 for more details.

[57] See section 5 for more details.

The Exclusive Private Gene Bank Model should be rejected on both ethical and economic grounds. From an ethical point of view, an exclusive project would unduly constrain the sort of commercial research that might be done in the province. From an economic point of view the just mentioned uncertainty regarding the economic value of commercial human genetic research cuts the other way. That is, it could be that there are in fact significant economic benefits to be gained from such research. The province might thus cut itself off from access to a huge market if the rosier predictions regarding this research turn out to be accurate.[58] In addition, an exclusive gene bank would be unacceptable for the ethical reasons outlined in section 4 and in section 5.3. Clearly, an exclusive deal would prevent other sorts of research from being carried out. In addition, selling exclusive access to one company seems unavoidably to 'commodify' the genetic material of Newfoundland and Labrador.

Having said all this, we note that the Provincial Approval model ultimately recommended by this report does not rule out the possibility of a *non-exclusive* private 'mega-project' approach. If commercial interests consider such a project viable, the project could be submitted to the approval process outlined below, where it might win approval.

8.2 Rejecting the No Governance and the No Commercial Human Genetic Research Approaches

In a similar fashion, the No Governance and No Commercial Genetic Research approaches can be quickly rejected. Neither approach is true to the conception of human DNA outlined in section 7. The No Governance approach treats human DNA as something to be governed entirely by economic forces in the marketplace. Not only does it display a naïve sense about the market's ability to distribute pure economic goods efficiently and fairly, it fails to respect the hybrid nature of human DNA. At the other end of the spectrum, the No Commercial Human Genetic Research approach draws too harsh a line. There is no reason to declare that commercial interests are completely incompatible with legitimate human genetic research. Here we must keep in mind that there is a difference between recognizing that human genetic research has a commercial value and treating human genetic material as just another commodity. As noted in section 7, human DNA's hybrid nature requires that we not treat it as *simply* another commercially valuable commodity. Nevertheless this does not mean that DNA *cannot* play a role in a process that produces something of commercial value.

[58] This consideration points to the difficulty of negotiating adequate provincial compensation if it were to grant an exclusive license. Given the uncertainty it would be extremely difficult to negotiate appropriate compensation.

What we want to avoid is to treat human DNA as though its *only* or *overriding* value is economic. This is possible as is indicated by the preferred model settled on below.

8.3 Rejecting the Advisory Agency Model

We are left with the Provincial Advisory Agency and Provincial Approval Models. Ultimately, our conclusion is that there are persuasive reasons for selecting the Provincial Approval Model. This is not to say, however, that the Advisory Agency Model has nothing to recommend it. It has the virtue of being relatively easy and inexpensive to implement. It could also be quite easily combined with the PHREB process. However, despite these virtues it should be clear from previous sections that the Advisory Model alone is not acceptable. This is so for the same reason that the No Additional Governance Model is unacceptable. Essentially the Advisory Model treats human DNA as just another tradable commodity. This is inconsistent with the view of human DNA argued for in the previous section.

One response to this observation would be to supplement the Advisory Model with additional measures aimed at properly respecting the value of human DNA. Such a response is, however, doomed to failure. The view of human DNA as property is at the heart of the advisory model and no amount of tinkering with the model can change this.

An additional problem facing the Advisory Model is one that arises anytime subjects are paid to participate in medical research, namely the problem of undue incentives. The Tri-Council Policy Statement *Ethical Conduct for Research Involving Humans* warns that incentives may undermine the legitimacy of consent to participate in research (Section 2.4). In the case of genetic research:

> The potential source may overvalue the likelihood of commercial value and, thus, see participation in research as a way to obtain a particularly valuable lottery ticket (Greely, 1999, 758).

This is not to say that the Advisory Model could not solve this problem, but it would at least have to address it. An analogue of this problem might arise in the case of the Provincial Approval Model. If the research is lucrative enough for the province, its representatives may put undue pressure on its residents to participate. One way to avoid this problem would be to include a requirement that the government not be allowed to advocate for particular projects. Such a requirement is part of the model adopted in Estonia.

Yet another problem facing the Advisory Agency Model is the possibility that allowing individuals to profit from the sale of DNA could pose a threat to the viability of academic human genetic research. Academic projects suffer from serious funding constraints at present. Allowing for the payment of research subjects will likely worsen the situation. When academic and commercial projects compete for access to the same research subjects, allowing for the payment of DNA donors may have a chilling effect on academic research. Subjects may well be less willing to give to academic projects if commercial projects offer payment while academic ones do not. On the other hand, if academic projects do offer payment their funding situation will be further compromised. What's more, there may be a chilling effect even where there is no competition for research subjects. If it is known that research subjects sometimes get paid for participating, there may be an expectation on the part of potential subjects that they will get paid for *any* project in which they participate. There is some empirical support for this claim. Singer (1973) and Titmuss (1971) argue that this pattern emerges when one compares countries in which the blood system runs on the basis of entirely voluntary donations to those in which people may donate blood either voluntarily or for a fee. This point should not, however, be overstated. The empirical support for this claim is far from conclusive. Nonetheless, it does provide a *prima facie* reason to take this possibility seriously.

Together the foregoing considerations build a strong case for rejecting the Advisory Agency Model. A better option is to adopt the Provincial Approval Model. As the following sections explain, it is more easily able to accommodate the view of human DNA taken in this report and, in the process, it addresses a number of the ethical challenges raised in Section 4.

8.4 An Argument for the Provincial Approval Model

As noted in section 6, the province of Newfoundland and Labrador treats health care as a common good, i.e., a communally held responsibility. Insofar as it is possible, it is our collective responsibility to attend to the health problems of individual residents of the province. Individuals are not, in other words, required to bear the costs of their bad luck in suffering from particular harmful medical conditions.[59] But, if this is how we treat harmful medical conditions, then symmetry and fairness require that individuals not benefit from these conditions either. If the residents of Newfoundland and Labrador collectively bear the

[59] Can all medical conditions be properly described as the product of bad luck? It would appear that in the case of a genetic predisposition to a wide variety of conditions the notion of luck could play a significant role.

burden of treating your psoriasis and it turns out that your genetic predisposition to psoriasis is valuable to a pharmaceutical company, then this benefit should be shared just as the burden is. This points to the need to adopt something like the Provincial Approval model. Such a model allows the provincial government to negotiate benefit-sharing agreements with commercial human genetic research ventures that operate here. These benefits should then be turned back into the public health care system.

An obvious objection to this line of argument is that the envisioned end products of most of this research are pharmaceutical products. For the most part such products are not publicly provided in Newfoundland and Labrador. One reaction to this objection is to wonder why pharmaceutical products aren't covered. This is not, of course, an adequate response, since it is unlikely that this gap in the medical system will be closed. A more satisfying response would point to the fact that there *are* non-pharmaceutical benefits that will come from such research. Diagnostic tests, for example, may be developed. To the extent that such tests are offered through the public health care system the objection loses force. Indeed, this should be part of the focus of any provincially negotiated benefits. The province could negotiate for free access to such tests and/or the equipment and personnel to perform them. To the extent that this is done, the province's claim on any benefits that can be negotiated becomes stronger.[60] Conversely, the less seriously the government of Newfoundland and Labrador takes the claim that health care is a communally held matter, the less convincing this position becomes.[61]

At present the provincial government makes a very significant, but not entirely comprehensive effort to treat health care as a commonly held responsibility. To this extent it has a significant but not unassailable claim to a portion of whatever benefits are generated from commercial human genetic research in this province. Any regulatory scheme adopted by the province of Newfoundland and Labrador must recognize the somewhat tenuous nature of this claim. One way to do so would be to use the Provincial Approval process to negotiate free access to whatever processes and pharmaceutical products that might result from genetic research conducted in the province. Depending on the nature of the study and the

[60] For this reason, it is important that government not use the benefits that may be generated by commercial human genetic research to simply replace funding it would have had to put into the health care system anyway. Recall that it is only because health care is viewed as a collective responsibility that the licensing model is plausible. To the extent that the government is not otherwise living up to its responsibility the case for the licensing model is weakened.

[61] In the limiting case, if the province abandoned socialized medicine, it would have no such claim at all.

product that is produced, this access might be available to those who provide the genetic material that made the research possible in the first place. Among other things this would be a way of acknowledging the personal property aspect of human DNA. At the same time it has the merit of relieving some of the burden on the public health care system associated with treating these individuals. There are problems with this suggestion, however. First, given the length of time it will take to develop new therapies and tests as a result of this research, the original donors may not be in a position to benefit directly. Second, it is in some respects a matter of chance that some affected individuals are included in a genetic study while others are not. It is unlikely, for example, that a study on psoriasis would include every citizen of the province that is affected by this disorder. Thus a policy that permitted free access to potential therapies only to those who happened to participate in the research in the first place would be somewhat arbitrary and patently unfair. These problems can be circumvented, however, by negotiating free access to therapies and tests for all Newfoundlanders and Labradorians affected by these conditions. Such benefits would be accessed irrespective of whether individuals had provided genetic samples for the initial research. Consistent with the hybrid value of human DNA argued for in this report, this approach respects both the personal property *and* the communal resource aspects of human DNA.[62]

A further reason in favour of the Provincial Approval Model is found in the communal nature of DNA as discussed in section 7.3. By opting for a communal payment rather than the sort of individual payment proposed by the Advisory Agency Model, the communal nature of DNA is recognized.

A final reason in favour of the Provincial Approval Model is that to treat Commercial Human Genetic Research in this way is to take a political stance in the best sense of the word. By rejecting individual payment we refuse to treat human DNA as just another tradable commodity. In so doing we affirm the idea that human beings have a worth beyond the utility of their components.

8.5 Additional Strengths of the Provincial Approval Model

The previous section provides a powerful argument in favour of the Provincial Approval Model. This section supplements that argument by indicating how this model answers many of the ethical challenges raised in section 4 of this paper.

[62] That is, the reason for this condition is rooted in the individual property aspect of human DNA. The way it is executed is rooted in the 'provincial resource' aspect of human DNA.

8.5.1 Rejecting Commodification—If the benefits negotiated through the approval process are directed to the improvement of health care and the health related research capability of this province, the charge that the DNA of the province's citizens has been inappropriately commodified can be avoided. Instead commerce is utilised to promote the idea that health care is a common good in this province. Commercial human genetic research is permitted because in so doing the people of the province will benefit. Furthermore, since an improved capacity for health research provides benefits beyond the province of Newfoundland and Labrador, the 'common heritage' aspect of human DNA is also respected.

8.5.2 Recognizing the Obligations of Commercial Entities—Given that the Provincial Approval process would apply specifically to commercial human genetic research, it is recognized that the moral obligations of companies doing commercial human genetic research are different than those engaged in other sorts of research.

8.5.3 Unskewing the Research Agenda/Warming Academic Research—Some of the benefits paid as a result of the approval process should be used to combat the tendency of commercial research to skew the research agenda and chill academic research. That is, a portion of these benefits could be used to improve the research infrastructure of the province either through the in-kind donation or purchase of necessary research equipment, or through funding additional research positions. In this way the capacity for academic health research in the province will be enhanced. Furthermore academic researchers will be better able to continue the necessary work on so-called 'orphan diseases' that affect a significant number of residents in the province, but whose relatively small numbers make their conditions largely unattractive to commercial entities.

8.5.4 Compatibility with the PHREB—The Provincial Approval Model fits well with the already discussed PHREB proposal. This compatibility with what is already expected to become government policy should count in favour of the Provincial Approval Model.

8.6 Remaining Ethical Issues

Although the Provincial Approval Model provides more effective responses to a number of the ethical challenges raised in section 4 than do the other various options discussed, some of the points raised in section 4 have still not been addressed. Those few remaining points are taken up here:

8.6.1 Patenting & Intellectual Property Rights—The province has no power in these matters, and the country may not have much more, due to international agreements such as the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement. Nonetheless, it is important that the province of Newfoundland and Labrador join the national dialogue on these matters. In particular, it is important that all the provinces harmonise their innovation policies with their health care policies. It makes little sense for a government to push for companies to develop intellectual property such as patents in biotechnology and then to complain when health costs are driven up by the cost of patented technologies (Caulfield, draft). It may well be, as many have suggested, that the patenting system needs adjusting, but if so, governments should be consistent in stating this view.

8.6.2 Personal Privacy and Private Companies—The PHREB proposal provides an adequate response to this issue.

8.6.3 The Blurred Line Between Commercial and Academic Research—This is addressed in section 9.

Section 9: The Provincial Approval Model

The Provincial Approval model accommodates well the view of the status of human DNA developed in this report. In addition it meets many of the ethical challenges posed by commercial human genetic research. This section considers how such a model might be implemented. The case is made that not only is such a model ethically appropriate, it also can be implemented without sacrificing the viability of commercial human genetic research in this province. More discussion of appropriate levels of benefit-sharing is required, but there is good reason to think that a consensus on reasonable levels is possible. As such the goal outlined at the beginning of this report, namely that economic and health related goals must be balanced, is achievable after all.

9.1 A Possible Scheme for Implementation—The following steps constitute a plausible plan for implementing the Provincial Approval mode:

- Anyone proposing to do research that includes a human genetic component in Newfoundland and Labrador should be required not only to seek approval from the PHREB but also from a Standing Committee on Human Genetic Research (SCHGR). The researcher sponsors would be required to submit a proposal for benefit-sharing to the SCHGR, along with a rationale for this proposal.

    - Notice that this requirement would apply to *all* research projects whether academic or commercial in origin. In this way the problem of the blurred line between academic and commercial research (see section 4.1.3) can be avoided. The only difference envisioned between the treatment of the two kinds of projects is that academic research projects would be expected to make their benefit-sharing agreements largely conditional on future potential commercialization. However such arrangements need not be entirely conditional. An academic project might, for instance, provide access to enhanced medical testing to the subjects of its research.

- The SCHGR would consist of people with expertise in genetics, medicine, pharmacology, business, law, health policy and medical ethics. Committee members would be appointed by the Minister of Health and Community Services on advice from the PHREB

Provincial Advisory Committee, the President of Memorial University of Newfoundland and the Minister of Industry, Trade and Rural Development.

- There is a limited pool of such expertise in Newfoundland and Labrador. As such, care must be taken not to structure the committee so that the province lacks the expertise to fill it. For this reason, the SCHGR should be kept to a manageable size, perhaps consisting of 5 or 6 members. Such a size is not unreasonable for such a committee since it would consider far fewer projects than the PHREB (namely, only those that involve a genetic component). Furthermore, the SCHGR is only responsible for assessing one aspect of a research proposal (unlike the PHREB whose mandate is considerably broader). Depending on the type of study in question the role of the SCHGR may be simply to ensure that the proposed research conforms to a previously negotiated benefit-sharing agreement. This would be the case, for example, with genetic add-on studies in which a general time limited benefit-sharing agreement was previously negotiated between the sponsor and the province.

- To avoid any impression of undue influence in the ethics review process, the PHREB committee must conduct its review of a project in ignorance of any decision on the project that may have been reached by the SCHGR. However, a project that had been reviewed by the PHREB would only gain final approval upon receipt of a report from the SCHGR to the effect that a satisfactory benefit-sharing agreement had been arranged.[63]

- Although the two streams of approval would function separately, they would also function in parallel. Hence the addition of the SCHGR should not slow down the overall process of ethics approval. Although we anticipate some delays at the outset as the initial procedural wrinkles are ironed out, once established the review process involving

[63] Doing this would fulfill a suggestion from the recent WHO report *Genomics and World Health*:

> "Nevertheless, genomic and pharmaceutical companies may have more expertise and experience in negotiation than the governments of developing countries. There is a need therefore for countries to acquire
> the capacity to carry out such negotiations" (WHO, 2002, 145).

the SCHGR should take no longer than the 'normal' operation of the PHREB process.

- Appeals of the SCHGR's decisions would be dealt with on an ad-hoc basis. An appeals committee consisting of members agreeable to both the SCHGR and those filing the appeal would be appointed by the Minister of Health and Community Services.

- The SCHGR would make general guidelines available to researchers concerning the type of benefit-sharing proposals the committee would view as appropriate.

- The SCHGR would be expected to consider both whether a particular benefit-sharing proposal lives up to the ideal of communal benefit-sharing, and whether the proposal makes sense in conjunction with other such proposals. For example, if a particular proposal involved the provision of a medical service to certain residents of the province, or a piece of equipment to a hospital or health board, the committee would consider whether or not there was a need for this service or equipment in the first place. Assuming the need was in fact legitimate the committee would consider any associated costs that might be incurred in implementing the service or in operating the equipment.

- In the event that a benefit-sharing proposal involves payment rather than an in-kind contribution, the committee's first responsibility would be to use benefits arising from that project to improve care for those who suffer from the medical condition that is the subject of the particular research project. When this is not possible the committee's responsibility would be to use the funds to improve the province's ability to care for patients in general. Towards this end, the committee should maintain an awareness of the infrastructure needs for health care and research in this province.

9.2 Reasonable Benefit-sharing Agreements—A 'one size fits all' approach to deciding whether a benefit-sharing agreement is reasonable or not must be avoided. As discussed in the introduction to this report, human genetic research may take a variety of forms, from attempts at gene discovery, to validation studies, to phramacogenomics trails. The differences between these various kinds of research and the potential financial rewards that might accrue, must be taken into account when assessing particular benefit-sharing proposals. Likewise, the portion of the project carried out in Newfoundland and Labrador must be

considered. In some cases the bulk of the research may be done in this province and the provincial contribution would be significant; in other cases there may be numerous cites participating in the research on an international scale, and the province's relative contribution may be small. Research sponsors would be expected to provide such rationale to the SCHGR when submitting their benefit-sharing proposals.

Given this diversity of projects and the variability in the relative contribution made by the province to the success of any given project, it would be unwise to stipulate in advance the precise form and content that benefit-sharing arrangements must take. Nonetheless, it is possible to give some general guidelines:

- Benefit-sharing may be both 'in kind' (e.g., making equipment available to researchers, providing jobs for researchers or support staff) or monetary. In the case of in kind benefit-sharing it is important for the Standing Committee to consider how useful the in kind benefit would be to the province and/or the group the benefit is meant to serve.

- As far as it can be anticipated in advance, the size of the benefit should be proportional to the significance of the contribution of Newfoundland and Labrador to the over-all success of any given project. In those cases where it is difficult or impossible to make a reasonable conjecture as to the overall contribution or eventual payoff, a graduated scheme of benefits tied to significant research "milestones" would be appropriate.[64]

- The amount of activity to be carried out in Newfoundland and Labrador (e.g., amount of employment, training for students) as well as any contribution to research infrastructure in the province should be taken into account as part of the project's benefit-sharing proposal.

- In general, different types of benefits are appropriate depending on whether a commercial research project is a 'fee for service' project or part of an attempt to make a patentable discovery. In the case of discoveries at least some part of the benefit should generally be based on a portion of revenue that might flow from the discovery. In the case of a fee for service project, the benefit generally should be clearly spelled out and should be non-conditional.

[64] The province already has some experience with this from negotiating a benefit-sharing agreement with Xenon Genetics. See Sec. 3.3.

- In the case of benefit-sharing agreements that are based on a portion of possible revenues, the agreement should be structured so that a benefit will continue to flow even if another company takes up the commercialization of the project. This is particularly important in human genetic research since it is generally the case that a company or investigator whose research produces a commercially valuable result will not be able to take the discovery to market alone. Typically partners will be needed or the result will be sold or licensed to another commercial entity. In such cases it is important that the benefit-sharing 'follow' the result through receipt by the province of a portion of any payment that is received for the result.

- Where the population of the province of Newfoundland and Labrador is projected to make a substantial contribution to some discovery, residents of the province should generally receive free access to any test or treatment based on this discovery during that period when the test or treatment is considered to be protected intellectual property.

- As noted in section 9.1, in general, academic research projects would be expected to make their benefit-sharing agreements largely conditional on future commercialization. They need not, however, be entirely conditional. An academic project might, for instance, provide access to enhanced medical testing to the subjects of its research.

- In some cases benefit-sharing agreements that cover more than one project may be appropriate. Consider, for example, the increasingly common practice of adding a genetic research component to traditional pharmaceutical trials. In most cases the genetic component is not essential to the trial, but it is added because it might provide researchers with a useful tool for future research in the form of a database of genetic information and trial results. Indeed it could well be that the majority of DNA currently collected in this province is gathered through such "add-ons".

  The usual practice in such "add-ons" is to include a statement in the consent document by which the research subject waives any claim to commercial benefits that might be forthcoming from future research. It is our considered view that such waivers are inappropriate. Our recommendation is that all such studies should be required to submit an appropriate benefit-sharing arrangement as well.

It would be onerous to submit individual proposals for each study, especially when it is often unclear as to how the DNA collected in any given study might be used in the future. Nevertheless it could be appropriate to negotiate an arrangement that would allow a company to collect DNA in such add-on studies for a limited period of time. That is, if a particular pharmaceutical company wishes to include genetic add-on components as part of its regular clinical trials, the company would make a benefit-sharing proposal that dealt with all such trials in general for a specified period of time (say three to five years). In effect the company would be negotiating a licensing arrangement to allow it to collect DNA as part of its regular clinical trial work for a specified period of time. This arrangement would apply only to the potential commercial aspects of the proposed research, and would not circumvent the general ethical requirements imposed by the PHREB that allow individual subjects to maintain a degree of control over non-anonymised samples, etc. Neither would such a general agreement obviate the need for each proposed study to be reviewed by the SCHGR. Instead it would allow the sponsor to refer to the previous general agreement as its benefit-sharing proposal for the study in question. The SCHGR would then ensure that the proposed study did in fact fit the criteria agreed upon for the general agreement.

9.3 Should Individual Payment for Providing Human DNA Be Banned?—It might be thought that the view argued for in this report leads to the conclusion that the province of Newfoundland and Labrador should make it illegal for individuals to receive payment for providing their DNA to researchers. This is not, however, a recommendation of this report. First, such a ban would be unenforceable in practice. How, after all, are such transactions to be tracked? Second, such a ban is unnecessary. There is good reason to think that Newfoundlanders and Labradorians will be willing to participate in human genetic research without individual payment, particularly if a benefit-sharing agreement has been worked out between the province and the researchers. Finally, if a fair and efficient benefit-sharing regimen is in place, it is anticipated that research sponsors will have little or no incentive to purchase DNA from individual donors. Given these considerations there is no reason to make the potentially divisive move of banning individual payment.

9.4 Limitations on the Use of the Collected DNA—Just as we argue that individuals should not treat their DNA as a form of property, the provincial government should take steps to ensure that those researchers or companies that collect DNA do not treat their collection as a piece of property. In particular, the provincial government must anticipate the possibility that a commercial research

company might go bankrupt. Thus it will be necessary to establish guidelines for what would happen to collected DNA samples in that case. It is possible, for example, that a company in receivership might attempt to use its DNA bank as collateral in future negotiations, or that a creditor would attempt to seize the DNA bank as an asset. We recommend that the province consider legislation that prohibits the ownership of human DNA. Such legislation should specify that such samples cannot be used as collateral nor attached as a result of a debt.[65] In the event of a bankruptcy or any other ceasing of a project with an existent collection of human DNA, the SCHGR would assume stewardship of the collection and determine whether the collection should be passed on to another research project or else destroyed.

[65] This is the approach taken in Iceland's Act on Biobanks (see article 10). An English translation of the Act on Biobanks is available on the website of the Icelandic Ministry of Health and Social Security at http://brunnur.stjr.is/interpro/htr/htr.nsf/pages/Act-biobanks.

Section 10: Recommendations

10.1 Main Recommendations—The main recommendations of this report are as follows:

- **The ethical challenges raised by commercial human genetic research can be dealt with best by implementing the Provincial Approval model.**

- The most effective and efficient manner by which to implement the Provincial Approval approach is in conjunction with the proposed PHREB. Together these two initiatives address the ethical challenges common to both commercial and academic human genetic research. Thus **it is imperative that the province move expeditiously to implement the PHREB.**

- It is clear that as the science and industry of genetics grows, issues such as the ones discussed in this report will continue to arise. For this reason **the province should establish a Standing Committee on Human Genetic Research (SCHGR)** that can assess these issues as they arise. If the proposal for a Provincial Advisory model made in this report is accepted the advisory committee needed to implement that model could also serve the dual purpose of a standing advisory committee.[66]

Some more specific recommendations follow from these main points.

10.2 Inform Potential Research Participants about Benefit-Sharing—As part of the informed consent process research subjects go through before participating in scientific research, a passage often appears in the consent document declaring that the research subject agrees to waive any claim on financial benefits that might result from the research. Even ignoring what has been argued for earlier in this report, this is unacceptable since it runs counter to the purpose of the informed consent process. The purpose of the consent process is not to protect the financial interests of researcher sponsors. Rather

[66] Establishing an advisory committee such as this would be consistent with a similar recommendation for the Ontario Provincial Advisory Committee on New Predictive Genetic Technologies (OPACNPGT, 2001, 6).

its purpose is to inform potential research subjects of the nature of the research they are being asked to take part in so they can make an informed choice as to whether or not to participate. Furthermore, the position argued for in this report suggests a better approach, one that *is* in keeping with the purpose of the informed consent process. Rather than asking the participants to waive their financial rights, the consent document should contain language such as the following:

> 'You will receive no direct financial benefit from participating in this research. However, as part of the ethics approval process for this research, the researchers have agreed to provide the province of Newfoundland and Labrador with a share of any financial benefits that may result from this research. Any share received by the province will be used to enhance health care and/or to further health care research in this province.'

More specific information about the details of the relevant benefit-sharing agreement could be made available on request.

10.3 Participate in National Debate on Patenting—As noted in section 8.6.1, while it is not within provincial authority to alter the patenting system, this province should play an active role in the on-going debate regarding the patenting of genes and gene fragments, as well as of living things more generally.[67] Furthermore, if the province proceeds with implementation of the PHREB and acts on this report's recommendations it will establish the province's leadership role regarding the regulation of human genetic research. As such the province will be well situated to influence the national debate.

10.4 Develop a Biotechnology Strategy for Newfoundland and Labrador—This report's main focus has been the ethical challenges posed by commercial human genetic research. Although it has made occasional comments about the economic potential of biotechnology for this province, it does not claim any particular authority on this matter. It is clear, however, that biotechnology does have significant economic potential and that many regions are seeking to take advantage of this potential (Crane, 2002). As such this province should develop a strategy for nurturing the biotechnology industry here. This would constitute a natural follow-up to this report in two ways. First, if the recommendations made in this report are implemented this would provide a feature of this province that could be promoted to those who

[67] The Ontario Ministry of Health and Long-Term Care recently made a similar recommendation (2002).

consider doing human genetic research here, namely, stable and efficient governance of such research. Second, developing a biotechnology strategy would involve an estimate of the economic potential of such research for this province. This would be very useful information in assessing the benefit-sharing proposals that would pass through the Provincial Approval process.[68]

[68] John Bear, a member of the project group that helped develop this report, has made preliminary contact with the Boston Consulting Group regarding an economic model the BCG used to estimate the overall economic potential of genomics research for the pharmaceutical industry. The BCG has indicated some willingness to allow researchers in Newfoundland and Labrador to have access to their model for the purpose of estimating the economic potential of human genetic research in this province.

Section 11: Conclusion

The challenges posed by commercial human genetic research are formidable. Nonetheless, this report demonstrates that they can be met in a way that sacrifices neither economic, health, nor ethical considerations. So long as the unique nature of human DNA is respected, commercial human genetic research poses no insoluble ethical problems.

Newfoundland and Labrador has the potential to lead the nation in setting standards for the regulation of human genetic research in general, and for establishing appropriate guidelines for benefit-sharing and a mechanism for implementing them in particular. We urge the province to move expeditiously to implement the recommendations presented herein.

Appendix A – Research/Writing Team

The principal investigator for the project was Daryl Pullman, Ph.D., Associate Professor, Medical Ethics, Memorial University of Newfoundland.

The members of the project team were:

John Bear, Ph.D., Professor, Population Genetics[69]
Maria Mathews, Ph. D., Assistant Professor, Health Policy
Paul McDonald, L.L.B., Lawyer, Cox Hanson O'Reilly Matheson
John Usher, Ph.D., Associate Dean, Faculty of Business Administration
Ban Younghusband, Ph. D., Interim Chair, Division of Genetics[70]

Andrew Latus, Ph.D. served as a post-doctoral research fellow for the project. Latus and Pullman are the authors of this report.

[69] Although Dr John Bear was actively involved in the discussions and work resulting in this report, his assessment of the issues it addresses is substantially different from that of this report. He has therefore chosen to disassociate himself from the report's conclusions and policy recommendations.

[70] With the exception of Paul McDonald, a lawyer with the St. John's firm Cox Hanson O'Reilly Matheson, all members of the project team were at Memorial University of Newfoundland. During the course of the project, John Usher left his position at MUN to become Dean of the Faculty of Management at the University of Lethbridge.

Appendix B – Provincial Health Research Ethics Board Terms of Reference (Working Draft # 4)

Purpose

The purpose of the Provincial Health Research Ethics Board (PHREB) is to protect and safeguard research participants. The Board will review; approve, propose modifications or reject; terminate and monitor any proposed or ongoing human health research conducted within the province of Newfoundland and Labrador, according to Tri-Council Guidelines.[71]

Composition of the Board

The Board shall consist of at least ten members, including both men and women, who shall possess one or more of the following:

a) expertise and experience in quantitative and qualitative research methods;
b) expertise and experience in the areas of research to be reviewed by the board including, in particular, pharmacology and genetics;
c) expertise and experience in clinical trials research;
d) knowledge in ethics;
e) knowledge in privacy protection; and
f) knowledge in the relevant law.

The voting members of the Board shall be appointed by the Minister of Health and Community Services, upon recommendation of the President of the University and the PHREB Provincial Advisory Committee, usually for terms of three years. Appointments may be renewed for one term. The Minister of Health and Community Services, in consultation with the President of the University and the PHREB Provincial Advisory Committee, will appoint a Chairperson from the voting members of the Board. The Board's decisions will be reported to the Minister of Health and Community Services, the President of the University and the PHREB Provincial Advisory Committee.

Quorum

A quorum shall be fifty per cent of the current voting membership.

[71] Or such guidelines as may supercede these.

Legal Representation

The Lawyer members, who should have experience in ethical issues, will **not** act as legal counsel to the Board.

Additional Members

Additional members may be appointed on the recommendation of the Board. The Board, at its discretion, may co-opt additional members to review specific applications. Co-opted members shall not vote.

The Board may also seek the opinion or advice of qualified persons outside the Board when deemed appropriate.

Role of the Board

The role of the Board is to review; approve, propose modifications or reject; terminate and monitor any proposed or ongoing human health research conducted within the province of Newfoundland and Labrador. Its primary tasks are:

(a) to review research projects and ensure that approved projects meet the appropriate ethical and scientific standards, and
(b) to monitor ongoing research projects to ensure continuing compliance with the appropriate ethical and scientific standards.

The term "health research" refers to research involving human beings and may include human remains, cadavers, tissues, biological fluids, embryos or foetuses in projects involving biomedical research, clinical and population research, research respecting health systems and health services, and research into the societal and cultural dimensions of health and environmental influences on health.

Guiding Principles

The Board will protect the interests of health research participants by using the highest quality, nationally accepted, standards for research review - the Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans[72];

[72] Tri-Council Policy Statement Ethical Conduct for Research Involving Humans; 1998. This document is a combined effort of three organizations: Medical research Council of Canada,

or such guidelines as may supercede these. The Guiding Principles are as follows:

- Respect for Human Dignity
- Respect for Free and Informed Consent
- Respect for Vulnerable Persons
- Respect for Privacy and Confidentiality
- Respect for Justice and Inclusiveness
- Balancing Benefits and Harms

Natural Sciences and Engineering Research Council of Canada, and the Social Sciences and Humanities Research Council of Canada.

Appendix C—PHREB Guidelines for Human Genetic Research in Newfoundland and Labrador (Working Draft #4)

INTRODUCTION

The Provincial Advisory Committee on Health Research Ethics Policy endorses the following guidelines for the ethical review and conduct of all human genetic research pertaining to the population of this province. The guidelines are intended as a supplement to the Tri-Council Policy Statement (1998) *Ethical Conduct for Research Involving Humans*, and are not intended in any way to replace or supplant that statement. These guidelines will serve as the standard by which the Provincial Health Research Ethics Board will assess all proposed human genetic research to be conducted in this province. The guidelines should also be useful to researchers in the planning and implementation of their research.

Objectives

The distinction between scientific research and clinical practice is often difficult to maintain in health research in general and in genetic research in particular. In recognition of this reality these guidelines aim to achieve the following broad objectives:

- To ensure that all subjects in genetic research understand the implications of their participation.

- To ensure optimal care for all subjects involved in genetic research in Newfoundland and Labrador with regard to pre- and post-test genetic counselling, genetic testing, interpretation and reporting of results, and subsequent treatment and/or therapy when applicable.

- To ensure appropriate storage and management of genetic samples and information for purposes of research and continuing patient care.

- To ensure the just and equitable distribution of the benefits and burdens associated with genetic research for all stakeholders including patients and families, researchers, research sponsors, and the people of Newfoundland and Labrador.

ETHICAL REVIEW GUIDELINES

I. Informed Participation in Genetic Research

The research team must obtain the free and informed consent from the individuals that participate in the study. Often genetic studies require the participation of multiple family members which raises a number of unique issues. A potential tension exists between the individuals who choose to participate in the study and other family members. Therefore as far as is practical and possible, free and informed consent should involve the family. The researcher should be aware that some individuals within a family might be coerced by other family members to join the study. Alternatively, conflict may develop if some family members hold that the rights of the family to genetic information override the rights of the individual. When the wishes of the family are in conflict, enhancing communication is preferable to compelling either the group or the individual to overcome their reluctance.

Informed participation often involves a 2-stage process:

A. Identification and first level contact of the potential study population.

The following shall be addressed:

- Where appropriate, efforts should be made to make the community aware of the study and its goals.

- The research team should describe the nature of community discourse, plans to minimize community risk and the nature of advertising for the purpose of recruitment.

- Will minors be involved in the study, and if so, how will they be identified?

- How will the initial offer of participation be made and by whom?

- Are there situations that could alter the planned method of contact?

- Will potential subjects be provided with material describing the methods and goals of the study? If not, why not?

B. Second level contact and informed consent:

The researchers should describe the process by which willing subjects will be connected to the research team. For the purpose of recruiting relatives, there should ordinarily be no direct contact between the research team and the family members of the proband. In order to respect the privacy of the family, only the proband should contact other family members with the initial offer of participation.

The person(s) responsible for obtaining informed consent should be clearly identified in the research proposal. This individual must ensure that the subject understands the goal of the research, as well as his or her own role in the research project.

In addition to the standard requirements for informed consent (see *Tri-council Policy Statement on Ethical Conduct Involving Human Subjects*), the informed consent document should include the following:

- Identification of the members of the research team.

- Description of the study including its goals and limitations, the anticipated length of the study and the methods that will be used.

- Description of where and how the research data will be analyzed and

stored.

- Description of the methods that will be taken to protect patient confidentiality.

- Description of a subject's options for future use of his or her sample following completion of this study.

- Description of the psychological and socioeconomic risks related to participation, for example occupational or insurance discrimination and the disclosure of non-paternity.

- Possibility of withdrawal from the study. The document should describe the process for withdrawal. Except in the case of an anonymized sample, this ordinarily includes the right to have a sample destroyed. The document should make it clear that information obtained up to the point of withdrawal will usually not be destroyed.

- Where applicable, the subject should be given the option of whether or not to be informed of the results of the research.

- Description of the predicted commercial gain and benefits-sharing arrangements.

- Potential impact of results on family members.

II. Communication of Results

Overall findings of the study should be regularly reported to the subjects. A process should also be developed for communicating individual results where appropriate. Communication of genetic research results is often complex, but should be as full and accurate as possible. A clinician or genetic counsellor should be associated with the research project to ensure appropriate support and counselling during and after the communication process.

A plan for communication of research results shall include:

- Opportunities for subjects and interested members of the public to learn about the general results;

- Provision of lists of publications on request;
- Where indicated, a process for communicating individual results, including:
  - communication by the treating physician where results have health implications for the individual and prevention or treatment is available;
  - full consideration of choices made by the individual, availability of clinical services and implications for the individual's family;
  - provision of appropriate genetic counselling as required;
- A schedule indicating when and how results will be communicated;
- A process for addressing the following specific situations:
  - where family members are found to be carrying a mutation in the study gene but are unaware of it; and
  - the circumstances under which genetic information will be disclosed to members of the subject's family against the subject's wishes.

III. Confidentiality

In light of the personal and familial nature of the data to be gathered, special safeguards need to be provided to protect confidentiality. The researcher will be required to provide strict controls over access to and disclosure of information concerning study subjects, and will need to ensure that the encoded data itself does not permit identification of individuals or familial relationships.

The researcher will identify those persons who will be authorized under the study protocol to have access to the subjects' medical (or other) records and genetic information.

The researcher will describe the measures being taken (physical, electronic or otherwise) to control access to the records of information collected during the study.

The researcher will describe the steps to be taken to protect the identity of subjects and their familial relationships in the data.

The researcher will specify how and when genetic information may be disclosed, and to whom; and

The researcher should address the issue of whether there will be any limits to the protection of confidentiality, and make provision for disclosure of this fact.

IV. Commercial Applications of Research

Commercially-sponsored research is accepted in many health-related fields. The issues are not particularly different when considering genetic research. Disclosure of the commercial connection – to both the REB and to the research subjects – is the important requirement.

The application to the REB and the consent form shall disclose specific details of any commercially funded research. They shall disclose whether any researcher is an employee of the sponsoring company and whether any researcher could financially benefit, directly or indirectly, from the research.

A question and answer sheet may be provided as additional information to prospective research subjects.

V. Storage and Transfer of Human Biological Material

Tissue or DNA specimens collected for one study could conceivably be used in future – possibly unrelated – studies. A research application should clearly state the purpose for which DNA is being collected. If it is proposed to keep the DNA when the present study is complete, the consent form should provide REB-approved options for restricting the future use of the samples.

If a subject at any time revokes consent or requests the return or destruction of unused DNA, the researchers shall comply with this request. It is understood that it may not be possible to return samples that have been anonymized.

In the event that Human Biological Material are to be transferred from one researcher and/or institution to another, a Materials Transfer Agreement must be completed (see attached).

VI. Archived Pathology Specimens

Pathology specimens, taken for clinical purposes and usually stored in hospitals, are a valuable source of genetic material, especially in the case of people no longer alive. The use of such specimens is not uncommon. With respect to the use of such material for genetic research:

- If use of such specimens is contemplated, the applicants shall include a description of the circumstances of their use, including a plan for obtaining appropriate consent or permission.

- If the subject is still alive, the researcher shall obtain consent from the subject.

- If the subject is deceased, then the researchers shall make a 'best efforts' to obtain permission for the use of archived specimens from a close family member and the nature and extent of these efforts shall be documented.

Materials Transfer Agreement

Re: Human Biological Material identified as
********** *(hereinafter referred to as "Human Biological Material")*

Dear *********:

In response to your request for the above-identified Human Biological Material, *the provider of the material (hereafter referred to as the "provider"*), requires that you and your Institution *(hereafter referred to as the "recipient")* agree to the following before you receive the Human Biological Material:

1. This Human Biological Material is the property of the *provider* and is made available as a service to the research community.

2. The Human Biological Material will be used for non-commercial research purposes only. Any commercial application of the research will require a separate agreement with the provider.

3. The Human Biological Material will not be distributed to others without written permission from the *provider*.

4. The recipient agrees that all Human Biological Material will be returned to the provider or destroyed at the request of the provider and the recipient shall provide written confirmation of such destruction.

5. The source of any Human Biological Materials will be acknowledged in any publications.

6. The Human Biological Material is experimental in nature and it is provided without any warranties, express or implied. All liability for damages that arise from your use, storage or disposal of the Human Biological Material is assumed by the recipient and the recipient's institution.

7. The Human Biological Material will at all times be kept safe and secure, and access to it will be restricted solely to those persons using it for

research purposes, and then only for those times when the Human Biological Material is actually being used for such purposes.

8. The Human Biological Material will be used only in a manner consistent with accepted standards of ethical practice and in compliance with all applicable laws and regulations, including, for example, those relating to research involving the use of human and animal subjects or recombinant DNA.

To indicate your agreement to these conditions, please sign and have your Institution sign both copies of this letter and return one signed copy by Fax to the *provider* at (709)*** ****. The Human Biological Material will then be forwarded to you.

_____ _____
Provider (date)

Accepted by - RECIPIENT:

_____ _____
(Signature) (date)

_____ _____
(Printed Name) (date)

Institutional Approval

_____ _____
(Authorized Signature) (date)

Name: _____

Title: _____

Address:_____

_____

Appendix D – Cases

1. Introduction

What follows is a series of descriptions of some commonly discussed commercial human genomics research (CHGR) projects. While this is far from an exhaustive catalogue, it does cover a number of the case that are referred to most often in the literature, as well as presenting a number of different models of CHGR projects.

The longest section deals with the infamous Icelandic deal with deCODE Genetics. This is partly because the Icelandic case is by far the best documented one, but also because virtually any project proposed since the Icelandic situation became well known has been designed with the outcry over that situation in mind. Iceland's arrangement with deCODE has been widely criticized on several grounds and there is widespread, although by no means universal, agreement that the arrangement is seriously flawed. Most post-deCODE proposals take pains to say how their approach differs from deCODE's.

2. Iceland

Although, as was just noted, deCODE's arrangement with the government of Iceland is the best known example of a commercial human genomics project, the details of the arrangement seem to be broadly misunderstood. People tend to focus only on Iceland's 1998 Act on a Health Sector Database (HSD Act), but this is just one part of the story. Roughly, the situation is this: the HSD Act gave the government of Iceland the power to grant a licence to a private company to assemble a database of the medical records of the people of Iceland. In January of 2000, this licence was granted to deCODE Genetics. Also in 2000, Iceland's government passed the Biobanks Act. This Act sets out the conditions under which a 'gene bank' can be assembled. The intent of this act is clearly to govern deCODE's project of assembling a database of genetic information on Icelanders that would be linked to the Health Sector Database and to a database of genealogical information deCODE has assembled. These arrangements are described in much greater detail below.

The deCODE project appears to have its origins in 1994. In that year, Kari Stefansson & Jeffrey Gulcher, two Harvard based clinical neurologists, took

part in a study that aimed to find a genetic cause of Multiple Sclerosis. Although this study did not produce much in the way of concrete results, it gave Stefansson, a native of Iceland, the idea of using the Icelandic population for further study. (Rose, 2001, 9) Stefansson and a number of others have cited several reasons for doing human genomics research in Iceland. Among them are the following:

> (1) The county is 'manageable' both in terms of size and number of inhabitants (approx. 275,000 inhabitants, mostly located in and around Reykjavik).
>
> (2) "Icelanders are not only a wealthy population, but distinctly technophile." (Rose, 2001, 12)
>
> (3) Iceland was settled around 930 AD, but the population was relatively isolated until the 19th century. For this reason, Iceland is often described as having a genetically homogenous population. (However, both the truth of this claim and how useful genetic homogeneity is are matters of some debate. For more on this, see Greely, 2000, 160 and Rose, 2001, 13-14)
>
> (4) Iceland has had universal healthcare and good record keeping since 1915. Since 1945, the collection and preservation of tissue samples has been centralized. (Greely, 2000, 159)
>
> (5) The Icelandic people have a history of being generally willing participants in medical research. (Greely, 2000, 159)
>
> (6) Genealogy is a national pastime, so excellent genealogical records of Icelandic population exist.

In 1996, Stefansson founded deCODE Genetics with $12 million in venture capital from 7 venture capital companies.[73] (Winickoff, 2000, 2) The company was incorporated in Delaware, U.S.A. but is physically located in Iceland.[74] In

[73] The companies were: Alta Partners, Atlas Venture Partners, Polaris Venture Capital, Arch Venture Partners, Falcon Technologies, Medical Science Partners and Advent International.

[74] In June, 1999, five million of the founder shares were sold to several Icelandic financial entities (which in turn sold 40% of these shares to private investors in Iceland). At this time, there seem to have been about 24 million shares in existence. (Greely, 2000, 169) In July, 2000 the company began to be listed on the NASDAQ Stock Exchange (DCGN). The stock closed its first day of trading at $25 and 7/16. In the period shortly after this, the stock went even higher, but has dropped significantly since then ($1.87 US as of Dec. 19, 2002).

December of 1996, deCODE labs opened in Reykjavik with 45 employees. (Winickoff, 2000, 2) deCODE's business model was a 'typical' one, i.e., to investigate genetic causes of health problems and develop new treatments or diagnostic tests based on this research or else strike deals with other companies that would carry out this development. They have, however, pursued this research in two quite distinct ways:

> (i) By 'traditional' disease gene hunting, i.e., studying genetic variations amongst afflicted and non-afflicted members of a highly afflicted family.
>
> (ii) By attempting to construct a database containing health, genealogical and genetic information on much of the population of Iceland.

It is this second project I will focus on here. deCODE has been handling the genealogical part of the project by itself, drawing on the national fascination with genealogies. In early 2001, it was reported that deCODE had "computerised and coded the genealogies for some 600 000 past and present individuals." (Rose, 2001, 10) The Act on a Health Sector Database (HSD Act) and Act on Biobanks provide a framework for the construction of the health and genetic parts of the database, respectively.

The Act on a Health Sector Database

deCODE actively campaigned for legislation that would allow it to construct a database of health information. In fact, it has been reported that, in September of 1997, deCODE faxed a draft version of what would become the HSD Act to the Ministry of Health. (Rose, 2001, 15) In March, 1998, the first version of the act was introduced in the Althingi, the Icelandic parliament. Among other things, the act presumed universal consent on the part of all Icelanders to inclusion in the database. For this and other reasons, the bill was widely condemned and soon withdrawn.[75] A second version, significantly revised but still controversial, was introduced in September, 2000 and passed by the end of the year.

Some of the main details of the HSD Act are as follows:

Another notable aspect of deCODE's business operations is a1998 deal it struck with Hoffman LaRoche. The deal is potentially worth $200 million (US) over 5 years agreement and is not supposed to be conditional on the setting up of the HSD. (Exactly how much of the $200 million deCODE will receive as part of the deal is a matter of some controversy.)

[75] One other prime source of controversy was the lack of consultation with Icelandic experts during the drafting of the bill. This was partially resolved during the revising of the bill.

(1) **Overview:** The Act gives the government the power to grant an exclusive, up to 12 year licence to a private company to create a database of health information on the people of Iceland based on existing and future records. (Article 3) The database is to be physically located in Iceland and all processing of it is to be done there. (Articles 5 & 10) The act makes a point of noting that it applies only to databases of health information and not "to the storage or handling of, or access to, biological samples." (Article 2) This is left to the later Act on Biobanks.

(2) **The Supervising Committee:** The operations of the database, as well as contracts between the licensee and health agencies that will be providing it with data, are to be overseen by a three person committee appointed by the Minister of Health. This committee is to consist of a lawyer (as chair), a health professional with expertise in epidemiology and an expert in information technology. This committee will also oversee the operation of the HSD in the event that the licence is revoked at any point. (Article 6)

(3) **Presumed Consent:** While presumed consent to participation in the HSD was not removed from the Act, allowance was now made for revoking this consent. This requires submitting a form to the Ministry of Health. (Article 8) In 1999, all households in Iceland were mailed information about this, although not a copy of the form.[76] (Rose, 2001, 20) Although the HSD Act is not entirely clear on this point, the provisions on 'opting out' only clearly apply to not having your data entered into the database. Once it is in the HSD, there seems to be no right to remove it. However, in a recent joint statement by deCODE Genetics and the Icelandic Medical Association, both agree that if information on a patient's health is entered into the Health Sector Database and "the patient wishes that this information be deleted from the database, it shall be done immediately after the wish has been put forth." deCODE has agreed to pay the costs for fulfilling such a request. (deCODE Press Release, August 27, 2001)

[76] Mannvernd, the Association of Icelanders for Ethics in Science and Medicine, the leading organization in opposing deCODE's plan has actively campaigned to get Icelanders to opt out of the HSD. As I write this, Mannvernd's website reports that approximately 20,000 Icelanders have opted out. (www.mannvernd.com)

The HSD Act makes no special provisions regarding opting out for children or those who are not legally competent. "[T]he same rules shall be applied as with regard to other decisions made on their behalf by responsible persons."[77] Notice that this means children don't have a clear right to remove information about themselves once they reach the age of majority (although keep in mind deCODE's compromise on this point). Likewise, health records of the dead are to be automatically included.[78]

(4) **Privacy Protection:** Seeking information from the HSD on particular individuals is explicitly prohibited. (Article 10) In addition, the data in the HSD is to be rendered personally unidentifiable.[79] It is to be entered into the HSD only after *one-way encryption* of identifying information. This encryption is to be done by those who supply data to the licensee (not by the licensee itself, as was provided for in the initial legislation.) No key for this encryption is to exist. (Article 7) It is worth noting, however, that the effectiveness of this proposal with regard to rendering the data unidentifiable has been questioned. (See the articles listed below by Arnason and Anderson.) This debate is important since the claim that the data in the HSD will not be personally identifiable has been a crucial part of the case the government and deCODE have made in favour of the standard of presumed consent to participation.

(5) **Access to the HSD:** In the original version of the HSD Act, the licensee was to have exclusive access to the HSD. In the final version, the ability of others to access the HSD was strengthened. The government is always to have access to statistical data from the HSD "for the making of health reports and planning, policy-making and other projects." This information is to be provided free of charge. (Article 9) The government's notes on Article 9 also provide for other researchers to have access to the

[77] This comes from explanatory notes attached to the HSD Act. See www.mannvernd.com for a translated version.

[78] Greely raises the question of what will happen to the health records of those people who opt out of the HSD after they die. (Greely, 2000, 174) This question, however, is answered in the explanatory notes that accompany the bill. (See previous note) In the comments on Article 8 of the bill it is noted that: "Provision is made here for the patient to request, on a special form, that data on him/her not be entered on the health-sector database. The request may apply to all data, or some specific data, and it must be complied with, also after the death of the patient."

[79] As such, the HSD is intended only as a research tool. In theory, it will be useless in treating particular patients. This represents another revision to the first version of the HSD Act. The first version envisioned the HSD as a tool for both research and treatment.

database. A committee consisting of representatives of the Director General of Public Health, the Faculty of Medicine of the University of Iceland, and the licensee will have the authority to grant access to data from the database to researchers working for organizations that provide data to the database. The researchers would only have to pay the extra costs for coming up with this data. However, the committee may not grant this access if "the committee foresees the research in question adversely affecting the licensee's business interests." This is another highly controversial aspect of the HSD Act.

As a further form of privacy protection, the licensee is not permitted to grant others direct access to the database. The access discussed above is to the results of *queries* on the database. (Article 10)

(7) **Payment by the Licensee:** The Act explicitly requires only two fees to be paid by the licensee. One is to "meet the costs of preparing and issuing the licence." The other is a yearly fee "equivalent to the costs of the work of the committees" set up as a result of the HSD Act and "other costs pertaining to service and monitoring of the operation." The act also grants the Minister of Health the right to negotiate further payments by the licensee. (Article 4) Greely reports that deCODE has agreed to pay the Icelandic government a $1 million (US) annual licensing fee and to provide the Icelandic government with a share in deCODE's yearly profits, up to $1 million per year. (Greely, 2000, 188) deCODE also struck a deal with Hoffman La Roche (see note 2) under which drugs developed by Hoffman La Roche as a result of deCODE's research would be provided to Icelanders who need them free of charge. (Rose, 2001, 26)

(8) **Protection of the Database:** During the period of the licence, the licensee is required to provide the supervising committee with a regularly updated copy of the database. (Article 5)

(9) **After the Licence Expires:** At the end of the licence, the Minister of Health (or someone assigned by him) shall receive "indefinite use of all software and right required for the maintenance and operation of the database."

The National Bioethics Committee

Having passed the HSD Act, the next major source of controversy came in 1999 and concerned the government's treatment of its own National Bioethics

Committee (NBC). This body had been created by the government in 1997. In July, 1999, it was dissolved and replaced with a new one. Prior to this, members of the NBC were appointed by the Minister of Health based on nominations from the University of Iceland, the Icelandic Medical Association and the Icelandic Nurses Association. The sole exception was the committee chair who was appointed by the minister with no need for nominations. The reorganized committee, however, was appointed by the minister of Health based on nominations from government ministers and the Director General of Public Health. Interestingly, only the chairman of the NBC had voted to support the HSD Act in 1998. Shortly after that vote, this same chairman became the Director General of Public Health. He was one of those responsible for the new design of the NBC.

The Biobanks Act

As already noted, the HSD Licence was awarded to deCODE, to little surprise, in January, 2000. In April of that year, the Biobanks Act was introduced in the Althingi.[80] It was passed with some amendments in May and took effect on January 1, 2001. A discussion of some of the main points of the Biobanks Act follows.

> (1) **Overview:** The Act "applies to the collection of biological samples, and their keeping, handling, utilisation and storage in Biobanks." (Article 2) The Act requires that Biobanks be set up only under a license from the Minister of Health (who is to receive advice on this from the Director General of Public Health and the National Bioethics Committee).[81] (Article 4) It does not apply, however, to samples taken for the purpose of testing, treatment or scientific study provided that the samples are only kept temporarily (usually, this will mean fewer than five years) and that the samples are destroyed once the tests, treatment or research is completed. (Article 2) It also does not apply to the storage of gametes or

[80] Like the HSD Act, a preliminary version of the Biobanks Act had already been introduced and withdrawn.

[81] Some have complained that the wording of parts of the act like articles 2 and 4 causes the act to be ambiguous regarding the status of already existing collections of biological samples. (See, for example, Winickoff, 2000) It is worth noting, however, that a provisional clause of the act clearly states that, as noted above, consent is to be presumed for materials that have already been collected unless the donor of the material has stated otherwise. It appears that any ambiguity regarding existing collections must concern the question of whether these existing biobanks *themselves* can continue to exist without needing to seek a licence from the Minister of Health.

embryos for reproductive purposes or to bodily organs collected for the purpose of transplantation. (Article 2)

(2) **Location:** Biobanks are to be located in Iceland. (Article 5.2)

(3) **Consent:** The requirements for consent for acquiring a sample depend on how the sample is collected. If the sample is collected for the specific purpose of inclusion in a biobank, then written "free, informed consent" by the donor is required. (Article 7) The donor is to be informed of the purpose of the biobank, the benefits and risks of donating, the fact that the sample will be stored permanently in a biobank and of the possible uses that the sample may be put to in the bank (more on this shortly). A donor may withdraw this consent at any time. If so, the sample is to be destroyed, but this is not necessary for material that has already been produced from the sample in the process of a study. (Article 7)

Samples may also be acquired in another way. If a biological sample has been collected for the purpose of performing "clinical tests or treatment", consent for inclusion in a biobank may be assumed provided that "general information on this is provided by a health care professional or health institution." (Article 7) So, for instance, consent may be assumed so long as the clinic at which the sample was taken posts notices about this on site. The Director General of Public Health is obliged by the act to promulgate "in detail" this standard of consent (and the terms of the Act in general). (Article 13) Assumed consent may be withdrawn by a (potential) donor at any time, by notifying the Director General of Public Health. The Director General is to make a coded list of those who have withdrawn their assumed consent available to the boards of all operating biobanks. (Article 7) It is worth noting, however, that, when discussing the right to withdraw assumed consent, the Act makes note of a provision in Article 9 that allows the Minister of Health to "issue regulations defining more precisely the use of biological samples."

The Act also requires the minister to answer queries from individuals as to whether samples taken from them are stored in any biobank. (Article 13)

A "Provisional Clause" to the act notes that samples gathered before the Act came into force "may be stored in a biobank, unless the donor of a biological sample declares his/her opposition to this." In the absence of such opposition, the terms of the act apply to the sample.

(4) **Privacy:** A number of provisions aim at protecting privacy. Any members of the staff of the Director General of Public Health who deal with the withdrawing of assumed consent are to take an Oath of Confidentiality. (Article 7) The staff members of biobanks are also required to safeguard confidentiality, a requirement that continues even if their employment ceases. (Article 11) The samples themselves are to be stored "without personal identification." (Article 8) As for reidentifying samples, this is only to be done in keeping with standards laid down by the Data Protection Agency.[82] (Article 8) (The DPA is the Icelandic authority charged with overseeing issues of personal privacy.)

(5) **Access:** The biobank is allowed to negotiate with scientists for access to the biobank. Access may be granted for "quality control" and "development of methods and tuition" provided that the samples are not personally identified. Access may also be granted for "further diagnosis of diseases." (Article 9) Access for medical research must be approved by the DPA. In addition a protocol for the research must have been approved by the NBC or the local ethics committee of the relevant health institution. (Article 9) This access may be for purposes other than those for which the samples were originally collected *provided that* "important interests are at stake, and that the potential benefit outweighs any potential inconvenience to the donor of a biological sample or other parties." (Article 9) As already noted, the act empowers the Minister of Health to issue more precise regulations on the use of samples.

(6) **Ownership of Samples:** The licensee for a biobank is not the owner of the samples, "but has rights over them." The samples may not be passed on to anyone else, nor used as collateral. (Article 10)

The Present Situation

It is surprisingly difficult to get information about the present state of deCODE's project. The company frequently announces promising results of its research, but does not seem to have made a great deal of progress at developing the HSD. In fact, it seems to have slowed down work on the HSD in an attempt to overcome the many objections to the project. (See, for instance, the already mentioned joint statement with the Icelandic Medical Association.)

[82] Notice that this is a different form of privacy protection than the one way encryption seen in the HSD Act. Here, relinking is allowable under some circumstances.

3. Estonia

Estonia plans to set up a 'Gene Bank', a combined database of health records and genetic information about its individual citizens.[83] Toward this end, the Human Genes Research Act was passed on December 13, 2000. (Bartha Knoppers, a well known Canadian expert in health ethics and law, consulted on the design of the law.) In keeping with the provisions of the act, the Estonian Genome Project Foundation was set up on March 6, 2001 to coordinate the project. The Foundation is overseen by a board consisting of nine members, six appointed by government and three by the Estonian Academy of Science.

The plan is to set up a database over the next five years containing health, genealogical and genetic information on about 1 million of Estonia's 1.4 million inhabitants. While Iceland's/deCODE's database is intended solely as a tool for research, the Estonian database is intended to function both as a research tool and as centralized resource for individual health care. (Any other use of the database is forbidden.)

The EGP Foundation touts Estonia's relatively small (and so, manageable) population, the high education level of its population, low labour costs (particularly for doctors), and well developed IT infrastructure as reasons why it makes sense to pursue the project in Estonia. It also, in contrast to Iceland and Newfoundland, highlights Estonia's genetic heterogeneity. A considerable focus is also placed on the efforts that have been made to ensure the project is ethically acceptable. (http://www.genomics.ee/genome/GeneBank.pdf)

Unlike the Icelandic database, all the material in the database is to be acquired on the basis of written, informed consent. (Those who cannot give consent cannot be donors.) Primary care physicians are to approach their patients about participating in the database. If consent is received, an extensive medical and family history of the donor is to be gathered by means of an interview with the physician, as well as from existing records the physician may have on the donor. A blood sample is also to be taken. The donor is "not entitled" to request a fee for providing these things. The medical and family history are to be entered into the database. The blood is to be sent to a central laboratory for genetic analysis. (The analysis will likely involve 60,000 - 100,000 SNPS with a portion of the sample being retained for later analysis.) The results of this analysis will then be added to

[83] Much of the information contained in this section is derived from the website of the Estonian Genome Foundation (http://www.genomics.ee).

the database. In similar fashion, the database will be updated as the donor's health develops (unless the donor forbids this). The Estonian Genome Project Foundation will be the legal owner of the information in the database and the genetic material.

The privacy of donors is to be maintained by replacing identifying information with a unique 16 character (or more) identifier. The meaning of these identifiers is to be stored on a computer available only to the Chief Processor of the database (an arm of the Estonian Genome Project Foundation). In certain circumstances, the information in the database may be relinked with personal identifiers. These circumstances are:

1. In order to destroy a sample, DNA information, health data, or data which enables decoding (24.2.1) (Notice: no mention is made here of genealogical data.)
2. In order to allow a donor, on the basis of a written request from the donor, access to his own genetic or health (but not genealogical) information (24.2.2)
3. In order to "renew, supplement or verify" health information on a donor without contacting the donor (unless the donor has forbidden this). (24.2.3)
4. In order to, on the recommendation of the Chief Processor and with the permission of the Ethics Committee, contact a donor to seek his permission to renew, supplement or verify health information on the donor. (24.2.4)
5. In order to seek a new blood sample from a donor if his blood sample is destroyed or cannot be properly analyzed (24.2.5)
6. In order to amend a donor's genealogy if the results of DNA research provide new genealogical information or contradict the current genealogy (24.2.6)
7. In order to provide a donor's doctor with health information about the gene donor. This must be done with the donor's permission except in urgent cases. (24.2.7)

Donors will also have the right to have their identifying material destroyed at any stage of the project. However, the right to destroy the genetic sample and health record itself only applies if the donor's identity is improperly revealed. (The Act, by the way, makes it illegal for anyone to reveal that a particular person is a donor without that donor's permission.)

A 5 million dollar pilot project which would gather information and samples on 10-20,000 people is supposed to have been underway as of October, 2001. The estimated cost for implementing the whole project is $100-150 million dollars (US). Financing is to be accomplished through EGeen, a company set up by the Estonian Genome Foundation. (EGeen is incorporated in Delaware, USA with a subsidiary set up in Estonia.) Initially, the EGF will be 100% owner of EGeen, but this is to be watered down later. EGeen will have exclusive commercial access to the database, but will be in the business of reselling this access. Genetics researchers and state agencies of Estonia that are involved in genetic research will be granted free access to the database. Any intellectual property created as a result of such free access will belong to the EGF.

4. Tonga

The Australian biotech company Autogen has a substantial collection of biological samples and accompanying medical/genealogical histories.[84] Autogen's website claims the company has a collection of some 44,000 samples accompanied by health records of varying detail (www.autogenlimited.com.au). What is of particular interest, however, is the agreement Autogen entered into with the Kingdom of Tonga.[85]

Tonga, a South Pacific nation made up of approximately 170 islands, has a population of 108,000, mostly of Polynesian descent. (It is the only constitutional monarchy in the South Pacific.) For some time, Autogen has been investigating obesity and diabetes there, conditions which have become increasingly common in Tonga in recent years. In late 2000, the company struck a broader agreement with the Kingdom of Tonga. Under the agreement, Autogen was to assemble a library of biological samples from Tongan citizens along with health information

[84] Autogen is a publicly traded company (AGT on the Australian Stock Exchange). One of its major shareholders – holding about 15% of ordinary shares – is the German company Merck KGaA. Autogen also "has a major strategic alliance with Lipha s.a., a wholly owned subsidiary of Merck KGaA of Darmstadt, Germany for its diabetes and obesity research." (ASX Announcement, Nov. 17, 2000)

[85] This agreement has apparently since been abandoned (Burton, 2002), although its form is still instructive.

about those citizens.[86] This database would have been used in an attempt to identify genetic causes of common diseases. (ASX Announcement, Nov. 17, 2000) Tonga would have retained ownership of all serum or DNA samples. (ASX Announcement, Nov. 17, 2000) However, Autogen would have had exclusive access to the database of samples and accompanying information. (Griggs, 2000) In return for this:

> (1) Tonga was to receive access to the health database in order to "enhance the islands [sic.] own health initiatives"
>
> (2) Autogen was to establish a research facility in Tonga for carrying out the research
>
> (3) "Any new therapeutics developed from the research will be provided free of charge to the people of Tonga"
>
> (4) Tonga would share in benefits from royalties or profits arising from new therapeutics developed as a result of the research at a rate that is in keeping with HUGO's "Statement on Benefit Sharing." This document recommends that for-profit companies "dedicate a percentage (e.g. 1% - 3%) of their annual net profit to healthcare infrastructure and/or to humanitarian efforts." (See Autogen's Ethics Policy for all four points)

Autogen stablished its own ethics policy for this project, based on the policies of Australia's National Health and Medical Research Council. The company also planned on seeking ethics approval from the International Diabetes Institute Human Ethics Committee and setting up a Human Ethics Committee of its own for the Tongan project.

Autogen's ethics policy requires that information about Tongans be collected only on the basis of fully voluntary informed consent. Such information would be coded so that it would not be personally identifiable.[87] The policy also requires that donors to the database be able to specify whether their samples and health information are to be used only for a particular study (or studies) or whether they

[86] Tongan families tend to be large and, traditionally, people have lived in extended family groups (although this has begun to change in recent years). These factors have been cited as virtues of doing this sort of research in Tonga (Barkham, 2000).

[87] The approach to encryption here appears to resemble the Estonia approach (in which it *is* possible to reidentify banked material) rather than the Icelandic model of one-way encryption.

may be kept and used in an open-ended fashion. For a more detailed presentation, the sections on "Respect for Individuals" of the Ethics Policy are reproduced below.

1. All patients and volunteers will be provided with information at their level of comprehension about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results).

2. Patients can make a voluntary choice about whether or not they wish to participate in the research without any consequences to their treatment.

3. Informed consent will be obtained from all individuals who agree to participate.

4. The welfare, rights, beliefs, perceptions, customs and cultural heritage of individuals and collectives participating in the research will be respected.

5. Participants may elect how their samples and data can be used (e.g. for research on a variety of diseases or a defined few).

6. Samples will be securely stored and will be discarded once the purpose for which the sample was collected has been achieved or at the donors request.

7. All information provided by participants about family members will be kept confidential.

8. Any information used by Autogen for the purposes of research will be encrypted and the anonymity of the individual will be ensured as the donors will not be able to be re-identified.

5. Framingham, Massachusetts

A project proposed in Framingham, Massachusetts is noteworthy because of the reasons why it was abandoned (Philipkoski, 2001b; Kolata, 2002). Since 1948, residents of Framingham have participated in a series of studies on heart-disease. This project has been very successful and is now into its third generation of research subjects. Over these generations, the study has assembled an enormous collection of materials and data. In early 2001, for instance, it was reported that the study had produced 500,000 x-rays and electrocardiograms and 5,000 blood

samples (Philipkoski, 2001a). The project had also yielded detailed medical records on more than 10,000 residents of Framingham (Craig, 2001). Recently, a for-profit company called Framingham Genomic Medicine proposed taking over the project.[88] The company proposed, among other things, to take the collection of materials just referred to and assemble it into a modern database (at present, much of this material is only on paper). Essentially, their proposal was to use the Framingham project's past and future research to develop a health database much like those discussed in the previous case studies in this paper. Access to the database would be provided at cost to academic researchers, but FGM would sell analysis of the data to private companies for profit. A portion of the company's profits would be returned to the town of Framingham through an institution called the Framingham Charitable Trust. The proposed commercialization of this project was, however, abandoned in the face of substantial opposition.

One of the main objections to the project revolved around the informed consent under which samples and records had been gathered thus far. Implementing FGM's proposal would have meant that these materials would have been used in a different way (and, in part, for different reasons) than the research subjects were informed of. Some argued that this would undermine the legitimacy of the subject's consent.

The final straw for the project stemmed from the fact that much of the Framingham Project's funding since 1948 had come from the U.S. government (approximately $40 million dollars by the end of 2000 through the National Heart, Lung and Blood Institute) (Philipkoski, 2001a). The NHLBI was reluctant to allow a publicly funded project like this to be turned into a profit making enterprise. The sticking point that led to the abandoning of FGM's plan concerned how quickly the 'enhanced' data FGM would assemble (e.g., genetic information) would be added to the already assembled database (and so, become more or less freely available to academic researchers). The NHLBI insisted on a time frame that FGM considered too short to give the enhanced data enough commercial value to justify the project. (Craig, 2001)

[88] Framingham Genomic Medicine was founded with $21 million (US) from venture capital investors and a 20% equity investment from Boston University (which has helped fund the Framingham study since 1971). Only about $3 million had been spent by the time the project was abandoned. The rest was returned to the investors.

6. Gioi (Cilento)

Approximately ten villages from a traditionally isolated area of Italy known as Cilento (approximately two hours south of Naples) are forming a 'genetic park.'[89,90] Like Newfoundland, this is a region that experiences plenty of emigration, but not much immigration. A number of the region's leaders hope the genetic park project "will bring visitors and jobs, reversing generations of poverty and emigration." (Carroll, 2000) Some speak of 'scientific tourism' as something that will halt the area's economic decline.

Researchers from the International Institute of Genetics and Biophysics in Naples plan to draw on church records covering the last approximately 500 years to construct detailed genealogies of the area's residents. In addition, they will seek permission from local residents to collect blood samples and health information about them. The goal is to assemble an extensive genetic data bank over the next couple of years for use in investigating common ailments in the area such as diabetes and cholesterol.[91] The project is initially being funded by Italy's National Research Council (CNR) but private backers are being sought for it. (Carroll, 2000) Residents will receive no direct benefit from the project, although many in the area hope for economic stimulus as a result of the project. Any payments generated by the project will go to the CNR.

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[89] 'Approximately' because one source (Carroll, 2000) claims ten villages are involved in the project while another (Follain) claims that nine villages are involved. Carroll also reports that another seventy Cilento villages will eventually join the project.

[90] The villages, which have a total population of approximately 15,000 people, are located in the Cilento nature reserve, a region that has been declared a protected area by UNESCO. (Carroll, 2000) The village that has taken the lead in getting the project going is Gioi. In particular, an endorsement of the project by Gioi's priest seems to have been crucial in getting it off the ground.

> "I told them there was this project, and that they had nothing to fear … I recommended that they start thinking about helping the researchers. I said it would bring progress and work, especially for the young." (Father Don Gugliemo Manna, quoted in Follain)

Despite this endorsement, Follain reports that there is still substantial suspicion about the project among the area's residents. At this point, it is by no means clear the project will succeed.

[91] In October of 2000, Carroll reported that the project's target was to have the database 'ready' within two years.

Appendix E – Individuals Consulted[92]

Burgess, Michael. Chair in Biomedical Ethics, Centre for Applied Ethics, University of British Columbia, Vancouver, British Columbia

Caulfield, Timothy. Canada Research Chair in Health Law and Policy, Research Director, Health Law Institute, University of Alberta, Edmonton, Alberta

Cave, Susan. Development Officer, Advanced Technology, Research and Development, Department of Industry, Trade and Rural Development, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

Clarke, Beverly. Assistant Deputy Minister, Policy and Program Services Branch, Department of Health and Community Services, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador,

Coady, Siobhan. Chief Operating Officer, Newfound Genomics Ltd., St. John's, Newfoundland and Labrador

Fernandez, Bridget. Director, Provincial Genetics Program, Health Sciences Centre, St. John's, Newfoundland and Labrador

Gold, E. Richard. BCE Chair in E-governance, Faculty of Law, McGill University, Montreal, Quebec

Greely, Henry. C. Wendell and Edith M. Carlsmith Professor, Director, Program in Law, Science, and Technology, Faculty of Law, Stanford University, Palo Alto, California

Green, Jane. Associate Professor, Medical Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador

Gulliver, Wayne. Chairman/Medical Director, Newlab Clinical Research Inc., St. John's, Newfoundland and Labrador

Hefferton, Donna. Clinical Manager, Newfound Genomics Ltd., St. John's, Newfoundland and Labrador

[92] Titles reflect position held when consulted.

Juengst, Eric. Associate Professor of Biomedical Ethics, Case Western Reserve University School of Medicine, Cleveland, Ohio.

Keel-Ryan, Juanita. Director Advanced Technology, Research and Development, Department of Industry, Trade and Rural Development, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

King, Dave. Chief Operating Officer, Genesis Group Inc., Memorial University of Newfoundland, St. John's, Newfondland and Labrador

Knoppers, Bartha Maria. Law Professor and Senior Researcher, Centre for Public Law Research, Université de Montréal, Montreal, Quebec

Laberge, Claude. Professor of Medicine and Pediatrics, Faculty of Medicine, Laval University, Quebec City, Quebec

Miller, Margaret. Research Marketing Manager, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador

Moody-Corbett, Penny. Assistant Dean for Research and Graduate Studies, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador

Pond, Morgan. Adult Policy Analyst, Policy and Program Services Branch, Department of Health and Community Services, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

Rahman, Proton. Chief Scientific Officer, Newfound Genomics Ltd., St. John's, Newfoundland and Labrador

Rolleston, Francis. Consultant, Health Canada. Ottawa, Ontario

Skanes, Verna. Interim Director, Newfoundland and Labrador Centre for Applied Health Research, St. John's, Newfoundland and Labrador

Sweeney, George, Member of the House of Assembly Carbonear-Harbour Grace, Parliamentary Secretary to the Minister of Industry, Trade and Rural Development on Information and Advanced Technologies, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

Thompson, Robert. Deputy Minister, Department of Health and Community Services, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

Wade, Brian M. Manager-Industry Development, Advanced Technology, Research and Development, Department of Industry, Trade and Rural Development, Government of Newfoundland and Labrador, St. John's, Newfoundland and Labrador

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