Biotechnology and the Health of Canadians

Canadian Biotechnology Advisory Committee

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A Report from the Canadian Biotechnology Advisory Committee

on

Biotechnology and Health Innovation: Opportunities, Challenges and Public Policy

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Message from the Chair of CBAC

The Canadian Biotechnology Advisory Committee (CBAC) prepared the report, *Biotechnology and the Health of Canadians*, as part of its ongoing examination of biotechnology and Canadian society.

In the report, we describe some of the current and emerging opportunities and challenges associated with biotechnology-based health innovation. We propose a policy framework along with a series of initiatives that would enhance Canada's capabilities and performance in research and development, regulation and commercialization, and technology assessment and uptake; and would contribute to the realization of Canada's potential as an effective and responsible leader in this important field.

Arnold Naimark

Canadian Biotechnology Advisory Committee Mandate

The Canadian Biotechnology Advisory Committee is a body of external experts established in September 1999 by the Government of Canada. CBAC provides comprehensive advice on current policy issues associated with the ethical, social, regulatory, economic, scientific, environmental and health aspects of biotechnology. It is also tasked with providing Canadians with easy-to-understand information on biotechnology issues, and opportunities for them to voice their views on these matters.

CBAC provides its advice through the Biotechnology Ministerial Coordinating Committee (BMCC), which is comprised of the federal ministers of Industry, Agriculture and Agri-food, Health, Environment, Fisheries and Oceans, Natural Resources and International Trade. CBAC's reports are available to the general public.

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- the individuals who examined our draft reports and provided valuable feedback.

Special thanks are also due to the members of CBAC who served on the BHI Steering Committee – led by its co-chairs, Mary Alton Mackey and Barry Glickman — and to all the staff of the Canadian Biotechnology Secretariat who served as project managers (Brian Colton and Richard Konchak — summer of 2003), and as policy/project officers (Marnie McCall and Stephanie Wilson). The overall guidance of the work of the Canadian Biotechnology Secretariat by Kimberly Elmslie, its Executive Director, and Roy Atkinson, former Executive Director, are greatly appreciated.

CBAC is grateful to the members of the Biotechnology Ministerial Coordinating Committee for their ongoing support.

Overview

The federal, provincial and territorial governments have a pivotal role to play in creating policies and mechanisms that guide the use of biotechnology to improve the health of Canadians. A proactive and forward-looking approach to policy development is essential in a field characterized by fast-paced science, exciting new opportunities, rising public expectations and growing demands for access to beneficial new technology, and controversies about the social and ethical implications of particular applications of biotechnology.

Realizing the promise and meeting the challenges of biotechnology-based health innovation (BHI) in the context of economic, social and political realities will create pressures in Canadian society. How we respond will be our prerogative, but ignoring the pressures for change will not make them disappear — more likely it will simply compound the costs and complexities of dealing with them later. Unless governments effectively address the policy imperatives associated with BHI, Canadians may fail to capture its benefits or may adopt innovations that are ill-suited to Canada's health care system. With proper planning and by building on the investments already made in new technological development, governments have the opportunity to make biotechnology work for all Canadians.

Biotechnology-based health innovations over the past century (from the development of vaccines and antibiotics, to organ transplantation and gene-based medicine) have contributed significantly to the remarkable improvements in the health of Canadians. Recent advances suggest that biotechnology may play an even more significant role in the future. Indeed, some predict that BHI may well induce fundamental transformation in how we organize, manage and deliver preventive, diagnostic and therapeutic services.

In *Biotechnology and the Health of Canadians,* the Canadian Biotechnology Advisory Committee (CBAC) describes the potential role of biotechnology in relation to the various factors that influence health, discusses some of the social and ethical considerations involved in the applications of biotechnology, sets out a policy framework, and recommends actions necessary to equip our systems to meet the challenges that the unfolding era of modern biotechnology will present.

The Promise of Biotechnology

The recent surge of interest in biotechnology is rooted in the rapid expansion of knowledge about the molecular basis of health and disease, and of our ability to use that knowledge in prevention, diagnosis and treatment of disease and disability.

In prevention, biotechnology plays a role in addressing both genetic and environmental influences on health through advances in screening populations for susceptibility to disease; in reducing exposure to noxious agents in the environment and enhancing the body's ability to block or ameliorate the effect of such agents; in the application of genomics and proteomics to the development of vaccines and other preventive strategies against infectious agents long-associated with human disease and those

emerging in recent years (e.g., HIV, the SARS virus and West Nile Virus); and in the application of pharmacogenomics to the development of anti-microbials for preventive use in special circumstances.

In diagnosis, advances in biotechnology broaden the array of sensitive and specific tests that speed diagnosis and permit greater individualization of treatment. In the case of emerging infectious diseases, new techniques to detect the presence of infectious agents will be applied both to persons who are symptomatic and to populations at risk.

In treatment, biotechnology will play a significant and, in some cases, pre-eminent role through the application of genomics and proteomics to therapeutic drug development, the development of immunological approaches to the treatment of cancer, the use of stem cells to repopulate diseased organs with normally functioning tissue-specific cells, tissue engineering and xenotransplantation to increase the supply of tissues to repair or replace defective anatomic structures, and gene therapy to correct primary defects within the genetic makeup of individuals.

Looking ahead one can reasonably anticipate that, as in the past, many BHIs will result from the application of advances in chemistry, physics, engineering, and computational and information sciences to biological systems. For example, the ability to design devices that operate at the molecular level or new materials through advances in nanotechnology could well provide powerful new tools for clinical application.

THE CHALLENGES OF BHI

The challenges in applying biotechnology to human health include the need to manage risks and prevent or ameliorate potential harms; to deal with the social and ethical implications of the use of technologies and the personal information resulting from that use; and to enhance access to an expanded array of beneficial BHIs.

There are also challenges related to both the process of policy-making and the implementation of strategies for governing and fostering the development and uses of BHI, including: the limited capacity of our systems and personnel to cope with the rapid pace of new technology development; the multiplicity of jurisdictions and stakeholders involved; the diverse levels of knowledge, interest and engagement within the body politic; the constraining effects of international obligations; and the complexity of scientific and ideological issues in debates about biotechnology.

POLICIES FOR BHI

The primary goal of public policy related to BHI is to improve health. This can be achieved by:

- optimizing access to the health and quality of life benefits of BHI in a cost-effective and efficient way;

- addressing and managing the potential challenges, risks and hazards that may be associated with BHI;
- ensuring the responsible and ethical development and use of biotechnology in the health care system; and
- building and sustaining the scientific and management capacity to generate, adapt and assimilate beneficial BHI.

As with public policy in general, specific policies for BHI should reflect the value that Canadians place on justice and equity, accountability and engagement, autonomy, beneficence, respect for diversity, objectivity, caution and dignity.

Our analysis has identified four sectors in which policy initiatives are required to expand capacities and remove barriers to optimum performance: research and development, regulation and commercialization, technology assessment, and health system adoption.
In proposing these initiatives, we are mindful that the use of biotechnology is but one of the ways to improve the health of Canadians. Other factors in the social and physical environments that have a powerful influence on health are also in need of further policy development.

Research and Development (Recommendations 1-3)

A vibrant and productive research enterprise is an essential underpinning of Canada's health system. Our researchers create new knowledge and tools for application in improving the health of Canadians; provide the scientific and technical expertise necessary to understand and adapt discoveries made elsewhere; and provide the advanced training of scientists, technologists and professionals required by health care institutions and agencies, and by the private sector.

In the past decade, there has been a significant increase in health research investment through the federal granting councils, research laboratories and institutes, and by various provincial agencies. Canada's per capita public funding of research in certain areas of the life sciences (e.g., genomics) compares favorably with that in other western countries. However, Canada's international position in biotechnology research cannot be taken for granted, given the priority that other industrialized nations have placed on increasing investment in this area. We call for the development of an integrated and coherent strategy to guide sustained growth in Canada's investment in health research generally, and in biotechnological innovation in particular.

The strategy should address the scale and modes of research investment required, and the need for collaboration among biological scientists, social scientists and humanists in advancing knowledge about the interaction of scientific and social dimensions of BHI. It should achieve an appropriate balance of investment between fundamental and applied research, and between investment in research involving the private sector and research on important topics that do not involve participation by the private sector.

Among the concerns raised by modern biotechnology, the ethical issues involved in the research process *per se* are of special importance. The privacy concerns surrounding the storage and use of genetic information, the implications of advances in pharmacogenomics with respect to the design and frequency of clinical trials, and the evolving concept of what constitutes truly informed consent,

are all factors that will impose additional pressures on the already strained capacity of research ethics boards in universities, hospitals and research institutes. We regard the further development of common standards, transparent methods, national and international harmonization, and public involvement as critical for maintaining public trust and confidence in the health research enterprise. Accordingly, we call for the establishment of a body both to set standards and to accredit organizations and institutions with responsibilities for research ethics boards, and for population health databases and banks of biological specimens used for research purposes.

Regulation and Commercialization (Recommendations 4 and 5)

Commercialization by the private sector is the predominant avenue through which new technology is made available to the health system. Bringing biotechnology products to market is a complex, expensive and time-consuming process that requires efficient and effective mechanisms of regulation and investment in order to facilitate Canada's competitiveness in a growing global marketplace and to provide Canadians with timely access to beneficial products.

Regulation is one of the most important and pervasive responsibilities of government. Confidence in the regulatory system on the part of both producers and consumers requires continuing improvement in how the regulatory system functions. The growing number and complexity of biotechnology products that require regulatory evaluation is placing intense pressure on federal regulatory bodies. Moreover, the development of therapeutic products targeting specific genetically defined groups may require new regulatory models. We call upon Health Canada to ensure that the regulatory regime it oversees is comprehensive (i.e., deals effectively with technologies that cross boundaries between departments or product types), efficient (i.e., meets the highest standards of timeliness in making and communicating regulatory decisions), responsive (incorporates leading edge scientific developments into its operations), and transparent (develops and publicizes standard operating procedures).

There are a variety of challenges to meet in order to increase the successful commercialization of BHIs in Canada. These include the lack of early stage capital for emerging enterprises; the shortage of bio-manufacturing capacity in Canada; the underutilization of public institutions for product testing; inadequate linkages among institutions and businesses and among disciplines, resulting in insufficient development of shared platforms for commercialization; and the lack of alignment of Canada's patent system with its major trading partners. Several initiatives to strengthen the commercialization of health-related biotechnology have been proposed in recent years, but relatively little progress has been made in implementing them. We share the view that in order to purposefully pursue such initiatives, and others that emerge from future technological advances, Canada requires a clearly articulated, comprehensive, coherent and integrated national health innovation and commercialization strategy that includes a specific focus on BHI.

Technology Assessment and Appraisal (Recommendations 6 and 7)

Canada's current health technology assessment (HTA) systems are reasonably well developed in a qualitative sense. However, they are more fragmented, receive significantly less funding on a per capita basis than HTA systems in certain other jurisdictions, and focus on a relatively narrow range of products and processes. The rise of genomic medicine and personalized approaches to treatment are

expected to fuel intensified public and provider demand for access to new technologies. As a result, HTA systems will be challenged to cope with an increased load, to develop and apply the expertise required to evaluate complex new products and processes, and to be rigorous in determining priorities for assessment within the available capacity.

Sound decision-making about the adoption of new technologies by the health system requires more than traditional HTA (evaluation of the objective evidence about the efficacy of health technology and its use); it also requires what, in the U.K., has been called technology appraisal (judgement about wider issues of priority, equity, fiscal capacity, ethical acceptability, etc.), and which may be better termed "analysis of potential health system impacts and implications." By comparison with traditional HTA, this broader approach to technology assessment is relatively poorly developed in Canada.

The Federal, Provincial and Territorial Advisory Committee on Information and Emerging Technologies has been tasked with developing a comprehensive strategy for HTA in Canada. We recommend that such a strategy include extending the reach of HTA by:

- broadening the array of products and processes subjected to assessment;
- establishing a national mechanism for complementing traditional HTA with evaluation of the social, ethical, economic and health system impacts of BHIs;
- developing rapid response mechanisms to deal with emergent demands;
- establishing mechanisms for conditional approval, in special circumstances, of BHIs where complete assessments and appraisal cannot be conducted in a timely fashion, and for assessment of BHIs after they have been introduced and used in the community; and
- incorporating a communication strategy that makes the processes and results of assessments readily available to health professionals, system managers and the public.

The effectiveness of HTA depends on its results being recognized and used by decision-makers in the health system. So far, HTA has had limited impact on resource allocations in part because of inadequate linkages between HTA agencies and decision-makers. A comprehensive strategy for HTA in Canada must also include measures to enhance its impact by:

- developing mechanisms that promote linkage and interaction between experts in HTA to experts and decision-makers in the organization, management and delivery of health services;
- establishing incentives and removing or ameliorating impediments to applying HTA in decision-making;
- establishing the tools required by decision-makers to model the impacts of introducing BHIs on institutions or the health care system generally; and
- developing and disseminating educational materials on HTA that are suitably customized for professionals, system managers and the public respectively.

Health System Adoption of BHI (Recommendation 8)

The adoption of BHIs by the health system is a complex process, strongly influenced by the internal dynamics of health care systems on the one hand, and health practitioners and consumers on the other. Health care system managers face difficult choices in regard to the adoption and funding of BHIs because of their technical complexity and "disruptive" effects (on costs, organizational structure, professional roles) and, in some instances, because of their ethical and social implications.

Canada's health care systems do not have a systematic approach to dealing with these issues. Practices vary among provinces, regional health care systems, hospitals, and health care practitioners, in part because there has been relatively little systematic study on how health technology is introduced and on the identification of best practices. The sustainability of this *ad hoc* approach is questionable in the face of increasing technological "push" and consumer demand. The challenge of making room for new technologies is compounded by impediments to discontinuing older, less effective technologies or technologies that have been shown to be ineffective, and by difficulties in estimating indirect costs and benefits. The systematic engagement of consumers in the process of health system adoption of BHI is generally regarded as essential, but has not been pursued effectively in Canada.

There is clearly a need to learn a lot more about the adoption of BHIs, and we therefore call for a body, sponsored by or involving the federal, provincial and territorial governments and other stakeholders (such as the newly formed Health Council of Canada), to develop the foundation for improving Canada's ability to adopt beneficial BHIs by:

- identifying barriers to health system adoption of BHIs and making recommendations to remove or ameliorate them;
- promulgating goals, strategies and guidelines for implementing best practices for citizen engagement in the process of adopting BHIs; and
- giving consideration to including such practices among the attributes evaluated in institutional performance reviews and/or in accrediting health care institutions.

FOUNDATIONS OF SUCCESS

As we considered the readiness of our systems for BHIs, it became clear that in addition to specific initiatives related to research and development, regulation and commercialization, health technology assessment and health system adoption, successful policy-making must be enabled by general strategies that:

- foster the collaboration among jurisdictions, sectors and disciplines necessary to realize the potential of biotechnology to contribute to improving the health of Canadians;
- respond to the urgent need to build and sustain the range and depth of scientific and managerial expertise required to generate, adopt and assimilate beneficial BHIs and to ensure their responsible use;
- facilitate public participation at appropriate points in the development and adoption of BHIs including fostering public education — in part through the development and communication of reliable, clear information about BHIs;
- facilitate special education of patients and providers about the clinical application of BHIs; and
- support evidence-based decision-making by ensuring that the information tools required are developed and maintained.

CONCLUDING OBSERVATIONS

The development and beneficial application of health-related biotechnology must be a central element in the articulation and implementation of Canada's overall innovation strategy. We believe that implementation of the recommendations in this report will assist the federal government and its provincial and territorial partners in addressing the development of biotechnology, and will complement the efforts of other bodies that are considering the development of policies on health-related aspects of biotechnology. Realizing the benefits of advances in biotechnology in a socially responsible manner is likely to entail significant transformations of important institutions in Canadian society — transformations that will be influenced by the need to strike a sustainable balance among competing objectives and social values.

RECOMMENDATIONS

Research and Development

1. In order to capitalize on investments already made and to ensure continued progress in enhancing Canada's research talent, infrastructure and capacity to conduct leading edge research related to biotechnology-based health innovations, we recommend that the Government of Canada, through an interdepartmental/interagency mechanism (facilitated by the National Science Advisor), develop an integrated and coherent strategy to guide increased and sustained investment in research and development in this area.

   This strategy should:
   - Include a commitment to sustain and enhance programs of basic and applied research related to BHI through the development of a clear and specific plan for long-term growth of investment in this area, including research required to support regulatory risk assessment.
   - Without limiting the foregoing, ensure that special programs, such as those currently implemented by the Canada Foundation for Innovation, Genome Canada, the Canada Research Chairs, Networks of Centres of Excellence, and the Canadian Health Services Research Foundation, are sustained over the long term by appropriate means. These programs should take into account the evolving imperative for support of large-scale interdisciplinary research teams and networks.
   - Strengthen Canada's research endeavors on the social dimensions of BHI by fostering the collaboration among biological scientists, social scientists and humanists that is needed to address important questions related to processes of innovation, regulation, commercialization, technology assessment and uptake, social and physical environmental impacts, public engagement strategies, and the development of tools to manage and adapt to change at the system and institutional levels.

2. In order to ensure that long-term growth in investment in research and development is guided in such a way as to maintain an appropriately balanced approach to funding of research related to BHI, and in view of concerns about the impact of private sector influence on publicly funded

research, we recommend that the National Science Advisor to the Prime Minister, in consultation with funding agencies and academic bodies:

- Assess the extent to which federal programs that support research in public (not-for-profit) institutions, which involve or require co-sponsorship by the private sector, have affected the scale of and balance between fundamental and applied research.
- In the case of applied research, assess the scale and balance of funding between research on topics in which there is an identified commercial interest and those topics of scientific importance in which there is little or no commercial interest.
- Make recommendations to address any impediments to achieving an appropriate balance.

3. In order to ensure the ethical and safe development and use of biotechnology in the health care sector, we recommend that the departments of Health and Industry, in collaboration with counterparts in the provinces and territories, and in consultation with the National Council on Ethics in Human Research and stakeholder groups, establish or facilitate the establishment of a body or mechanism both to set standards and to accredit organizations and institutions with responsibilities for research ethics boards, and for population health databases and banks of biological specimens used for research purposes. Satisfactory compliance with standards should be an eligibility criterion for federal research funding**.**

   The body should:

   - Operate at arms-length from research funding agencies and institutions.
   - Include representation of the general public.
   - Establish standards with respect to the ethical conduct of research that strike a reasonable balance between serving the interests and needs of Canadians and facilitating research that will improve the health of Canadians.
   - Serve a developmental role by fostering collaboration among agencies and institutions in meeting the education and training needs associated with the foregoing regulatory functions, and in developing methods to improve efficiency and reduce the burden of meeting regulatory requirements related to research (e.g., by developing standardized common templates for regulatory submissions; by encouraging reciprocal recognition of review processes that meet national standards).
   - Work cooperatively with agencies such as the Canadian Council on Animal Care (CCAC) to ensure that best practices are applied in the humane use of animals (including genetically modified animals) for biotechnology-related research.

Regulation and Commercialization

4. In order to achieve effective and efficient evaluation, and the timely introduction of beneficial BHIs in Canada, we recommend that Health Canada ensure it has a comprehensive, responsive and transparent regulatory regime that:

   - Through exemplary governance, organization and operational arrangements, coordinates the regulatory evaluation and approval mechanisms applicable to biotechnological products and processes, and effectively addresses the regulatory challenges presented by technologies that cross boundaries between departmental jurisdictions (“molecular pharming”) or between categories of innovation (combinations of drugs and devices).

- Achieves the highest standard of performance with respect to efficiency, timeliness and effectiveness in evaluation, and in making and communicating decisions.
- Is responsive in incorporating new scientific and technical knowledge into its evaluation and decision-making criteria and processes. Works with counterparts in other countries, directly or through appropriate international bodies, to develop and encourage the adoption of best practices; share risk assessments; and standardize application and information requirements to make applications in multiple jurisdictions easier for applicants and to streamline processes for products previously approved elsewhere, in order to reduce delays in access for Canadians.
- Systematically reviews — including by international expert panels — the capacity and expertise of regulatory agencies, particularly their in-house capacity, with a view to establishing appropriate strategies and tools to respond to the needs and opportunities presented by scientific and technical advances.
- Develops and publishes standard operating procedures in order to increase public understanding of and enhance confidence in the regulatory system.

5. In order to optimize the return on investment in publicly funded research and development, we recommend that Industry Canada, in collaboration with the federal research funding agencies, develop a coherent, integrated commercialization strategy that:
   - Clarifies the legal and regulatory framework for ownership and licensing of intellectual property to strike an appropriate balance between the interests of innovators, developers and the public seeking access to the benefits of BHI.
   - Facilitates the financing of commercialization efforts by small- and medium-sized enterprises — for example, by refining the taxation regime so that it is more responsive to the needs of small enterprises (e.g., through the Scientific Research and Experimental Development tax credit provisions).
   - Promotes the development of greater access to early stage capital by such means as mergers of small companies that result in economies of scale; expanded scientific and managerial capacity; bundling of product lines to attract investment; and the development, in partnership with the private sector, of special investment funds that focus on early stage capital financing needs.
   - Creates commercialization platforms and networks to enhance the commercialization efforts of universities, research hospitals and institutes.
   - Identifies instruments (financial, legal and commercial) that would allow the private sector to benefit from producing technologies that more clearly contribute to improved health within existing levels of health expenditures.
   - Nurtures the capacity of the private sector to develop and deliver products that are valued and purchased by the health care sector, by fostering linkages between entrepreneurs in small- and medium-sized firms with experts in the health sector who can identify areas of need and opportunity.

Technology Assessment and Appraisal

6. In order to ensure that HTA is developed sufficiently to provide the comprehensive evaluations required for decision-making on the adoption of beneficial BHIs, we recommend that the federal, provincial and territorial governments, in the context of their current efforts to develop and implement a comprehensive Canada-wide strategy on HTA, put a priority on the following key actions:
   - Extend the existing models of Canada-wide HTA (e.g., Common Drug Review) to assessing a wider array of biotechnology-based health innovations (products, processes and tools).
   - Complement HTA with an appraisal of broader social, ethical, economic and health system impact factors by a body composed of experts equipped to assess such factors (e.g., a National Biotechnology Appraisal Committee linked to the Health Council of Canada).
   - Establish a rapid response mechanism to provide conditional assessments that meet urgent decision needs and that incorporate commitments to follow-on full assessments.
   - Mount coordinated field trials on a demonstration basis when there is insufficient HTA evidence available to determine the direct and indirect impacts of adopting a biotechnology-based health innovation.
   - Develop comprehensive mechanisms for assessing the efficacy, safety, and health system impacts of innovations after they have been introduced in the community, and for supporting research on methods to facilitate such assessments.
   - Establish programs to maintain the capacity and expertise of the HTA system to respond to emerging needs and opportunities (e.g., effective horizon scanning). Promote capacity-sharing domestically and internationally to increase quality and efficiency, and to reduce cost burdens (e.g., inter-regional or international agreements might be reached whereby specific regions or countries specialize in assessing particular types of technology).
   - Develop a comprehensive communication strategy that provides balanced and objective information about assessment results (both positive and negative) to professionals, system managers and the public.

7. In order to support the adoption of beneficial BHIs by health care systems, we recommend that the federal, provincial and territorial governments commit themselves to the collaborative development and implementation of a comprehensive Canada-wide system that:
   - Links experts in technology assessment and appraisal to experts and decision-makers involved in the organization, management and delivery of health services, and to the public — for example, through a network of researchers, HTA practitioners, knowledge brokers, health care practitioners, and decision-makers engaged in setting priorities, synthesizing results, gathering data from national and international sources, and interpreting international findings in the Canadian context.
   - Establishes incentives and removes or ameliorates impediments to applying technology assessment and appraisal in decision-making.
   - Establishes standardized information systems and linked databases required to model the impacts of introducing BHIs on institutions or the health care system.
   - Develops and disseminates educational materials related to technology assessment and appraisal, which are suitably customized for professionals, system managers and the public.

- Makes HTA results public in plain language documents, so that the public can meaningfully participate in the uptake process and make informed decisions about BHIs for personal purposes.

Health System Adoption

8. We recommend that a body, sponsored by or involving the federal, provincial and territorial governments and other stakeholders (such as the newly formed Health Council of Canada), contribute to improvements in Canada's ability to adopt beneficial BHIs by:
   - Sponsoring studies to systematically identify barriers to the adoption of BHIs by the health system, and make recommendations to remove or ameliorate the barriers.
   - Addressing the challenge of how the health care system can deal with the adoption of BHIs for which assessments and appraisals are incomplete or unavailable — including by determining the desirability and feasibility of establishing mechanisms to provide conditional approval for adoption.
   - Identifying best practices in Canada and abroad for public (consumer) engagement in all stages of technology appraisal and assessment, and promulgating goals, strategies and guidelines to implement them on a Canada-wide basis. Specific consideration should be given to including the use of appropriate engagement practices among the attributes evaluated in institutional performance reviews and/or in accrediting health care institutions.

Introduction

Canadians have enjoyed remarkable improvements in their health status over the past century and place a high value on the contribution of health to general well-being. However, there are still many challenges to overcome by finding new and better ways to promote health, and to prevent, detect and treat disease and disability. Whether individuals are healthy or not is influenced by their biological and behavioral responses to the interaction of environmental (physical and social) factors and genetic endowment. This means that health innovations must be sought that address both individual and societal factors involved in determining health status.[2]

Although the importance of genes in health and disease, and the applications of genetic technologies to health care, were well described over a decade ago, few had predicted how rapidly advances in biological science would result in new and powerful tools for application in the prevention, detection and treatment of disease and disability — tools that may not only contribute to improving the health of Canadians but also help to reduce inequities in health status between the developed and developing world.[3] [4] Some contend that these new biotechnology tools will lead to health innovations that are so extensive and pervasive in their application, or so powerful, that they will change the fundamental nature and direction of the health system and/or professional practice — in other words that they are "transformative."[5] A report prepared by Ontario in 2002 for the provincial premiers stated that "genetic technologies hold out the potential to fundamentally redefine medicine within the lifetime of many Canadians."[6] The European Union has dedicated almost $4 billion for research in this area.[7]

Whether or not one accepts such declarations as a reasonable premise to guide future policy development, the potential applications of new knowledge such as the unraveling of the function of genes, or how variations in DNA sequences cause people to have differing susceptibility to disease and treatment, will have a significant influence on health and health care. At the same time, some applications of biotechnology may pose potential risks to humans and the environment, or challenge some of the core values of Canadian society, or both. Canada needs to be prepared with policies, systems and structures that will facilitate the adoption of advances in biotechnology in a socially responsible way — a way that captures benefits without taking unacceptable risks and that reflects commonly shared ethical and social values.

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2 For the purposes of this document, a health innovation is deemed to occur when a new or improved product, service or method is introduced and used in the course of providing health care to individuals, or in the course of organizing, managing and delivering health services from a population/public health perspective.

3 Science Council of Canada, *Report 42: Genetics in Canadian Health Care* (Ottawa: 1991).

4 P. Singer et al., *Top 10 Biotechnologies for Improving Health in Developing Countries* (Toronto: University of Toronto Joint Centre for Bioethics, 2003).

5 Some health innovations may be based on biotechnology inventions but a biotechnology invention is not in itself a health innovation until it is introduced and applied.

6 Government of Ontario, Ministry of Health and Long Term Care*, Genetics, Testing and Gene Patenting: Charting New Territory in Health Care, Report to the Provinces and Territories* (Toronto: January 2002).

7 "Life Sciences, Genomics and Biotechnology for Health" is one of the programmatic themes of the Sixth Framework Program of the European Union. For the period 2002-2006, 2514 million € (almost $4 billion) has been budgeted, which is divided roughly equally between applications of advanced genomics for health and combatting major diseases: www.cordis.lu/fp6/lifescihealth.htm. (Accessed: September 29, 2004.)

Under the overarching theme of *Biotechnology in Canadian Society,* CBAC has assessed the role of biotechnology in health innovation and the implications of recent and prospective developments for Canadian public policy. This report provides an overview of the role or potential role of biotechnology in relation to the various factors that influence health; discusses some of the social and ethical considerations involved in the application of biotechnology; describes a framework for public policy related to biotechnology; and uses the framework to make a series of recommendations to the federal government that are specifically related to biotechnology-based health innovation.[8]

[8] The term federal government is used in this report to mean the departments of the federal government and agencies established by the federal government.

Part 1
The Promise of Biotechnology – Based Health Innovation (BHI)

Biotechnology in a formal sense may be defined as a body of technical knowledge about living organisms and their constituent parts. Applied biotechnology is the use of this knowledge to serve some scientific, social or economic purpose. Some kinds of applied biotechnology date from antiquity (the use of organisms in fermentation) and others appeared much later (the development of vaccines and antibiotics). Biotechnological applications are now pervasive in the industrialized nations. They play an important and increasingly prominent role in agriculture and food processing, forestry, fisheries, the chemical and textile industries, and environmental management, and are especially prominent in industries related to human and animal health.

The most recent surge of interest in biotechnology has its roots in the biological revolution marked by the emergence of our ability to study phenomena at the molecular level.[9] In 1944, it was demonstrated that the DNA molecule carried genetic information, and in 1953 Watson and Crick announced that they had determined its structure. These seminal events, together with major advances in instrumentation, launched a tidal wave of scientific and technical progress that mark the modern era of biotechnology.

In 1972, a method to clone DNA was developed and, shortly afterward, this "recombinant DNA" technique was used to produce human insulin. This innovation prevented many (sometimes fatal) allergic reactions to animal insulin. In 1983, the location of a disease-causing gene was determined for the first time (the gene for Huntington's disease on chromosome 4).[10] Since then, scientists have decoded the sequence of bases in the DNA of humans and several animal species, established the function of more than 1,500 genes, and determined that the human genome contains some 30,000-40,000 genes. The rapid pace of these advances was made possible by the development of automated techniques of DNA analysis, facilitated by the huge increases in computing power and the development of methods of computational and statistical analysis now known as "bioinformatics."

Research on the molecular basis of disease is leading to new ways to prevent, predict, identify and treat many disorders, ranging from those with relatively straightforward causation to chronic diseases with complex causes. These applications include the manipulation of cells, tissues, organs or whole organisms (e.g., assisted human reproduction, transplantation of organs and cells, and cloning), and the analysis and modification of molecules such as DNA and proteins found exclusively in living

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[9] Many of the techniques and tools used in biology are direct applications of or are derived from the basic tools and techniques of physics, chemistry, mathematics, engineering and information sciences.

[10] J.F. Gusella et al., "A polymorphic DNA marker genetically linked to Huntington's disease," *Nature* 36 (November 17-23, 1983), pp. 234-238.

organisms (e.g., identification of genes involved in predisposition to disease, modification of the genetic makeup of plants and animals, and production of diagnostic tools and novel compounds such as new therapeutic agents).

Biotechnology also offers great promise for improving health in less developed countries by addressing problems such as infectious disease, malnutrition and environmental degradation.[11] Canada has the potential to be both a leader in setting an international research agenda that supports developing countries and a strong participant in its implementation.

In the following sections of this chapter, we illustrate how recent advances in biotechnology have led, or are likely to lead, to innovations in the protection of public health and in the prevention, diagnosis and treatment of disease and disability.

1.1 PREVENTION

Biotechnology plays a significant role in addressing both genetic and environmental influences on health. This includes the use of techniques both to block the effects of noxious agents in the environment (including highly infectious and lethal microbes used as weapons of warfare or terrorism) by developing vaccines to prevent infection, and to decrease such exposure by identifying and removing noxious agents from air, water and food. Modern biotechnology also provides the tools needed to characterize and combat biological threats to health and safety from spontaneously arising infections (e.g., SARS) or from the malevolent use of biological agents as weapons of war or terrorism.[12]

The role of biotechnology in relation to the social determinants of health is, for now at least, largely indirect. By expanding our ability to characterize genetic susceptibility to disease we may be better able to identify populations at risk and to take steps to intervene and ameliorate aggravating factors in the social environment.[13] Even more indirectly, a vibrant biotechnology industry, by contributing to economic growth and with appropriate public policies in place, can influence health through an improved standard of living and greater affordability of expanded public health services.

Screening Populations for Susceptibility to Disease

Advances in biotechnology and bioinformatics have some of their most important applications in epidemiology (the study of the distribution and determinants of disease) and in assessments of the health status of populations. New techniques are anticipated for faster and easier detection and monitoring of a broad array of genetic markers and other characteristics in large population samples.

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[11] Singer, *Top 10 Biotechnologies*. [See note 4.]

[12] New biotechnological techniques are dramatically increasing the speed of product development. For example, a Canadian team announced the sequence of the SARS viral genome on April 11, 2003. On July 15, 2003, Roche released a test for the SARS virus to research laboratories (the shortest ever development time for a research test at Roche). On August 20, 2003, Abbott Laboratories and a German company released a test for SARS for use with patients.

[13] Possibilities for direct biotechnology intervention may emerge from advances in our understanding about the mechanisms by which social factors influence biological responses — for example, how early childhood experience influences the development of the brain and biological response systems to produce long-term effects on behaviour and health status.

In Iceland, a massive database is being created to link the genetic material of all 270,000 inhabitants with their medical records.[14] In Quebec, a proposed population genomics project, CARTaGENE, led by Dr. Claude Laberge, Director of the Quebec Medical Genetics Network, will assess genomic variation by collecting genetic information on 50,000 people representing 1.5% of the Quebec population.[15] The Lifelong Health Initiative proposed by the Canadian Institutes of Health Research[16] plans to collect data to assess the interaction of genetic and environmental exposures on developmental and aging processes.

DATABASES OF GENETIC INFORMATION [17]

PROPOSED	PARTICIPANTS
Quebec CARTaGENE	50,000
Lifelong Health Initiative (Canada)	30,000
Icelandic Health Sector Database	280,000
Estonian Genome Project	1,000,000
UK Biobank (Britain)	500,000
Marshfield Personalized Medicine (U.S.)	40,000
National Children's Study (U.S.)	100,000
Latvian Genome Database	60,000
EXISTING	
Västerbotten, Sweden	80,000
Mayo Clinic (U.S.)	100,000
EPIC (Europe)	500,000
Nurses' Health Study (U.S.)	115,000
American Cancer Society (CPS-II)	180,000
CDC NHANES III (U.S.)	7,300

[14] L. Sheremeta, *Population Biobanking in Canada: Ethical, Legal and Social Issues* (prepared for the Canadian Biotechnology Advisory Committee, September 2003).

[15] CARTaGENE Quebec: www.cartagene.qc.ca. (Accessed: October 25, 2004.)

[16] Canadian Institutes of Health Research, "The Canadian Lifelong Health Initiative (CLHI) includes two study components — the Canadian Birth Cohort Study and the Canadian Longitudinal Study on Aging. The CLHI will enable large, multi-centered longitudinal cohort studies of Canadians to analyze the role and interaction of different genetic and environmental exposures involved in developmental and aging processes over the life course, the multifactorial causes and evolution of common diseases, and the utilization of health care services." See: www.cihr-irsc.gc.ca/e/strategic/18542.shtml. (Accessed: September 5, 2004.)

[17] Adapted from: J. Kaiser, "Population Databases Boom, from Iceland to the U.S.," *Science* 298 (2002), p. 1158.

Preventing Infection

Vaccines

Vaccines play an important role in preventing illness and death from infectious disease. Smallpox has been eradicated, polio is a distant memory (at least in developed countries), and most serious childhood infections have been significantly reduced. Even those who choose not to be vaccinated are protected through "herd immunity" whereby the immunized majority prevents the spread of disease outbreaks. In the near future, we can realistically expect to see an increase in the number of diseases against which vaccines have been developed, changes in how potential vaccines are identified, and new methods to produce and administer vaccines.

It is now possible to search the genome of an infectious agent to identify antigens that may stimulate an antibody response ("vaccine candidates"), and to analyze the results of injecting vaccine candidates into mice in order to quickly select the most promising antigens to test in humans. Vaccines currently being tested in humans include those against tuberculosis, malaria and sexually transmitted diseases, including chlamydia, HIV and human papilloma virus (the cause of cervical cancer).

New methods of producing vaccines are under development that will make vaccines available more quickly and economically by, for example, using bacteria, special strains of yeast, animals and plants that have been genetically modified to produce the antigens required.[18]

Currently available vaccines require refrigeration and are mainly given by injection. However, work is underway to formulate vaccines so that they have an extended shelf life, can be stored and transported without the requirement for constant refrigeration, and can be taken by mouth or simply applied to the skin. These features are particularly advantageous in countries where facilities for transport and cold storage are limited, and where the use of non-sterile needles can lead to the spread of hepatitis and HIV.

Controlling Vectors of Infectious Disease

In 2001 malaria killed 1.1 million people worldwide. One of the approaches being pursued to prevent the spread of malaria involves modifying the genetic structure of the *Anopheles* mosquito so that the malaria parasite cannot live within the mosquito's body.[19] Once this has been accomplished, the plan is to release the genetically modified mosquito into the wild.[20]

Environmental Protection and Food Safety

Biotechnology-based strategies can be used to remedy the effects of environmental pollution ("bioremediation").[21] Genetically engineered or naturally adapted bacteria can remove or detoxify

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[18] The process of modifying plants and animals to produce novel molecules is referred to as "molecular farming," or when the novel molecules are produced for therapeutic purposes as "molecular pharming."

[19] M. Enserink, "Two New Steps Toward a Better Mosquito," *Science* 293 (September 28, 2001), pp. 2370–71.

[20] See generally: *Bugs in the System? Issues in the Science and Regulation of Modified Insects* (Washington, D.C.: Pew Initiative on Food and Biotechnology, 2004).

[21] Iogen, an Ottawa company, has developed an enzyme, BioBrite, which breaks down the cellulose in wood fibres. Pulp and paper companies using BioBrite can produce wood products more efficiently. They also use less chlorine during

both organic waste and heavy metal contamination (e.g., pesticides, PCBs, arsenic, mercury and radioactive uranium). The number of pollutants amenable to bioremediation is steadily growing.

Genetically modified plants can break down organic waste and extract, and store toxic heavy metals in their leaves. Harvesting the plant rids the area of the pollutant. Some of the heavy metals can even be extracted from the plants and recycled. Genetically modified bacteria or animal cells can be used as biosensors to detect the "bio-available portion" of contaminants — the component that causes the damage to living organisms.[22] [23]

Techniques have been developed to rapidly detect food contamination by *E. coli* and other pathogens, using genetic probes to identify their unique DNA sequences.[24] Intensive research is underway to reduce the susceptibility of food animals to diseases such as BSE, thereby improving the health of the animals and reducing the possibility of transmission to humans.

Nutrition

Genetic engineering is increasingly being used to produce foods with enhanced nutritional value either by modifying the concentration of nutrients that are normally present, or by introducing nutrients that are not normally present in plants and animals. Research and development in this field has almost exclusively involved genetic modification of plants, although some work is underway on genetic modification of animals to produce nutritionally enhanced food.

1.2 DIAGNOSIS

Advances in biotechnology have produced a number of sensitive and specific tests that speed diagnosis, enhance patient response to treatment, and reduce the deleterious effects of delays in diagnosis. The latter include anxiety, unrelieved suffering, possible worsening of the underlying disease, and added costs to individuals and the health care system.

Testing for Infectious Disease

Traditional methods for identifying infectious agents can take up to 48 hours or more. In recent years, tests using antibodies (which bind to the surface of infectious agents that are present in body fluids) or

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manufacturing, which significantly reduces the production of toxic dioxins associated with pulp and paper production. See: www.iogen.ca/4100.html. (Accessed: September 5, 2004.)

22 The gene coding for luciferase, an enzyme involved in producing the glow of fireflies, can be incorporated into receptors for specific chemicals such as dioxin and estrogen in cells. When these cells are exposed to the chemical, they emit light that can be easily quantified as a measure of the amount and location of the chemical in the environment. Biodetection Systems: www.biodetectionsystems.com. (Accessed: September 6, 2004.)

23 Similarly, it is possible to create microorganisms that emit a bright fluorescence when they feed on explosive compounds. The movements of these bacteria can be monitored using sensitive photo detection equipment, thereby assisting in the detection of dangerous explosives (e.g., in landmines). F. Bolin, "Leveling land mines with biotechnology," *Natural Biotechnology* 17 (8) (August 1999), p. 732.

24 Warnex Ltd.: www.warnex.ca. (Accessed: September 6, 2004.)

antigens (which bind to antibodies circulating in an infected person's blood) have been developed in which the result is available within an hour, so that treatment can be initiated immediately. Some of these tests can be done at the bedside using a dipstick impregnated with antibodies that changes colour in the presence of the infectious agent.

More complex tests using DNA analysis allow the rapid detection of specific strains of infectious agents and the identification of those that are resistant to certain antibiotics.[25] Tests are also available for chlamydia, HIV, gonorrhea, pneumonia and herpes, and others will soon be on the market. Tests that allow rapid detection of the presence of infectious agents provide critical information for physicians who have to decide quickly which antibiotic to use. For example, Group B streptococcus infection is responsible for severe infections in neonates, and it is crucial to determine rapidly if the mother is carrying the bacterium at the time of delivery.

Genetic Testing

Sixty percent of Canadians will, in their lifetime, suffer from a disease with a genetic component.[26] Early detection of an individual's strong predisposition to developing a disease provides the opportunity for early intervention to ameliorate or remove risk factors, and significantly reduce the probability of disease.

Although genetic testing has been used for many years in prenatal diagnosis (e.g., for Down Syndrome) and to test children for rare genetic abnormalities, the availability of genetic tests for other conditions has increased sharply in recent years. For example, there are currently 600 genetic tests available in Ontario.[27] Over the next decade, as the number of genes shown to be associated with an increased risk of specific diseases grows, the number of genetic tests is expected to increase into the thousands.[28]

Recent technical innovations even make it possible and economical to perform genetic tests at home. However, such genetic tests are not without error and, in the absence of professional counseling, may do more to confuse the public than shed light on their future risk of developing disease. As the genes responsible for more genetic disorders are identified, the number of such tests is bound to increase. For example, a 2002 Internet search revealed 12 commercial genetic testing companies, three of which offered genetic testing direct to consumers.[29] One U.S. company uses the Internet to advertise genetic tests to assess the risk of developing heart disease, osteoporosis and other conditions.[30]

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[25] IDI-Strep B developed by IDI, Quebec City, Quebec: www.infectio.com. (Accessed: September 6, 2004.)

[26] C.R. Scriver, "Genetic Disease: An Orphan in Canadian Health care?" *ISUMA: Canadian Journal of Policy Research* 2, 3 (Autumn 2001).

[27] Government of Ontario, *Genetics, Testing and Gene Patenting*. [See note 6.]

[28] It is also now possible to determine whether a person carries a gene that predisposes them to certain forms of colon cancer. A positive test would call for frequent colonoscopies to detect the cancer and excise it before it metastasizes. Similarly, a test has been developed to detect a gene associated with an increased risk of developing breast cancer. A positive test requires more frequent and careful monitoring of the patient and early surgical intervention where appropriate.

[29] B. Williams-Jones, "Where There's a Web There's a Way: Commercial Genetic Testing and the Internet," *Community Genetics* 6 (2003), pp. 46–57.

[30] Genovations: www.genovations.com. (Accessed: September 6, 2004.)

In addition to predicting the risk for disease, genetic testing may be useful in predicting how a person will respond to medication. Some people metabolize drugs quickly. As a result, the levels of drugs in their blood and tissues required to achieve a therapeutic effect are often not reached. Other people metabolize drugs slowly, with the result that excessively high blood levels are reached, producing toxic effects. A few people will not respond at all to certain drugs. For example, 5% of the population receives no analgesic effect from codeine because their brains do not contain an enzyme to break the codeine down into morphine. Of greatest concern are those individuals that have severe, sometimes fatal, reactions to the medication.[31]

Genetic tests allow physicians to be more efficient and effective in the selection of appropriate medication. Although this field is in its infancy and the tests are not yet widely available, a book with an accompanying computer database has already been published and marketed to family physicians that lists the genetic variations known to affect response to medications.[32] This may well represent the beginning of what some predict will be a flood of information on this subject.

1.3 TREATMENT

Pharmaceutical agents, biological compounds, and devices or procedures for monitoring treatment constitute the majority of biotechnology-based tools for treating disease and disability that are approved for and adopted widely into clinical practice. Others, such as bone marrow transplantation or anti-infertility treatments, are used in limited circumstances. Other treatment modalities such as gene therapy, administration of modified stem cells, and xenotransplantation are still in the experimental stage.

New Therapeutic Agents

Recent advances in genomics and proteomics are being used to accelerate the identification of therapeutic targets for drug development (i.e., the specific molecules and metabolic pathways that play a role in the development of disease) and to improve the ability to predict the efficacy and safety of candidate drugs on the basis of molecular composition and conformation. While current drug therapies are directed at about 500 metabolic processes, the mapping of the human genome has opened up some 3,000–5,000 potential new targets for therapy.[33]

"Pharmacogenomic" approaches are being used to develop therapeutic drugs that are tailored to meet the specific characteristics and needs of genetically defined subsets of persons with a particular disease syndrome, in terms of efficacy and safety. Possible implications of this customization include the testing of prospective participants in clinical drug trials in order to exclude those who are predisposed to adverse reactions and, in the case of drugs approved for clinical use, a requirement that

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[31] There are no data in Canada on the number of adverse drug reactions, other than the 8,500 cases reported to Health Canada each year. Extrapolating from U.S. data, there are 5,000–10,000 deaths in Canada each year from adverse drug reactions and 200,000 serious reactions in hospitalized patients. While many of these reactions are caused by errors in prescribing or administering drugs, a significant number are likely due to genetic factors that prior testing might detect.

[32] L. Humma et al., *Pharmacogenomics Handbook* (Hudson, Ohio: Lexi-Comp Inc., 2003).

[33] World Health Organization, *World Health Report* (Geneva: 2003), p. 63.

patients be tested in advance in order to determine if they have the appropriate genetic profile to benefit from the drug and are not predisposed to adverse reactions.

The new approaches to therapeutic drug development are being actively pursued in relation to cancer. Advances in molecular biology have increased our understanding of the genetics of cancer, and the interaction of genetic predisposition and the environment in its etiology. These advances have opened up many possibilities in terms of identifying novel molecular targets for preventive and therapeutic intervention and for customizing treatment. For example, pathologists may use new analytical tools to identify gene patterns in biopsy specimens, and use the results to indicate which therapies are likely to be most effective in a given individual.

Another goal of cancer research is to find treatments that specifically target cancer tissue and spare normal tissue. With this goal in mind, Aventis Pasteur has developed vaccines for colorectal cancer and melanoma, which are currently in clinical trials in Canada and elsewhere. Analogous to vaccines against infection that stimulate the immune system to fight viruses or bacteria, cancer vaccines stimulate the immune system to attack cancer cells.[34] The U.S. National Cancer Institute estimates that there are more than 100 drugs in clinical trials that are designed specifically to attack cancer cells. One such drug, Gleevec, which was recently approved by the Food and Drug Administration, interferes with the development of a protein complex that stimulates uncontrolled growth in leukemia cells.[35]

In addition to new approaches to drug discovery and treatment planning, novel methods are being used in the production of therapeutic agents. For example, as noted earlier, the genetic modification of plants, animals and microorganisms is being used to produce molecules that the organisms do not normally produce and are of nutritional or therapeutic value. In the latter category are compounds such as vaccines, hormones and enzymes — so called "biologics."

Stem Cell Therapy

Stem cells are generic cells that have the potential to develop into several specialized cell types such as nerve, muscle and liver cells. Stem cells have usually been obtained from embryos, placentas, cord blood and bone marrow, but more recently they have also been found in a variety of adult tissues. Blood stem cells derived from normal bone marrow have saved lives when transplanted into recipients with certain blood-related disorders. No other stem cell procedure has been perfected to date, and it may be a decade before the use of transplanted stem cells to repair the nervous system, or replace the insulin-producing cells in the pancreas to cure diabetes, moves from clinical trials to standard practice.

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[34] Cancer Vaccines: www.cancervaccines.com. (Accessed: September 6, 2004.)

[35] A. Von Eschenbach, "Presentation to House Appropriations Subcommittee on behalf of the National Cancer Institute" (March 13, 2002).

Xenotransplantation

Research on xenotransplantation (the transplantation of cells, tissues or organs from animals into humans) is currently focused on transplantation of cells (e.g., to treat Parkinson's disease and diabetes), tissues and whole organs such as hearts, kidneys and livers. While the potential advantages are huge, given the limited supply of suitable human donors, there are numerous technical difficulties to overcome, including tissue and organ rejection, and the potential transfer of infectious agents to humans. Some progress has been made on the problem of rejection. The Scottish firm that owns the Roslin Institute (where the sheep Dolly was cloned) announced it has cloned pigs that are genetically engineered so that the human immune system would not reject a transplanted pig organ. However, the clinical efficacy and safety of this approach has not yet been determined.[36]

Tissue engineering

Tissue engineering is a related technology in which cells (e.g., of tissues such as skin, cornea or blood vessels) are grown outside the body to form tissue for transplantation. Canada has the largest hospital-based, tissue-engineering laboratory in the world, attached to Université Laval in Quebec City.[37] Researchers at the laboratory plan to assess whether it is possible to enhance tissue development using gene therapy.

Gene Therapy

Successful gene therapy has been the "Holy Grail" of molecular medicine. For over a decade, there has been intensive research on gene therapy as a potential cure for such "mono-genetic" disorders as haemophilia, sickle cell anemia, acute immunologic deficiencies, inborn errors of metabolism, and for more complex "poly-genetic" disorders such as arthritis, macular degeneration (a common cause of blindness in older people), and coronary heart disease.

There are more than 500 trials of gene therapy currently underway, but none has yet been approved for widespread medical use. There are two broad classes of gene therapy. In somatic gene therapy, a healthy gene is inserted into a carrier such as an inactivated virus that delivers the gene to somatic cells in the body. Somatic cells are cells other than germ cells (i.e., eggs or sperm). The second class of gene therapy, called germ-line therapy, involves genetically altering human eggs or sperm. Since these changes will be passed on to an individual's descendants, germ-line therapy is currently banned on the grounds of both risk and moral unacceptability.

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[36] See: www.ri.bbsrc.ac.uk/news/articles/106.html. (Accessed: September 23, 2004.)

[37] Laboratoire d'organogenèse expérimentale, Laval, Quebec: www.fmed.ulaval.ca/loex/default.html. (Accessed: September 6, 2004.)

1.4 Looking Further Ahead

The examples illustrating the promise of biotechnology were chosen to reflect developments that are likely to be feasible in the next three to ten years. The policy initiatives we recommend later in this report should, however, be developed so that they can be readily adapted to developments that may lie further in the future. As part of its background work on BHI, CBAC commissioned an analysis of potential longer-range developments by the Office of Technology Foresight of the National Research Council. One of the key conclusions of that analysis was that many of the new products and processes relevant to BHI are likely to result from the convergence of technologies (biotechnology, nanotechnology, information technology). Hybrid products and processes (e.g., combinations of drugs and nano-scale devices) may require a reconceptualization of approaches to regulation and technology assessment.

Part 2
The Challenges of BHI

Recent advances in health-related biotechnology, like many advances in medicine in the past, bring with them a variety of challenges. However, while there may be a familiar ring to many of the contemporary challenges, some recent advances raise questions as fundamental as what it means to be a human being, and provoke particularly intense debate and even disagreements for which satisfactory resolutions are difficult to find.

The accelerating pace of innovation is itself a challenge because physicians, decision-makers, and the public have little opportunity to gain experience with new techniques and products before even newer techniques and products appear. As a result, gaining a sound understanding of both their potential and their risks can be difficult. Many of the issues that Canadians are grappling with are also being faced in other countries. While we need to be aware of how they are being addressed elsewhere,[38] Canada's political culture, ethnic diversity, geography, and the special features of its health system require solutions tailored to meet Canadian needs.

This section includes a discussion of some of the issues and challenges posed by BHIs, chosen to reflect the current heavy emphasis in public debates and discussion on advances emerging from the "genetic revolution."

2.1 Manipulation of Genes, Cells and Tissues

Modification to genetic structures inherently involves risk. Whether it involves bacteria induced to create antibodies, animals genetically modified to produce a therapeutic product or react like humans when exposed to a new drug, or the correction of inherited abnormalities in humans, there is a risk of an unintended result such as damage to the modified organism, or the escape of a genetically modified animal or infectious agent that harms the environment or other organisms. Some hold that there is also a serious moral risk involved in changing genetic structures, on the grounds that this could lead to a fundamental change in how we value life. For others, such manipulations offend deeply held religious beliefs.

Gene Therapy

There are a variety of challenges that remain to be overcome in relation to somatic gene therapy. These include the technicalities of introducing the therapeutic gene into the recipient and establishing the clinical efficacy and safety of gene therapy. Particular concern about the safety of gene therapy

[38] World Health Organization, *Proposed International Guidelines on Ethical Issues in Medical Genetics* (World Health Organization, Programme in Human Genetics, 1998): www.who.int/ncd/hgn/hgnethic.htm. (Accessed: September 6, 2004.)

has been heightened by events in short-term trials.[39] There are also important questions about the long-term effects of somatic gene therapy — for example, about the reversibility of genetic modification if it does not work or does not work as intended. The risks of germ-line therapy (widely banned with respect to human applications) were noted earlier.

Genetic Modification of Plants, Animals and Microorganisms

In an earlier report, we analyzed the regulatory challenges associated with the production and marketing of foods and feed derived from genetically modified plants, and commented on their implications for health and the environment.[40] Many of the same regulatory challenges apply to the use, in food production, of genetically modified animals, or animals obtained through recently developed cloning techniques. These matters are currently being examined by regulatory agencies.

As noted earlier, genetic engineering of plants, animals and microorganisms is being undertaken for a variety of purposes in addition to food production — for example, in the development of animal models of disease for experimental use, the production of animals with modified characteristics for xenotransplantation (see below), or the processes of molecular-farming/pharming. Each of these applications may present particular challenges as exemplified in a recent discussion paper on molecular-farming.[41] There are a variety of matters that require thorough consideration and the development of appropriate controls. They include the unintended introduction of a change in genetic structure that has serious deleterious effects on the welfare of animals or on the health of those who handle them, the escape of transgenic organisms into the wild, and the spread of traits that are damaging to other species or the environment.[42] [43] [44] [45] [46]

Stem Cell Therapy

The use of stem cells does not generally involve genetic manipulation. Nevertheless, the nature of the risks and ethical challenges is similar to techniques involving genetic manipulation. Not unexpectedly, therefore, there are sharp differences of opinion on the ethics of using stem cells both for research and therapy.

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[38] Jesse Gelsinger was the first person to die from a gene therapy experiment. Jesse, an 18-year-old whose rare metabolic disorder was well managed, volunteered in 1999 to receive a genetically modified virus that would insert a gene into his liver cells. Unfortunately the virus triggered an immune reaction that led to his death a few days later. See: S.G. Stolberg, "The Biotech Death of Jessie Gelsinger," *New York Times, Sunday Magazine* (New York: November 28, 1999).

[40] Canadian Biotechnology Advisory Committee, *Patenting of Higher Life Forms* (June 2002): www.cbac-cccb.gc.ca. (Accessed: September 6, 2004.)

[41] F. Arcand and P.G. Arnison, "Development of novel protein-production systems and economic opportunities and regulatory challenges for Canada." See: cpmp2005.org/pdf/NPPS_040412.pdf. (Accessed: September 10, 2004.)

[42] Committee on Defining Science-Based Concerns Associated with Products of Animal Biotechnology et al. (É-U), *Animal Biotechnology – Science-Based Concerns* (Washington, D.C.: National Academies Press, 2002).

[43] G.L. Comstock, *Vexing Nature? On the Ethical Case against Agriculture Biotechnology* (Boston: Kluwer Academic Publishers, 2000).

[44] A. Holland and A. Johnson, (eds.), *Animal Biotechnology and Ethics* (London: Chapman & Hall, 1998).

[45] B.E. Rollin, *The Frankenstein Syndrome: Ethical and Social Issues in the Genetic Engineering of Animals* (Cambridge: Cambridge University Press, 1995).

[46] P.B. Thompson, *Food Biotechnology in Ethical Perspective* (London: Blackie Academic & Professional, 1997).

Much of the public concern about research using stem cells relates to the destruction of human embryos in order to harvest stem cells. The creation of pre-implantation embryos in order to harvest stem cells is seen by some as incompatible with a fundamental respect for human life. While limiting stem cell use to "excess" embryos from *in vitro* fertilization is a compromise that has been adopted in several countries, it is not acceptable to those who ascribe full human value to an embryo. These disagreements make legislating in this area very difficult. Recent research demonstrates that it may be possible to use stem cells from adult tissue. This may help to alleviate some of the ethical concerns around the stem cell issue, but the clinical efficacy of transplanting cells derived from adult stem cells has not been determined.[47]

Xenotransplantation

The transplantation of animal organs into humans (which, in some applications, involves the genetic manipulation of animals to make their organs more suitable for transplantation) carries with it the risk of trans-species viral infections (e.g., pigs have 40 endogenous retroviruses embedded in their genome).[48] Health Canada developed draft guidelines in 1999 for research in xenotransplantation that propose a series of tests to detect infectious agents.[49] However, as stated in similar guidelines in the United States, infections may occur that are caused by agents that have not previously been recognized and therefore cannot be detected with available tests.[50]

A citizens' forum, hosted by the Canadian Public Health Association in 2001, found that the majority of the 107 participants believed that Canada should not proceed with xenotransplantation at this time. They favored a precautionary approach because the health risks are uncertain, the level of knowledge is insufficient, regulations are inadequate, and other alternatives, such as mechanical substitutes, stem cell research and an expanding human donor pool, are more worthy of support. It should be noted that the latter approach is likely to be insufficient to meet the growing demand for organs and tissues. There was also concern expressed about the well-being of animals involved.[51]

2.2 GENETIC TESTING

Genetic testing is expanding rapidly as the techniques to detect the presence, absence, mutation or variation of particular genes proliferate, and become more sensitive and specific. It will soon be possible to test for hundreds — perhaps even thousands — of genes simultaneously, using DNA micro-array chips. The challenges we face in order to benefit from such a development are not solely

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47 M. Körbling and Z. Estrov, "Adult Stem Cells for Tissue Repair — A New Therapeutic Concept?" *New England Journal of Medicine* 349 (August 7, 2003), pp. 570–82.

48 Tissues such as pig heart valves have been used to replace damaged valves in humans for many years. However, these tissues can be "sterilized" while whole organs cannot.

49 Health Canada, *Proposed Canadian Standard for Xenotransplantation*, Draft (July 14, 1999): www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/bgtd/xeno_std_e.html. (Accessed: July 20, 2004.)

50 United States Food and Drug Administration, *Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans*, Final Guidance (April 3, 2003): www.fda.gov/cber/gdlns/clinxeno.pdf. (Accessed: July 20, 2004.)

51 Canadian Public Health Association, *Animal-to-Human Transplantation: Should Canada Proceed? A Public Consultation on Xenotransplantation* (Ottawa: CPHA, 2001): www.xeno.cpha.ca/english/finalrep/page1.htm. (Accessed: July 22, 2004.)

technical. Will we know enough about the implications of the results of these tests to allow health professionals to counsel patients adequately? Does the health care system have the capacity to respond in both an ethical and cost-effective manner?

Limits to Predictive Value

As the media have often described the human genome as a blueprint,[52] it is not surprising that the public believes it is possible to read the genome as one reads the plans for a house, and know exactly what the finished product will be like. However, whether or not a particular gene causes a disease is influenced by other genes or by "epigenetic" factors, many of which are environmental in origin. Thus, although genetic testing can identify the presence of a genetic abnormality associated with a particular disease, in many cases it is currently impossible to determine with confidence the probability that the disease will in fact occur in the person with the abnormality. (Exceptions to this occur for diseases caused by a single gene mutation, as in Huntington's disease, where the predictive powers of genetic tests are considerably greater.)

While the benefits of genetic testing are clear for some diseases, for others the benefits may not outweigh the risks. The breast cancer gene, for example, has more than 200 mutations, which may influence whether cancer develops in a woman who tests positive for the gene.[53] People who test positive for a gene that causes disease and who never develop the disease may spend their entire lives in fear, and be impelled to undergo frequent diagnostic procedures or take drugs of questionable preventive efficacy. On the other hand, individuals who have a negative test yet develop the disease may not even have undergone the routine screening advised for the general population because they believed they would never get the disease. For these reasons, it is argued that genetic testing should be carried out only after a patient receives counseling and can give fully informed consent.

A recent report prepared by the Canadian Coordinating Office for Health Technology Assessment[54] identified six genetic tests for hereditary cancers that have become a part of standard clinical management. The report concluded that the implementation of genetic testing in the clinical management of the 14 other hereditary cancers (indicated in the report) was unjustified at that time. This is a developing field and it will take considerably more work to determine the clinical circumstances in which these new biotechnology techniques are best used.

Genetic tests, like other kinds of diagnostic tests, vary in efficiency, specificity and sensitivity. Low specificity leads to false positive test results (i.e., the subject has a positive result but does not get the disease). Low sensitivity leads to false negative results (i.e., the subject has a negative result yet does get the disease). The impact of such errors in relation to serious and perhaps life-threatening diseases creates regulatory challenges with respect to safety and reliability, and clinical challenges with respect to counseling of patients. This is particularly true in regard to genetic tests marketed by companies directly to the public — including through the Internet.[55]

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52 *Newsweek* (New York: January 27, 1997).

53 H. Healy, "BRCA Genes: Bookmaking, Fortunetelling, and Medical Care," *New England Journal of Medicine* 336 (1997), pp. 1448–49.

54 N.H. Chuong et al., *Molecular Diagnosis for Hereditary Cancer Predisposing Syndromes: Genetic Testing and Clinical Impact, Canadian Coordinating Office for Health Technology Assessment, Technology Report 41* (November 2003).

55 S.M. Suter, "The Routinization of Prenatal Testing," *American Journal of Law and Medicine* 28 (2002), p. 233.

In 1997, the UK Advisory Committee on Genetic Testing proposed a voluntary code of conduct for companies wishing to offer genetic testing directly to the public, and the U.S. Task Force on Genetic Testing stated that it "discourages advertising or marketing of predictive genetic tests to the public."[56] [57] In 2002, the UK Human Genetics Commission released a consultation document on this topic.[58]

Genetic Testing of Fetuses and Children

Genetic testing and pre-conception counseling allows families to avoid having children with severe genetic diseases. Prenatal testing followed by abortion, if indicated, also prevents the birth of children with genetic or chromosomal disease. As prenatal testing becomes less invasive, and is applied to a wider array of fetal characteristics, at what point do such interventions amount to eugenics? Disability rights groups have claimed that prenatal testing stigmatizes them because it implies that they should not have been born. While little change to current practice is planned, there remain at the heart of this issue fundamental questions about the concept of normalcy that merit continuing discussion.

Should children be tested for diseases that will not develop until adulthood? Should they be tested for diseases that have no cure? In the U.K. and the U.S., national advisory committees have recommended against performing genetic testing in children unless it is possible to take some action that will either treat or prevent disease. Norway is more prescriptive and prohibits testing of asymptomatic children for diseases that may develop in adulthood.[59] Some physicians and parents believe that informed parents are in the best position to make the decision as to whether their children should have genetic testing.

2.3 MANAGING GENETIC INFORMATION

Does a person own or have control of the genetic material he or she has donated for testing or scientific experimentation? It is unlikely that property law applies; however, the issue has yet to be tested in Canadian courts. What is clear is that consent must be obtained both to obtain a sample of genetic material and to carry out tests or experiments on it. Permission to use the genetic material must be explicitly given for each use of the material. An issue that requires careful consideration is whether an individual has the right to consent to the release of genetic information that also reveals information about the genome of his or her family or community. Who has the right of consent for the use of this information? How does one obtain the consent of the community?

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[56] United Kingdom Advisory Committee on Genetic Testing, *Code of Practice and Guidance on Human Genetic Testing Services Supplied Direct to the Public* (London: September 1997).

[57] N.A. Holtzman and M.S. Watson, (eds.), *Promoting Safe and Effective Genetic Testing in the United States: Final Report of the U.S. Task Force on Genetic Testing* (September 1997).

[58] Human Genetics Commission, *The Supply of Genetic Tests Direct to the Public: A Consultation Document* (London: July 2002): www.hgc.gov.uk/testingconsultation/testingconsultation.pdf. (Accessed: July 22, 2004.)

[59] Ibid., p. 17.

Recent research projects in Newfoundland demonstrate how a consent form may not adequately protect the interests of the donors of genetic material.[60] In the first case, researchers from Texas, studying an inherited heart condition that leads to sudden death, collected samples from people in remote Newfoundland communities. These "helicopter geneticists" (as they came to be called) provided no follow-up or genetic counseling for the affected families, and refused to provide provincial geneticists with the medical records so that they could counsel the affected individuals. In another study about inheritance patterns in psoriasis, a California company refused to provide samples to Memorial University, as previously agreed, because the company was concerned that a competitor might access the genetic information.

Maintaining the confidentiality of medical records is a pervasive concern in the health care system. Recent federal and provincial legislative initiatives on privacy protection have addressed many aspects of the concern, including the new challenges created by the introduction of electronic medical records.[61] However, there is continuing debate about whether genetic information requires greater protection than is currently required for other kinds of medical information, given the potential for its ostensible predictive value to be misused. On closer examination, one can find similar characteristics in current medical records that contain no direct genetic information.

Many people are concerned that employers may require genetic testing prior to employment. A number of countries, including Austria, Denmark, France, Norway and Spain, have outlawed the use of genetic testing by employers.[62] In the U.S., more than 40 states have enacted legislation to address the use of genetic information in the workplace. In October 2003, the U.S. Senate passed the *Genetic Information Nondiscrimination Act*, which prevents health insurers and employers from using genetic information to determine eligibility, set
premiums, or hire and fire people.[63] The legislation now requires approval by Congress. In Canada, federal and provincial laws deal only indirectly with this issue and do not specifically prohibit the use of genetic testing by employers. Most of the legislation that touches on this issue was drafted before genetic information could potentially be used to discriminate against employees.[64]

Life and health insurance is another concern. Insurance companies limit their risk at present by requiring a medical examination, and may adjust their rates if there is an increased risk of future disease and death. Why would they not include genetic testing in the medical exam to more accurately assess this risk? For now, uncertainty about the predictive value of genetic testing makes it less useful to insurance companies than more traditional methods of predicting illness or death. This

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60 D. Pullman and A. Latus, *Policy Implications of Commercial Human Genetic Research in Newfoundland and Labrador, Report for the Newfoundland and Labrador Department of Health and Community Services* (St. John's, Newfoundland: 2002).

61 *Personal Information Protection and Electronic Documents Act*, S.C. 2000, c. 5: laws.justice.gc.ca/en/P-8.6/index.html and www.privcom.gc.ca/legislation/02_06_01_e.asp. See also, for example: Government of Prince Edward Island*, Freedom of Information and Protection of Privacy Act*:: www.gov.pe.ca/foipp/index.php3; and Government of British Columbia, Bill 38, *Personal Information Protection Act*:: www.legis.gov.bc.ca/37th4th/1st_read/gov38-1.htm. (Accessed: July 22, 2004.)

62 C. Jamieson, *Genetic Testing for Late Onset Diseases: Current Research Practices and Analysis of Policy Development* (Health Canada Working Paper, September 2001), p. 23.

63 F. Collins, "Statement on the Senate's Passage of the Genetic Information Nondiscrimination Act of 2003 (S. 1053)," (Bethesda, Maryland: National Human Genome Research Institute, October 14, 2003): www.genome.gov/11009127. (Accessed: November 23, 2004.)

64 P. Roche, "The Genetic Revolution at Work: Legislative Efforts to Protect Employees," *American Journal of Law and Medicine* 28 (2002), pp. 271–283.

may change and, in recognition of the potential for abuse in the future, Belgium and Norway have prohibited insurance companies from access to genetic information.[65] The Netherlands prohibits insurers from demanding genetic information only when the insurance policy is below a certain limit. The U.K. has imposed a moratorium until 2006, during which time insurers will not use genetic test results in setting premiums for life insurance under £500,000.[66]

In Canada, the Ontario Human Rights Commission recently released a report that advised against using genetic information to deny insurance or invoke exclusionary periods on the basis of a "pre-existing condition."[67] The Canadian Genetics and Life Insurance Task Force[68] (created to debate the subject of life insurance and genetics in Canada) has put forward two options: (i) No use of genetic test results (excluding family history) for a set, moderate amount of insurance coverage for a limited period of time (five years); (ii) Creation of an independent standing body that includes consumers, government, clinicians, industry and researchers for ongoing review of criteria concerning the reliability of genetic information for underwriting purposes. This advisory body could also handle complaints and queries from consumers. The Task Force members view the articulation of these options as a way to focus ongoing debate on both the role of the life insurance industry and on the meaning of genetic research, testing and information, in the context of our universal health care system and the ability of Canadians to avail themselves of the health benefits of the genetic revolution without fear.

2.4 Patenting of Biological Material

The issues surrounding the patenting of living organisms was comprehensively reviewed in CBAC's report *Patenting of Higher Life Forms and Related Issues*.[69] There are, however, a number of issues that relate specifically to health and health care (e.g., the impact of biotechnology patents on health care costs), which were not addressed in the report because they were not central to its purpose.

The CBAC report did, however, support the recommendation in an Ontario report to Canada's provincial health ministers "that the provinces and the federal government work together to identify and then respond to negative effects of the patenting system on the public health care system."[70] This initiative was spurred by the cost implications of genetic tests for susceptibility to breast cancer.[71] The federal and provincial deputy ministers of health have created a Coordinating Task Group on

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65 Jamieson, *Genetic Testing for Late Onset Diseases*, p. 25. [See note 62.]

66 United Kingdom Department of Health*, Our Inheritance, Our Future: Realizing the Potential of Genetics in the National Health Service, Report to Parliament* (London: June 2003).

67 Government of Ontario, Ontario Human Rights Commission, *Human Rights Issues in Insurance: Consultation Report* (Toronto: February 2002): www.ohrc.on.ca/english/consultations/insurance-consultation-report.shtml.

68 B.M. Knoppers and Y. Joly, "Physicians, genetics and life insurance," *Canadian Medical Association Journal* 170, 9 (April 27, 2004).

69 Canadian Biotechnology Advisory Committee, *Patenting of Higher Life Forms and Related Issues.* [See note 40].

70 Ibid., p. 20.

71 Tests for two genes that increase the risk of developing breast and ovarian cancer were developed and patented by Myriad Genetics. In 2001, the company decided that the test could be performed only at its laboratory in the U.S. The test performed by Myriad costs $3,800 and is considerably more expensive than a similar test done in Canada. Several provinces decided that they would ignore Myriad's demands because of the cost implications for the Canadian health care system. The issue is yet to be resolved.

Genomics and Health. The Task Group's mandate is to assist in the development of a comprehensive coordinated framework for genetics. The Task Group's work focuses on five priority areas, one of which is gene patenting.

Since the release of the CBAC report, several organizations in other countries have released reports on patenting DNA sequences that echo CBAC's conclusions. In 2002, the Australian Law Reform Commission established a national inquiry on the protection of human genetic information, which considered the impact of patent laws on genetic technologies, the biotechnology industry, and the cost-effectiveness of health care.[72] The Commission released its final report to the Australian parliament in August 2004.[73] In Canada, the Romanow Commission supported the views of provincial premiers that the federal government should review the current provisions of patent law in relation to the issue of patenting genes and DNA.[74] CBAC is currently examining this matter and will report its findings to the Government of Canada in the spring of 2005.[75]

In spite of the strong interest in patents on genes and DNA, little empirical research has been carried out on the relationship between such patents and both research and access to health care.[76] There is clear evidence that limitations placed on testing by patent or licence holders have reduced access to genetic testing. A recent survey of 132 genetic laboratories in the U.S. found that genetic test patents have had a significant adverse effect on the ability of clinical laboratories to research, develop and provide genetic testing.[77] Tests for hemochromatosis and breast cancer have been the subject of patent challenges that led to a decrease in use of these tests. Ontario has proposed compulsory licensing of tests or therapies when required to preserve public health.[78] The debate is not about whether genes are patentable — more than 20,000 genes have been patented in the U.S. alone.[79] The key issue is how to preserve the economic benefits of patenting while preventing adverse impacts on research and access to health care.[80]

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72 Australian Law Reform Commission Inquiry (commissioned by the Attorney General), *Intellectual Property Rights over Genetic Materials and Genetic Related Technologies* (Sydney: December 2002).

73 Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health* (Sydney: August 2004): www.austlii.edu.au/au/other/alrc/publications/reports/99/. (Accessed: October 26, 2004.)

74 Commission on the Future of Health Care in Canada (Roy Romanow, Commissioner), *Building on Values: The Future of Health Care in Canada* (November 2002), p. 209.

75 "CBAC to Study Potential Implications of Gene Patents for the Health Care System" (news release): cbac-cccb.ca/epic/internet/incbac-cccb.nsf/en/h_ah00461e.html. (Accessed: October 28, 2004.)

76 R. Gold, "DNA Sequence Patents: Recent Developments," (paper prepared for the Canadian Biotechnology Advisory Committee, June 2003).

77 M. Cho et al., "Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services," *Journal of Molecular Diagnostics* 5, 1 (2003), pp. 3–8.

78 Government of Ontario, *Genetics, Testing and Gene Patenting.* [See note 6.]

79 Associated Press, "Scientists race to patent SARS virus, Efforts to claim property rights spark ethical debate" (November 4, 2003): msnbc.msn.com/id/3076748/. (Accessed: February 27, 2004.)

80 T. Caulfield et al., "Patenting Human Genetic Material: Refocusing the Debate," *Nature Reviews/Genetics* 1 (December 2000), pp. 227–31.

2.5 General Challenges in Policy-Making for BHI

The fundamental challenge facing policy-makers in relation to biotechnology generally is that while applications of biotechnology hold the potential to provide significant social and economic benefits, they may also involve profound social and ethical concerns, or challenge current approaches to the protection of human and animal health and the environment. The difficult task of policy-makers, therefore, lies in crafting public policy that satisfactorily solves, in a pluralistic democratic society such as ours, the dilemma raised by the applications of biotechnology, and strikes a sustainable balance between innovation and values, use and control, opportunities and challenges.

To this point, we have discussed challenges pertaining to particular kinds of BHI. Meeting many of these challenges will require solving technical, safety and efficacy problems through further research. However, other problems faced by policy-makers are related to both the process of policy-making and the implementation of strategies for governing and fostering the development and uses of BHI. These problems include:

- the rapid pace of technical innovation and the stresses placed on the capacity and adaptability of regulatory systems and the health sector generally, and of institutions, providers and consumers in particular;
- the multiplicity of jurisdictions and stakeholders involved in Canada's health system;
- serving the needs of a population with diverse levels of knowledge and interest in influencing policy;
- operating in uncertainty (e.g., in circumstances when the risks are unknown or difficult to quantify; or where data resources are inadequately developed);
- differences between the public and experts in evaluation of risk and uncertainty;
- the pervasiveness of biotechnological issues among sectors resulting in overlapping mandates;
- the constraining effects of international obligations on domestic policy; and
- the tendency for controversies over biotechnology to involve the intersection of complex scientific and socio-ethical issues.

Since many questions about the uses of biotechnology are primarily about values, Canadians need to be involved in the debates on these questions so that decision-makers can discern the issues on which a consensus exists or is possible. However, biotechnological innovation is a highly complex topic. If Canadians are to be fully engaged in debating the public policy issues raised by such innovation, they need to understand the general nature of specific biotechnology advances and their implications. Achieving this objective will not be easy. Public opinion research, sponsored by the Canadian Biotechnology Strategy Secretariat, indicates that "Canadians exhibit a blend of high awareness of biotechnology mixed with low levels of engagement and knowledge. Most find the area too complex and technical to follow closely."[81]

While most Canadians may have little interest in participating in debates about biotechnology, they are interested in their own health. This creates both an opportunity and obligation to inform them as fully as possible about investigations and treatments they may receive. Family physicians, nurses, genetic counselors, nutritionists and other professionals involved in primary care are well placed to

[81] Canadian Biotechnology Secretariat, *Summary of Public Opinion Research into Biotechnology Issues in Canada* (2003): biotech.gc.ca/epic/internet/incbs-scb.nsf/vwGeneratedInterE/by00148e.html#2. (Accessed: July 23, 2004.)

play a leading role in this regard, since they are often asked by their patients to explain investigations and treatments ordered by specialists. Educating health professionals about new developments in biotechnology is therefore an important challenge, especially in view of the anticipated introduction of many new biotechnological innovations (e.g., pharmacogenetic testing) that may overwhelm physicians' ability to understand them well enough to provide appropriate advice and counseling to their patients. This challenge may be particularly salient when obtaining truly informed consent from patients for interventions that are complex, and for which the risks and benefits are uncertain.

In addition to the challenge of expanding the knowledge and awareness of the public and professionals about biotechnology and health, there is also a need to focus specifically on informing and educating legislators and other decision-makers in government. These individuals are charged with making critical decisions on complex and far-reaching issues, and they must be equipped with a solid understanding of the issues and their implications.

A Note on Biotechnology and Global Health

This report is focused on biotechnology and the health of Canadians, and does not address, except by occasional brief references, the opportunities and challenges of BHI that are of special relevance to developing countries — as outlined, for example, in the joint report of the Program in Applied Ethics and Biotechnology, and the Canadian Program on Genomics and Global Health.[82] Clearly, Canada has an important role to play in helping such countries realize the opportunities and meet these special challenges through policies and mechanisms that share Canadian expertise and remove access barriers to BHI — especially those directed at the primary causes of disease and disability. Political leaders have attested to the importance of Canada's responsibilities in this regard and have called for Canada to devote part of its investment in R&D to support new technological initiatives as part of development assistance.[83] [84]

[82] Singer, *Top 10 Biotechnologies*. [See note 4.]

[83] Hon. Allan Rock, Minister of Industry, Government of Canada, "Address to the Global Biotechnology Forum" (Washington D.C., June 22, 2003): www.ic.gc.ca/cmb/welcomeic.nsf/searchEnglish/$searchForm!SearchView&Seq=1. (Accessed: July 23, 2004.)

[84] Rt. Hon. Paul Martin, "Address in Reply to the Speech from the Throne" (February 3, 2004): pm.gc.ca/eng/sft-ddt.asp?id=2. (Accessed: May 21, 2004.)

Part 3
Policies for BHI: A Framework and Recommendations

It is imperative for Canada to have appropriate policies and programs that take advantage of the opportunities and deal with the challenges of biotechnology-based health innovations. The pace of new technological developments, combined with public pressure for access to the benefits of that technology in the face of limited resources and social controversy, will force choices and trade-offs — between old and new technologies, and between BHI and other kinds of health innovation. Clearly defined objectives, thoughtful planning, relevant and timely information and analysis, prudent investment in capacity building, and proactive change within the institutions where health innovations are implemented, are all needed in order to optimize those choices and trade-offs.

In this part of the report, we analyze the policy issues associated with BHI, and propose initiatives to address them within a framework that consists of an overall goal for BHI, a set of values that should inform the crafting and implementation of effective public policy, and the major sectors through which public policy can contribute to the achievement of the goal. We also identify the critical areas for strategic action that apply to several of these policy sectors and that constitute the foundations of success.

3.1 Goals and Values

The primary goal of public policy related to BHI is to improve health. This can be achieved by:

- optimizing access to the health and quality of life benefits of BHI in a cost-effective and efficient way;
- addressing and managing the potential challenges, risks and hazards that may be associated with BHI;
- ensuring the responsible and ethical development and use of biotechnology in the health care system; and
- building and sustaining the scientific and management capacity to generate, adapt and assimilate beneficial BHI.

The use of biotechnology is but one of the ways to improve the health of Canadians. There are many factors in the social and physical environments that have a powerful influence on health and in which biotechnology plays little or no role (at least for the present), which are in need of further policy development and additional investment. One must also be mindful that the use of technology to solve or ameliorate current health problems may have social or environmental consequences for human health in the more distant future.

As noted earlier, many questions about the uses of biotechnology are primarily about values. It is therefore essential that policies related to BHI should be crafted in the context of shared social values. In consultation with a range of stakeholders, CBAC has identified a set of such values. The values and the kind of commitments they entail are:

- *Justice and Equity* - a commitment to a fair distribution of benefits and burdens, and to ensuring that policies and practices do not contribute to the exploitation, exclusion, or oppression of vulnerable groups.
- *Accountability and Engagement* - a commitment to openness and responsiveness to the concerns and interests of citizens and consumers, and to engage them in the process of determining the nature and direction of public policy.
- *Autonomy* - a commitment to promote free and informed choice.
- *Beneficence* - a commitment to the primacy of the benefit to health care recipients over all other interests.
- *Respect for Diversity* - a commitment to respect diverse ways and forms of life.
- *Objectivity* - a commitment to basing decisions on objective knowledge.
- *Caution* - a commitment to adopt a precautionary approach when knowledge is incomplete.
- *Dignity* - a commitment to respect and safeguard the inherent dignity of the human person.

3.2 Policy Priorities and Recommendations

Discovering, developing, assessing, regulating, introducing and applying BHIs are all processes governed or materially influenced by public policy and, in some cases, by direct operational involvement of governments and public sector agencies. These processes are implemented within the following program domains: Research and Development; Regulation and Commercialization; Technology Assessment; and Technology Adoption.

In undertaking our analysis, we have been guided by the following fundamental questions:

> *"Do our systems, as now organized and operated, equip Canada to make the choices among the options available that will achieve the optimum health benefit? If not, what needs to be done?"*

What follows is our assessment of current capacity in each program domain, and our recommendations for actions required to support the goal of improving health.

3.2.1 Research and Development

A vibrant and productive research enterprise is an essential underpinning of Canada's health system. Our researchers create new knowledge and tools for application to improve the health of Canadians; provide us with the scientific and technical expertise necessary to understand and adapt discoveries made elsewhere; and provide the advanced training of scientists, technologists and professionals required by health care institutions and agencies and by the private sector.

Scale and Modes of Investment in Research

In the past decade, there has been a significant increase in health research investment through the federal granting councils (Canadian Institutes of Health Research, Social Science and Humanities Research Council, Natural Sciences and Engineering Research Council), federal laboratories/research institutes (including the National Research Council), special purpose entities such as the Canada Foundation for Innovation and Genome Canada, and programs such as the Canada Research Chairs.

In 2000, funding for genomics research from Genome Canada and the Canadian Institutes of Health Research (CIHR) totaled US$158 million. This compares with expenditures of US$627 million in the United States, US$353 million in Japan, and US$244 million in the United Kingdom.[85]

The lack of specific data on investments in human health-related biological research makes international comparisons difficult, but it is reasonable to argue that Canada's international position cannot be taken for granted. Other countries are committed to a growing investment in life science research over the long term, and Canada could quickly find itself losing ground. Much of Canada's enhanced support for research has been delivered through special purpose agencies (e.g., Genome Canada) to which the government has ceded program responsibilities. Although the agencies provide extensive public information about their activities and financial stewardship, concerns have been raised because the accountability arrangements typically do not include direct parliamentary oversight. Some have gone so far as to suggest that the agencies be abolished.[86] In addressing any concerns about oversight, it is crucial that the government ensure that the focus, flexibility and efficiency of these important programs are not compromised.

Building Canada's Biotechnology Research Capacity

In the increasingly intense competition to attract and retain the best researchers, it is critical that Canada continue to build its investments in publicly funded research, and that the power of its research funding agencies be used to pursue strategic objectives that allow Canada to seize new opportunities and participate in international research ventures. Canada's success in developing and commercializing biotechnology-based health innovations depends upon its research capacity. Accelerating the pace of discovery and the translation of new knowledge into health innovations will be key success factors. Governments' capacity to regulate these innovations depends on strong regulatory science in support of risk assessment and other aspects of health and environmental regulation. Clearly, a portfolio of research investments that supports both basic and applied research, builds interdisciplinary teams, and that targets investments to fill gaps in strategic areas, is necessary to maintain a healthy biotechnology research enterprise. Enhancing collaboration among research funding agencies would serve to increase the alignment of resources with research priorities to achieve maximum impact.

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[85] World Health Organization, *Genomics and World Health, Report of the Advisory Committee on Health Research* (Geneva: 2002), graph 1, p. 129: whqlibdoc.who.int/hq/2002/a74580.pdf. (Accessed: July 11, 2004.)

[86] Auditor-General of Canada, *Chapter 1: Placing the Public's Money Beyond Parliament's Reach* (Ottawa, April 2002): www.oag-bvg.gc.ca. (Accessed: July 6, 2004.)

Biotechnology raises important and, in some ways, unique social, legal and ethical questions that require investigation by researchers in law, social sciences and the humanities. The current supply of researchers with advanced training in these areas, and the amount of funding available, fall considerably short of meeting requirements. The Social Sciences and Humanities Research Council and the Canadian Institutes of Health Research have increased support for building research capacity. They have also increased support for what is broadly termed "knowledge transfer" initiatives. However, these important initiatives must be distinguished from research in law, the social sciences and humanities to improve our understanding of the social phenomena involved in the invention, development, commercialization, assimilation and use of BHIs. Without research in these areas, we will find ourselves ill-equipped to handle health innovations derived from biotechnology because we will lack the necessary understanding of the societal, institutional and individual factors that determine their uptake and diffusion.

This point was reinforced in the national consultation exercise (*Listening for Direction II*) carried out by the Canadian Health Services Research Foundation.[87] One of the top ten priority themes identified in 2004 was titled *Managing and Adapting to Change.* Researchers and decision-makers agreed on the need for "better tools to bring about change at the system level" including: breaking down organizational and professional silos, overcoming difficulty in responding to external forces, and supporting evidence-based decision-making (information systems, technology assessment, models of risk management and knowledge translation).[88] This need for better tools to effect system change is particularly germane to BHI.

Recommendation 1:

In order to capitalize on investments already made and to ensure continued progress in enhancing Canada's research talent, infrastructure and capacity to conduct leading edge research related to biotechnology-based health innovations, we recommend that the Government of Canada, through an appropriate interdepartmental/interagency mechanism (facilitated by the National Science Advisor), develop an integrated and coherent strategy to guide increased and sustained investment in research and development in this area.

This strategy should:

- Include a commitment to sustain and enhance programs of basic and applied research related to BHI through the development of a clear and specific plan for long-term growth of investment in this area, including research required to support regulatory risk assessment.

[87] The exercise involves the following sponsoring partners: CHRF, CIHI, CCOHTA, Advisory Committee on Government and Accountability of the F/P/T Conference of Deputy Ministers of Health and Statistics Canada, Health Statistics Division.

[88] See: www.chsrf.ca/other_documents/listening/index_e.php. (Accessed: July 23, 2004.)

Recommendation 1 (continued):

- Without limiting the foregoing, ensure that special programs, such as those currently implemented by the Canada Foundation for Innovation, Genome Canada, the Canada Research Chairs, Networks of Centres of Excellence, and the Canadian Health Services Research Foundation, are sustained over the long term by appropriate means. These programs should take into account the evolving imperative for support of large-scale interdisciplinary research teams and networks.
- Strengthen Canada's research endeavours on the social dimensions of BHI by fostering the collaboration among biological scientists, social scientists and humanists that is needed to address important questions related to: processes of innovation, regulation, commercialization, technology assessment and uptake, social and physical environmental impacts, public engagement strategies, and the development of tools to manage and adapt to change at the system and institutional levels.

A Balanced Approach to Research Investments

In Canada, direct and indirect public funding involves a mixture of untargeted and directed research, and of research in public and private sector organizations. However, as a general proposition, it remains true that the public sector has the main responsibility for funding much of the basic or fundamental research and the training of research personnel in Canada. This is because the benefits of such research and training are diffused so widely within society and realized over such long time frames that it is uneconomic for the majority of private firms to invest significantly in this type of research.

In the applied research sector, there has been significant growth in linkages between the academic and private sectors in recent years. While these linkages have been productive, concerns have been raised about conflicts between academic goals and commercial interests — for example, between the academic commitment to open sharing of research results and the need of private firms to protect intellectual property so they can profitably commercialize the resulting products.[89] There is also a concern that, in public–private collaborations, the priorities of the private sector will drive the direction of research along lines that are of commercial interest, to the exclusion of research on socially relevant issues (in Canada and the developing world) that are of relatively little commercial interest.

The current prominence of questions related to "the return on public investment in health research" in the minds of policy-makers is reflected in the published statements of research priorities of public agencies such as CIHR's Institute of Genetics.[90] It is also reflected in the eligibility criteria for one of Genome Canada's funding streams, which requires that research must be "directly linked to the delivery of predictive, preventive and/or personalized health care to individuals and populations."[91]

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89 T. Caulfield, "Sustainability and the Balancing of the Health Care and Innovation Agendas: The Commercialization of Genetic Research," *Saskatchewan Law Review* 66 (2003).

90 Canadian Institutes of Health Research: www.cihr-irsc.gc.ca/e/services/15761.shtml. (Accessed: July 23, 2004.)

91 Genome Canada, *Guidelines and Evaluation Criteria for the Competition in Applied Genomics and Proteomics Research in Human Health* (Ottawa: May 2003).

While achieving a suitable return on investment is appropriate, the definition of return should include the creation of an environment to attract and retain research talent, in order to train scientists in the full range of disciplines necessary for Canada's systems of advanced education and health care and for its health industries. Public investments in research are also one of the ways that Canada contributes to improving the health status and living standards of people in the developing world.

To judge whether Canada is achieving an appropriate balance in the biotechnological research enterprise requires empirical evidence about the effects of research policies and trends on outcomes — i.e., on relative research productivity in the various sectors of research. The issue is not whether research is basic or applied, or funded by grant or contract, government or industry, through individual projects or research networks — but whether important research questions bearing on human health are being addressed in an optimum fashion. The recent appointment of a National Science Advisor to the Prime Minister provides an opportunity for a systematic approach to address the question of balance in the support of biotechnological research.

Recommendation 2:

In order to ensure that long-term growth in investment in research and development is guided in such a way as to maintain an appropriately balanced approach to funding of research related to BHI, and in view of concerns about the impact of private sector influence on publicly funded research, we recommend that the National Science Advisor to the Prime Minister, in consultation with funding agencies and academic bodies:

- Assess the extent to which federal programs that support research in public (not-for-profit) institutions, which involve or require co-sponsorship by the private sector, have affected the scale of and balance between fundamental and applied research.
- In the case of applied research, assess the scale and balance of funding between research on topics in which there is an identified commercial interest and those topics of scientific importance in which there is little or no commercial interest.
- Make recommendations to address any impediments to achieving an appropriate balance.

Ethics, Standards and Accreditation

The governance and oversight of research ethics is an area where common standards, transparent methods, national and international harmonization, and public involvement are critical underpinnings that require government leadership and resources, both to protect research participants and enable Canadian researchers to participate effectively in the discovery process. Unless the highest ethical standards are rigorously applied to research on and implementation of BHIs, public trust and confidence in such research could be undermined and support for funding it weakened.

As noted earlier in this report, public policy initiatives have recently been introduced in the field of biotechnological research that reflect prominent ethical concerns. For example, the new legislation on

reproductive technology places limitations on the use of human embryos for research purposes.[92] But significant gaps remain and include the following:

- A coherent framework governing the development, oversight and use of databases containing genetic information (often called biobanks).

Privacy concerns associated with the use of health data (especially data containing genetic information of a predictive nature) and materials in tissue banks will have an impact on the ability to conduct population research. The very nature of DNA makes it uniquely sensitive and gives rise to concerns that employers, insurance companies or law enforcement agencies might obtain and misuse genetic information. Interestingly, in public opinion research completed in 2003, a small majority of Canadians viewed genetic information differently than other types of personal information and said they would like to see stricter rules governing it.[93] CIHR is developing Privacy Best Practice Guidelines[94] for protecting privacy and confidentiality in the design, conduct and evaluation of health research. These guidelines will help health researchers and research ethics boards both to understand and discharge their responsibilities.

Requirements for informed consent (and reconsent) must be clearly articulated in a research context where the future research uses of databases containing genetic material or information cannot be anticipated at the time that research participants provide initial consent. In Canada, strict application of existing law and policy would demand that fresh consent be obtained at the time of sample collection and for each novel use of an identifiable DNA sample or associated data in a biobank. However, traditional norms may be too onerous in the context of population genetic research, given that the future research uses of the tissue and/or data are unknown.[95]

Policy clarity and effective oversight will both facilitate the research enterprise and maximize public protection. Evidence that best practices are being executed consistently, and that adequate oversight is in place to prevent and correct deficiencies in a timely and effective manner, is essential to sustain public confidence in and support for the research enterprise.

- Assimilating the implications of pharmacogenomics for conduct and oversight of clinical research.

Pharmacogenomics is a new field of research that studies inheritable responses to drugs over the entire genome. It is widely anticipated that advances will lead to tailored drug therapy based on genetically determined variation in effectiveness and side effects.

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92 *Assisted Human Reproduction Act*, Statutes of Canada 2004, chapter 2: laws.justice.gc.ca/en/a-13.4/2294.html. (Accessed: November 24, 2004.)

93 Pollara Research, *Public Opinion Research into Genetic Privacy Issues: Final Report* (Ottawa: March 2003), p. 91.

94 Canadian Institutes of Health Research, *Guidelines for Protecting Privacy and Confidentiality in the Design, Conduct and Evaluation of Health Research: Best Practices*, Consultation Draft: www.cihr-irsc.gc.ca/e/pdf_22427.htm. (Accessed: November 24, 2004.)

95 T. Caulfield et al., "DNA Databanks and Consent: A Suggested Policy Option involving an Authorization Model," *BioMed Central Medical Ethics*, 4 (January 3, 2003), p. 1.

It is anticipated that pharmacogenomics will allow the development of therapeutic drugs specific to patient genotypes. This would facilitate the identification of drug targets specific to particular groups and the design of more efficient clinical trials. However, important social and ethical issues arise relating to the security and privacy of DNA samples and genetic data; the adequacy of current guidelines for informed consent for genotype-based clinical trials; criteria for determining who shall have access to drugs developed with particular genotypes in mind; the organization of health services and health policy more generally; and the regulation of new medicines.[96]

- Guidelines for sharing with public stakeholders the benefits from publicly funded research that result in data used for financial gain.

In our 2002 report, *The Patenting of Higher Life Forms and Related Issues*,[97] we recommended that the federal government, in consultation with other levels of government and other stakeholders, develop policies and practices that encourage sharing the benefits of research involving genetic material. In particular, we recommended that the benefits of medical and pharmaceutical research based on human genetic material (including its commercial exploitation) be shared with the groups or communities who provided the material.

- National Oversight of Research Ethics

Research ethics boards (REBs) in universities, hospitals and research institutes are primary vehicles in which these issues will be played out. In general, they have served Canadians well. However, the already strained capacity to cope with existing workloads will be magnified by the projected increase in the number of research proposals with high levels of biotechnological complexity, which directly impact upon the public's confidence in and willingness to participate in health research. There are also private/independent REBs in Canada that are utilized extensively in industry to meet the requirements of Health Canada with respect to clinical trials. While many private REBs function well, there is a concern that some smaller companies do not use REBs, or may use REBs that would not meet appropriate standards.

There are currently a number of guidelines, policies, standards and regulations in use in Canada related to research ethics, including the *Tri-Council Policy Statement: Ethical Conduct of Research Involving Human Subjects* and the *International Conference on Harmonization: Good Clinical Practice Guidelines*. They provide an important framework for both institutions and researchers. However, there is widespread recognition within the research and policy communities[98] of the need to modernize approaches to governing the ethical conduct of research involving humans. This stems

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96 G. Lewis et al., *The Clinical and Commercial Development of Pharmacogenetic Project*, Outline (funded by Wellcome Trust) (London: 2001-2003).

97 Canadian Biotechnology Advisory Committee, *Patenting of Higher Life Forms.* [See note 40.]

98 The Senate Social Affairs Committee Report on Health Reform in 2002 and a study by the Law Commission of Canada in 2000 recommended improvements to the consistency and quality of ethics review by research ethics boards, as well as the development and implementation of mechanisms to assure that research ethics instruments (e.g., the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans) are respected in practice. See: Standing Senate Committee on Social Affairs, Science and Technology, *The Health of Canadians – The Federal Role* (Interim Report), Volume Five: Principles and Recommendations for Reform – Part I (Ottawa, April 2002); Law Commission of Canada, *The Governance of Health Research Involving Human Subjects*: www.lcc.gc.ca/en/themes/gr/hrish/macdonald/macdonald.pdf (accessed: November 24, 2004); and Medical Research Council of Canada et al., *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (Ottawa: August 1998).

from the need to maintain public confidence in the research endeavour at a time of change in the nature and pace of research activities, the rise of new research methodologies, as well as shifts in the institutional settings in which research is conducted. Ensuring the ethical conduct of human research is a fundamental "building block" to promoting the commercialization of research discoveries.

These imperatives have prompted continued developments within existing agencies and some new initiatives, such as the introduction of new clinical trial regulations by Health Canada; further refinement of the Tri-Council Policy Statement and related communication and educational activities; the establishment, by the National Council of Ethics in Human Research (NCEHR), of a Task Force for the Development of an Accreditation System for Human Research Protection Programs; the creation of the Canadian Association of Research Ethics Boards; and the development of a variety of specialized mechanisms for quality assurance in particular fields (e.g., cancer research ethics boards).

While Canadian researchers and research sponsors are active participants in the international debate surrounding the ethics of research in the modern biotechnological era, and there are bodies (e.g., federal and provincial granting councils, NCEHR and Genome Canada) concerned with the promotion and implementation of appropriate ethical standards, current structures and policies may be inadequate to deal optimally with contemporary and emerging challenges.

The need seems clear to achieve greater coordination and collaboration among the various organizations and groups with responsibilities for governance and oversight of research ethics. However, we perceive a lack of movement in some areas, from issue definition and discussion to a clear and unambiguous policy response. For example, the identification of a need for a national governance/oversight body for research ethics boards has, to date, produced no tangible results. Unless there are national or, better still, international standards that are rigorously adhered to, it will be difficult if not impossible to achieve effective harmonization across institutional, regional and international boundaries.

Recommendation 3:

In order to ensure the ethical and safe development and use of biotechnology in the health care sector, we recommend that the ministries of Health and Industry, in collaboration with counterparts in the provinces and territories, and in consultation with the National Council on Ethics in Human Research and stakeholder groups,[99] establish or facilitate the establishment of a body or mechanism both to set standards and to accredit organizations and institutions with responsibilities for research ethics boards, and for population health databases and banks of biological specimens used for research purposes.[100] Satisfactory compliance with standards should be an eligibility criterion for federal research funding**.**

[99] Stakeholder groups should include the research granting councils and bodies representing universities and research hospitals and institutes.

[100] A review, conducted for CBAC, of the issues related to biobanks concluded that Canada should develop a regulatory framework that incorporates the legal and ethical norms governing research and corporate governance. The author of the review believes that Canada can learn from the experience of other countries that have created large biobanks and should

Recommendation 3 (continued):

The body should:

- Operate at arms-length from research funding agencies and institutions.
- Include representation of the general public.
- Establish standards with respect to the ethical conduct of research that strike a reasonable balance between serving the interests and needs of Canadians and facilitating research that will improve the health of Canadians.
- Serve a developmental role by fostering collaboration among agencies and institutions in meeting the education and training needs associated with the foregoing regulatory functions, and in developing methods to improve efficiency and reduce the burden of meeting regulatory requirements related to research (e.g., by developing standardized common templates for regulatory submissions; by encouraging reciprocal recognition of review processes that meet national standards).
- Work cooperatively with agencies such as the Canadian Council on Animal Care (CCAC) to ensure that best practices are applied in the humane use of animals (including genetically modified animals) for biotechnology related research.[101]

3.2.2 Regulation and Commercialization

Commercialization by the private sector is the predominant avenue through which new technology is made available for use in the health system. Bringing biotechnology products to market is a complex, expensive and time-consuming process. In order to secure Canada's competitive advantage in a growing global marketplace, and to provide Canadians with timely access to beneficial products, the systems we deploy to develop, regulate, evaluate and commercialize BHI must be equipped to optimize the benefits and minimize risks. The challenges are becoming progressively more intense because the rate at which novel (and often complex) BHIs are being developed is increasing steadily.

The market opportunity for BHIs is growing as illustrated by the following observations:[102]

- The global market for health-related technologies exceeds a trillion dollars.
- 97% of the market is accessible to Canadian firms.
- 50% of the opportunity is in the U.S.
- The health care market is expanding at an annual rate of 8%, more than double the rate of economic growth.

create an independent organization responsible for project oversight and surveillance. L. Sheremeta, *Population Biobanking in Canada: Ethical, Legal and Social Issues.* [See note 14.] Recently, researchers in Quebec have created a non-profit agency to oversee genetic research in the province. Institut de Population et Genetique (IPEG) has established an ethical and legal framework to guide population-based genetic research.

[101] The CCAC is currently revising its 1997 guidelines on transgenic animals to reflect developments in the field of animal biotechnology. See: www.ccac.ca/English_gui_pol/gdlines/TRANSGENE1.HTM. (Accessed: September 6, 2004.)

[102] National Research Council of Canada, Office of Technology Foresight, *Towards a Sustainable Health Care System: Capturing the Commercial Potential of Bio-Health Innovations* (Ottawa: April 2004).

- The demand for biotechnology-derived products is growing at more than 30% annually.
- The biotechnology market alone is expected to reach US$50 billion by 2005.

Canada's biotechnology sector ranks second in the world to the U.S. in terms of number of firms, and ranks third after the U.S. and the U.K. in generating revenues. In 2003, there were 418 companies, 84% of which were focused on health.[103] Annual revenues reported by the health biotechnology firms were almost $2.5 billion, up from $417 million in 1997, and it is estimated that such firms spent about $1.2 billion on R&D in 2001. Canada has exhibited the fastest rate of growth among G7 countries in the number of workers devoted to R&D, the number of external patent applications, and business expenditures on R&D. A strong capacity in biopharmaceuticals is developing based on growing expertise in genomics, proteomics, bioinformatics, immunotherapy, and also in protein engineering and new drug delivery systems.

While investments in R&D have placed Canada among the world leaders in generating discoveries and innovations, foreign interests too often realize the return on these investments. Canada's bio-health industry is a comparatively weak performer in the global marketplace. The weakness is particularly evident in the trade performance of the pharmaceutical and medical device sectors. In the medical device industry, imports are roughly double the level of exports, leaving Canada with a $1.9 billion trade deficit in this sector. Some predict that the medical device trade deficit will likely double within the next seven years. The trade deficit in pharmaceuticals runs far deeper. Last year, it exceeded $5 billion, more than double the trade imbalance in 1998. On its current trajectory, Canada's trade deficit in pharmaceuticals could reach $11 billion in 2010.[104]

There are serious concerns among leaders in the health biotechnology industry that, while Canada's biotechnology industry has a strong R&D focus, "Canada has become a "farm team" of discoveries, where ideas are generated but not developed into products."[105] One of the reasons for this situation, according to industry representatives, is the long approval process within Canada's existing regulatory structure. They also note that not enough priority has been given to market development. For example, the Canadian International Development Agency has facilitated exposure for Canada's engineering expertise worldwide, but little effort has been made to showcase Canadian-developed health care products.[106]

A Regulatory System that is Comprehensive, Transparent and Responsive

Regulation is one of the most important and pervasive responsibilities of government. Regulatory systems can be a key determinant of the tempo of commercialization of biotechnology-based health innovations. In 2002, CBAC presented the federal government with its analysis and recommendations on improving the regulation of genetically modified foods and feed. The importance of developing standard operating procedures, increasing transparency of decision-making, using leading-edge science, and making clear information accessible to the public were prominent in the report and in our

[103] Statistics Canada, *Biotechnology Use and Development Survey 2001* (Ottawa: March 2003).

[104] National Research Council of Canada, *Towards a Sustainable Health Care System*. [See note 102.]

[105] Ibid., p. 9.

[106] Public Policy Forum, *Roundtable on Canada's Knowledge Economy: New Models for Health Innovation* (Ottawa: August 27, 2002): www.ppforum.com/ow/ow_e_08_27_2002.pdf. (Accessed: November 24, 2004.)

recommendations. These are essential features of regulatory systems generally, and we reiterate the imperative of ensuring their prominence in systems that regulate BHI.

The federal government's External Advisory Committee on Smart Regulation (EACSR) recently released its report, Smart Regulation: A Regulatory Strategy for Canada,[107] which also identified the regulatory needs that the 2002 CBAC report had organized into four themes (good governance, transparency and public involvement; precautionary elements; information and consumer choice; and social and ethical considerations).[108] It is noteworthy that an increasing number of therapeutic drugs are biotechnology products. Moreover, from the perspective of improving the health of Canadians, it is essential that a national biotechnology regulatory strategy be both comprehensive and integrated — comprehensive in that it embraces therapeutic drugs and devices; preventive, diagnostic and therapeutic processes; foods and nutrition; and environmental biotechnology; and integrated in that there is coherence and effective articulation among the various regulatory agencies of government.

The number of biotechnology products being presented for regulatory approval from all sources has grown rapidly, and this growth is placing intense pressure on federal regulatory bodies. In 1997, there were 1,710 health-related biotechnology products in development or on the market. This grew to 3,400 in 1999 and reached 9,100 in 2001.[109] Although not all health-related products require extensive regulatory assessment, it is anticipated that the number that do require such assessment will continue to grow, and place even more intense pressure on the regulatory system. In addition to the increased rate of product development, regulatory systems are likely to be faced with products and processes that are more complex than the drugs and devices of the past (e.g., products that are combinations of drugs, diagnostics and devices), and that will require expanding the range of expertise and the level of methodological sophistication available in regulatory agencies.[110]

Recommendation 4:

In order to achieve effective and efficient evaluation, and the timely introduction of beneficial BHIs in Canada, we recommend that Health Canada ensure it has a comprehensive, responsive and transparent regulatory regime that:

- Through exemplary governance, organization and operational arrangements, coordinates the regulatory evaluation and approval mechanisms applicable to biotechnological products and processes, and effectively addresses the regulatory challenges presented by technologies that cross boundaries between departmental jurisdictions ("molecular pharming") or between categories of innovation (combinations of drugs and devices).
  Achieves the highest standard of performance with respect to efficiency, timeliness and effectiveness in evaluation, and in making and communicating decisions.

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[107] Government of Canada, External Advisory Committee on Smart Regulation, *Smart Regulation: A Regulatory Strategy for Canada* (Ottawa: September 2004): www.smartregulation.gc.ca/en/index.asp. (Accessed: November 24, 2004.)

[108] Canadian Biotechnology Advisory Committee, *The Regulation of Genetically Modified Foods* (Ottawa: August 2002).

[109] Statistics Canada, *Biotechnology Use and Development Survey 2001.* [See note 103.]

[110] G. Bruce Doern, *Regulatory Regimes for the Safety and Efficacy of Biotechnological Health Products: Changing Pressures, Products and Processes* (prepared for the Canadian Biotechnology Advisory Committee, July 2003).

Recommendation 4 (continued):

- Is responsive in incorporating new scientific and technical knowledge into its evaluation and decision-making criteria and processes. Works with counterparts in other countries, directly or through appropriate international bodies, to develop and encourage the adoption of best practices; share risk assessments; and standardize application and information requirements to make applications in multiple jurisdictions easier for applicants and to streamline processes for products previously approved elsewhere, in order to reduce delays in access for Canadians.
- Systematically reviews — including by international expert panels — the capacity and expertise of regulatory agencies, particularly their in-house capacity, with a view to establishing appropriate strategies and tools to respond to the needs and opportunities presented by scientific and technical advances.
- Develops and publishes standard operating procedures in order to increase public understanding of and enhance confidence in the regulatory system.[111]

An Integrated Biotechnology Commercialization Strategy

Canada faces several challenges in its efforts to increase the commercialization of biotechnology-based health innovations:[113]

- Many promising ideas are being stalled by a lack of early stage equity capital for emerging enterprises in the bio-health sector, and this is creating a blockage in the innovation chain. As a result, Canadian companies are failing to survive the phase between research and development, and early stage commercialization.
- Canada is funding the riskiest part of technology development. Foreign sources then acquire the intellectual property quite inexpensively, undertake lower risk product development, and sell products back to Canada at higher prices. Canada lacks a commercialization strategy that supports its entrepreneurs in developing their products.
- Investors in biotechnology firms tend to select a single compound for development. If this fails, the business often fails, leaving other potential compounds or applications unexploited. It is estimated that between 600 and 1,000 compounds are not being developed because of this practice.
- The shortage of bio-manufacturing capacity in Canada and worldwide is a major impediment to commercialization.

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[111] The standard operating procedures that CBAC identified regarding the regulation of food and feeds [see note 108] are also applicable to biological products and processes applied to human health. They include: organizational mandates; legislative authorities; relevant laws and responsibility centres; precise steps in a product's progression through the system and relevant time lines (including details regarding the stages of risk assessment); delegation of decision-making authority; procedures to insulate officials from inappropriate influence; decision-making procedures including the rationale for engaging non-governmental experts in regulatory processes; mechanisms to resolve differences of opinion with regard to regulatory decisions; preparation of draft decision documents for public review; and procedures for providing public input.

[113] This summary is taken from: National Research Council of Canada, *Towards a Sustainable Health Care System.* [See note 102.]

- The lack of expert or knowledgeable investors capable of assessing risks in an increasingly complex technological world is cited as a major impediment to the growth of Canada's biotechnology industry.
- The underutilization of public institutions (notably major hospitals) for product testing, clinical trials and technical innovation, and the sparse linkages among sectoral players and among professional and scientific disciplines, results in insufficient development of shared platforms for commercialization.
- The federal government's main vehicles for providing financial assistance to bio-health companies — Technology Partnerships Canada (TPC) and NRC's Industrial Research Assistance Program (IRAP) — are not well aligned with the needs of biotechnology companies. Applicants to these programs report concerns about TPC's repayment terms (namely, repayment from a biotechnology company's royalty stream can adversely impact the company's valuation) and the small amount of funding available under IRAP. (Anecdotally, the U.S. Small Business Innovation Research Program[114] is reported to have an excellent record in technology commercialization, and is attached to all U.S. federal organizations with extramural R&D budgets in excess of US$100 million.)
- The lack of alignment of Canada's patent system with those of our major trading partners, as well as a lack of clarity on the scope of patent protection, are cited as disincentives to investment and to a thriving research community. CBAC has addressed this issue in a previous report[115] and made specific recommendations.

Proposals have been advanced to address the biotechnology commercialization challenge. Their features include:

- Creating larger, more sustainable companies from the merger and consolidation of small enterprises that have survived the early commercialization stage. This will provide economies of scale and increase scientific critical mass, and will allow the distribution of risk among multiple products in the pipeline. Merged companies will increase their ability to attract and retain highly qualified personnel, particularly those with the essential mix of scientific and business skills.
- Establishing a Biotechnology Drug Development Accelerator (BDDA).[116] The BDDA is a novel initiative that would proactively evaluate all compounds in Canadian biopharmaceutical companies, qualify those with potential for improved health outcomes and global market potential, and fast-track the development of selected compounds in collaboration with other stakeholders to ensure maximum patient access to the latest scientific breakthroughs. The BDDA would:
  - manage the product development process to ensure maximum efficiency and return on investment;
  - take an active approach to seek out technologies and products that are not being advanced;
  - structure agreements with intellectual property holders; and

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[114] See: www.sbir.er.doe.gov/sbir. (Accessed: June 30, 2004.) The primary objective of the SBIR Program is to increase the incentive and opportunity for small firms to undertake cutting-edge, high-risk, high-quality research that would have a large potential economic payoff if the research were successful. No such program is available at the national level in Canada.

[115] Canadian Biotechnology Advisory Committee, *Patenting of Higher Life Forms.* [See note 40.]

[116] *Canada's Innovation Strategy*, 2 volumes (Ottawa: Industry Canada, 2001). See also: www.innovationstrategy.gc.ca.

- co-invest through an Innovation Development Fund (IDF) to accelerate their development.

- Establishing a Canadian Bioprocessing Initiative[117] (CBI). The CBI would contribute to Canada's global leadership in the manufacture of therapeutic proteins. To meet this objective, the CBI would create five distributed national networks: regulatory foresight, research, training, systems development, and contract manufacturing. The CBI would also construct a current Good Manufacturing Practices (cGMP)-compliant bio-manufacturing plant to concentrate on small batch production, and create a new national institute affiliated with the National Research Council of Canada, Agriculture and Agri-Food Canada, and Canadian universities.
- Health Innovation Canada (HIC)[118] has characterized Canada's health care system as lacking a culture of commercialization and innovation. The current system is focused on cost-containment and short-term planning, and acts as a constraint on entrepreneurial talent. HIC has articulated a challenge for Canada to use its investment in health research and the health care system to build a globally competitive health industry. Its draft proposal, Moving Health Innovations to Market (March 2004), calls for the creation of investment funds to address the early stage financing needs of small innovative firms; the establishment of commercialization centres in partnership with leading teaching hospitals and health authorities to catalyze hospital-based innovation; and the development of commercialization platforms in the form of networks and support structures and resources.

Patents are an essential element of a commercialization strategy for Canada. For Canadian companies, most of which are small or medium in size, the ability to attract investors to finance developmental work significantly depends on the company's patent portfolio.

The patent not only gives its holder the exclusive right to sell the invention, it allows the patent-holder to set the price. As was described earlier, the Myriad case illustrates the conflict between gene patents and affordable access to health care interventions.[119] The key issue is how to preserve the economic benefits of patenting while preventing, minimizing or mitigating adverse impacts on research and access to health care.

One of the key policy questions in this area is the extent to which the existence of patents in fact impedes research or affects access to services. The extent of these negative effects is unknown since most expressions of concern are based on relatively few documented incidents and anecdotal evidence.[120] Although research is being undertaken on questions such as the licensing and pricing practices of patent-holders,[121] much more needs to be done. In an earlier report, we recommended that

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[117] National Research Council of Canada, *Towards a Sustainable Health Care System.* [See note 102.]

[118] Health Innovation Canada is a body whose goal is to catalyze greater economic returns from investments that Canada makes in health-related R&D and in health care (currently about $2 billion and $120 billion respectively).

[119] Myriad's European patent claiming "a method for diagnosing a predisposition to breast and ovarian cancer," one of a number of patent claims on the BRCA1 and BRCA2 genes, was revoked by the European Patent Office Opposition Division on May 19, 2004, as being insufficiently novel. See: European Patent Office, "'Myriad/breast cancer' patent revoked after public hearing" (news release): www.european-patent-office.org/news/pressrel/2004_05_18_e.htm. (Accessed: July 20, 2004.) This ruling may be challenged before a Technical Board of Appeal.

[120] Centre for Intellectual Property Policy, "Recommendations for Canadian Genetic Patents and Health Care: An International Comparison of Patent Regimes of Canada and its Major Trading Partners" (paper prepared for the Canadian Biotechnology Advisory Committee, September 2004).

[121] See, for example: Organisation for Economic Co-operation and Development, *Genetic Inventions, Intellectual Property Rights and Licensing Practices: Evidence and Policies* (Paris: OECD, 2002); and "Study of the Canadian Biotechnology

the *Patent Act* be amended to include a provision that exempts research and experimental uses of patented inventions from claims of patent infringement.[122] Issues of licensing and royalty payments would only arise if a new product or process resulting from such research incorporated the patented invention. This would help to address the concern that scientists avoid certain lines of research out of fear of being sued for patent infringement, or because the transaction costs of identifying patents and negotiating licences or the royalty payments are too high.

Regarding affordable access to patented inventions, some methods of ensuring affordable access already exist. The Patented Medicine Prices Review Board (PMPRB) requires that the introductory price of a new drug in Canada fit within a range determined by the prices charged in selected comparable countries. It has been suggested that the PMPRB's mandate should be extended as a way of ensuring affordable access to new health biotechnologies, such as genetic tests. Another method of controlling costs is through bulk purchasing. If a provincial drug plan purchased the pharmaceuticals needed by its residents, the cost would be much lower than if they were purchased by individual pharmacies.[123]

CBAC is undertaking a more detailed examination of the interface between genetic patents and the health care system, and plans to issue a report on its findings in the spring of 2005.

The foregoing discussion indicates that there is no shortage of ideas about, and recommendations for, how to respond to the commercialization challenges in the health sector of the economy. What is required is a clearly articulated, comprehensive, coherent and integrated national strategy for health innovation commercialization that includes a specific focus on BHI.

Sector's Licensing Practices Regarding Patented Genetic Inventions" (unpublished paper prepared under the Canadian Biotechnology Strategy Fund, August 2004).

[122] Canadian Biotechnology Advisory Committee, *Patenting of Higher Life Forms*, p. 15, recommendation 5 [see note 40]:

> We recommend that the Patent Act be amended to include a research and experimental use exception that includes the following statement:
> It is not an infringement of a patent to use a patented process or product either:
> (a) privately and for non-commercial purposes, or
> (b) to study the subject-matter of the patented invention to investigate its properties, improve upon it, or create a new product or process.

[123] The U.S. government recently passed the *Medicare Prescription Drug, and Modernization Act of 2003*, which includes a provision denying state governments the right to negotiate prices with brand name drug companies: gordon.house.gov/NR/rdonlyres/68AF7486-66FF-4518-9FCA-C7E5A24E7956/0/medicareprescripdrubexplanation.pdf#xml=http. (Accessed: July 20, 2004.)

Recommendation 5:

In order to optimize the return on investment in publicly funded research and development, we recommend that Industry Canada, in collaboration with the federal research funding agencies, develop a coherent, integrated biotechnology commercialization strategy that:

- Clarifies the legal and regulatory framework for ownership and licensing of intellectual property to strike an appropriate balance between the interests of innovators, developers and the public seeking access to the benefits of BHI.[124]
- Facilitates the financing of commercialization efforts by small- and medium-sized enterprises — for example, by refining the taxation regime so that it is more responsive to the needs of small enterprises (e.g., through the Scientific Research and Experimental Development tax credit provisions).
- Promotes the development of greater access to early stage capital by such means as mergers of small companies that result in economies of scale; expanded scientific and managerial capacity; bundling of product lines to attract investment; and the development, in partnership with the private sector, of special investment funds that focus on early stage capital financing needs.
- Creates commercialization platforms and networks to enhance the commercialization efforts of universities, research hospitals and institutes.
- Identifies instruments (financial, legal and commercial) that would allow the private sector to benefit from producing technologies that more clearly contribute to improved health within existing levels of health expenditures.
- Nurtures the capacity of the private sector to develop and deliver products that are valued and purchased by the health care sector, by fostering linkages between entrepreneurs in small- and medium-sized firms with experts in the health sector who can identify areas of need and opportunity.

3.2.3 Technology Assessment

Health technology assessment is defined as the process of systematically reviewing existing evidence and providing an evaluation of the effectiveness, cost-effectiveness and impact, both on patient health and on the health care system, of medical technology and its use.[126]

[124] CBAC has made specific recommendations in this respect that are applicable to BHI. They are included in its *Report on Biotechnological Intellectual Property: Patenting of Higher Life Forms* [see note 40], and its advisory memoranda dealing with the implications of recent Supreme Court decisions on the Harvard Onco-mouse case and the Schmeiser case*: Higher Life Forms and the Patent Act* (February 2003) and *Rationalizing Patent Law in the Age of Biotechnology* (September 2004), both available at cbac-cccb.ca/epic/internet/incbac-cccb.nsf/en/h_ah00036e.html. (Accessed: November 24, 2004.)

[126] Canadian Coordinating Office for Health Technology Assessment: www.ccohta.ca. (Accessed: June 23, 2004.)

The term health technology appraisal has been applied to judgements about relative priority, equity, acceptability, feasibility and other features associated with the introduction of a technology.[127] Since the terms "assessment" and "appraisal" can be applied to both traditional HTA and an analysis of these broader features, and since the latter are increasingly viewed as integral to decisions on the adoption of new technologies, it is preferable, for contemporary purposes, to redefine HTA to reflect this integration.

HTA, whether in its traditional or expanded form, needs to be embedded in a robust policy framework that includes policies dealing with regulatory, social, economic, clinical, fiscal and governance dimensions, associated with decisions about the adoption or continuing use of technologies. Since policy frameworks and the processes of policy development vary across jurisdictions in Canada, mechanisms to facilitate the identification of areas of common policy interest and potential collaboration are highly desirable.

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) and Agence d'évaluation des technologies des modes d'intervention en santé (AETMIS) carry out the bulk of health technology assessments in Canada. Other provincial and inter-provincial agencies contribute valuable expertise and evaluations of new technologies that assist in decision-making. Annex 3 includes a summary of HTA agencies in Canada and their mandates.

Public and health care provider demands influence the selection of technologies for which HTA is undertaken. The rise of genomic medicine and personalized approaches to treatment are expected to increase demand and strain the capacities of HTA agencies even further. National coordination and international collaboration can help to reduce the strain by avoiding unnecessary duplication of effort through sharing the limited pool of personnel equipped to undertake HTAs for BHIs. International delegates to a Canadian symposium on health technology assessment highlighted the dangerous shortfall in expertise for the assessment of genetic technologies. They indicated a need for methodological innovations for analyzing and synthesizing different types of data than those methods used traditionally.[128]

An excerpt from the report, Genetics, Testing and Gene Patenting: Charting New Territory in Healthcare,[129] illustrates the challenge:

- "High levels of public interest in new genetic breakthroughs, combined with the rapid commercialization of genetic knowledge, will undoubtedly mean that publicly funded health systems will increasingly be required to evaluate claims and counter-claims regarding new genetic technologies and new approaches to treatment.
- For all jurisdictions, the capacity to incorporate new genetic technologies in a responsible and effective manner will require improving our collective capacity to assess, evaluate and monitor the relative effectiveness and cost-impact of new genetic technologies compared to existing treatments and procedures.

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[127] I. Blancquaert and L. Caron, HTA in Genetics: Challenges and Opportunities" (presentation at the Symposium on Health Technology Assessment in Genetics and Policy-making in Montreal, Quebec: September 12, 2003).

[128] *Symposium on Health Technology Assessment in Genetics and Policy-making in Canada* (Montreal, Quebec: September 11-12, 2003): www.aetmis.gouv.qc.ca. (Accessed: June 30, 2004). The September 9, 2004, version of the symposium summary was provided to CBAC through the courtesy of AETMIS.

[129] Government of Ontario, *Genetics, Testing and Gene Patenting.* [See note 6.]

- Without strengthened capacity, there is a real risk that misleading commercial marketing entering Canada from other jurisdictions and via the internet, combined with the risk of possible premature commercialization, could all play a very strong role in influencing the types of tests and interventions which are available or indeed which become publicly funded."

Emerging biotechnological innovations will highlight and exacerbate existing challenges for HTA in general. They will also, in some cases, require special approaches to deal with applications that diffuse rapidly throughout the health system, entail high costs, and/or are likely to require health service reorganization. Moreover, the inherent ethical and social issues that accompany particular biotechnological applications will change the type of information required by decision-makers.

Currently, total Canadian expenditures on HTAs are about $17 million. CCOHTA spends about $14 million annually on HTAs, and AETMIS and the Alberta Health Foundation for Medical Research (AHFMR)-HTA unit together spend about $3 million. By comparison, the U.K. spends $100 million.[130] It is therefore not surprising that a number of provincial task forces and commissions have commented on this issue. The Romanow Commission recommended that technology assessment in Canada should be streamlined and increased in scope to enhance its use in guiding decisions.[131] Romanow argues that HTA should serve as a driving force to encourage the adoption and implementation of appropriate health technologies. A national HTA body should ensure that provinces and territories are keeping pace in adopting new technologies, and that health professionals and decision-makers use technology assessments to guide their decisions.

In February 2003, the First Ministers' Accord on Health Care Renewal directed health ministers to develop a comprehensive strategy for health technology assessment. The Federal, Provincial and Territorial Advisory Committee on Information and Emerging Technologies is responsible for developing this strategy. At the same time, work is underway internationally, spearheaded by the Organisation for Economic Co-operation and Development, to assess the appropriateness of current HTA models in supporting decision-making processes for the adoption of biomedical technologies.

After reviewing background papers on HTA and BHIs,[132] [133] CBAC convened an "Expert Roundtable on Health Technology Assessment and Health System Adoption of Biotechnology-based Health Innovations" on April 26, 2004. During the roundtable discussions, the challenges to be addressed in enhancing the HTA system were grouped under two main categories: namely, extending the reach of HTA and enhancing the impact of HTA.

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[130] Jill Sanders, CEO, Canadian Coordinating Office for Health Technology Assessment, Testimony before the Senate Standing Committee on Social Affairs, Science and Technology (Senator Michael Kirby, Chair), *Study on the State of the Health Care System in Canada* (Ottawa: March 29, 2001).

[131] Commission on the Future of Health Care in Canada, *Building on Values: The Future of Health Care in Canada*, p. 249. [See note 73.]

[132] "Discussion Paper for Symposium on Health Technology Assessment in Genetics and Policy-making in Canada: Towards Sustainable Development" (Ottawa: April 2004): www.cbac-cccb.gc.ca; Government of Alberta, Alberta Health and Wellness, *Health Technology Assessment: Alberta's Needs and Future Directions, Summary of Results of a Consultation Workshop* (September 21 – 22, 2003): www.health.gov.ab.ca (accessed: September 6, 2004); R. Atkinson, "Discussion Paper: Biotechnology and the Challenge to Governance and Management of Medicare" (unpublished paper prepared for Canadian Biotechnology Advisory Committee, October 2003). [See also note 131.]

[133] I. Haertel et al., *New and Emerging Health Related Technologies: Policy Decision-making in the Field of Biomedicine* (Paris: Organisation for Economic Co-operation and Development, 2003).

Extending the Reach of HTA

An HTA approach that is confined to evaluating the technical effectiveness of a product is not sufficient for making decisions on the adoption of BHIs by the health system. What is needed is a system that provides:

- a comprehensive multidisciplinary evaluation of biotechnology-based processes and products (i.e., not only drugs) that includes analyses of clinical effectiveness; costs, social, ethical and legal issues; and quality of life measures;
- a comparison of the new technology with other technologies already in use; and
- an assessment of the impact of the new technology on the immediate organization and delivery of health care services and on the downstream implications of adoption.

Battista and Hodge[134] express the emerging paradigm shift as follows: health technology assessment will need to shift from providing information on how practitioners should use a technology to an interactive communication of information that will assist people in making decisions. Technology assessment in the future will likely be more focused on the evaluation of a package of care rather than a single product. Such analyses are resource-intensive and, with the current capacity, only a small percentage of the technologies that are developed each year can be assessed. The organizations that carry out the bulk of health technology assessment in Canada have limited financial resources, which are already insufficient to respond to the need to build expertise in genomics, proteomics and other new aspects of biotechnology.[135]

HTA is dependent on the availability of high quality data, but relevant data are not always available. This deficiency often limits the scope of HTAs to narrow evaluations that do not go much beyond assessing the data on safety and efficacy required for regulatory approvals. When coupled with public pressure for access to new technologies, the deficiency may lead to uninformed or misinformed decisions that are difficult to remedy even when better information does become available.

The HTA system needs the capacity to undertake field studies of new biotechnologies in order to assess their costs, benefits, health system effects, and broader social and ethical impacts. Such comprehensive "on-the-ground assessments" will be increasingly important to adoption decisions, as health care systems are confronted with new products and techniques that have the potential to produce significant impacts not readily detected by standard clinical trials.

The latter category includes genetic tests for which the public demand is growing, in part as a result of intensive commercial marketing. Responding to the demand creates economic pressures for payers.[136] Initiatives have been launched in Canada and internationally to develop guidelines for the appraisal of genetic tests, some for regulatory purposes, others for coverage and service planning decisions. What is missing is an integrated policy approach for genomic technologies that is capable of incorporating important ethical and societal considerations.

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[134] R. Battista and M. Hodge, "The evolving paradigm of health technology assessment: reflections for the millennium," *Canadian Medical Association Journal* 160 (May 18, 1999), pp. 1464-1467.

[135] R. Battista, "Opening from the Chair," *Symposium on Health Technology Assessment in Genetics and Policy-Making in Canada.* [See note 126.]

[136] M. Giacomini et al., "Confronting the "Gray Zones" of Technology Assessment: Evaluating Genetic Testing Services for Public Insurance Coverage in Canada," *International Journal of Technology Assessment in Health Care* 19, 2 (2003), pp. 301-306.

Blancquaert and colleagues[137] favour a two-step implementation process for genetic tests — first testing the analytical validity of the technology prior to deployment, and then evaluating the impact of the technology during a transitional phase of restricted use (e.g., in research-based institutions). Only if second phase results are satisfactory would the test be recommended for unrestricted use in clinical practice.

Our consultations with experts[138] have reinforced the merits of conditional approvals for selected high impact bio-based innovations, and of implementing controlled evaluation in field trials. Such conditional approvals may require the development of rapid response mechanisms that provide conditional assessments to meet urgent decision needs. CCOHTA will be implementing a rapid response service to address the demand for quick access to HTA information. The success of this approach, however, depends on pan-Canadian agreement that adoption decisions will await these results. We believe that the new Health Council of Canada has an important role to play in promoting consistency in this regard. Otherwise, the "whipsaw effect" — where one jurisdiction's adoption of a technology creates pressures for other jurisdictions to do likewise — will negate the benefits from field trial results. While we do not underestimate the pressures on jurisdictions to adopt technological solutions, we strongly believe that certain innovations require precaution and that the time invested in systematic evaluation is well worth it in the long run.

In situations where investment in full-scale field trials is not warranted, but where continuing data collection is necessary to better understand the impacts of adopting a technology, post-introduction monitoring should be considered. This approach can validate the claims made by those seeking to introduce new technologies into the system. It also acts as a quality check for adverse or unanticipated outcomes. Post-introduction monitoring is particularly relevant to biotechnological innovation because the full implications of using these technologies will often not be apparent until after they are in general use.

The U.K. National Institute for Clinical Excellence (NICE)[139] is extending the reach of HTA through an assessment-appraisal approach. Technical assessment of an intervention is first completed by the HTA agency. This assessment is subsequently considered by an "appraisal committee," which focuses on implementation issues. NICE synthesizes evidence on the effectiveness and costs of treatments, and reaches a judgement as to whether, on balance, the intervention can be recommended as a cost-effective use of National Health Service (NHS) resources. Its guidance provides the NHS

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[137] I. Blancquaert et al., "Oversight Mechanisms for Technology Transfer in Molecular Genetics: Meeting the Challenge," *ISUMA: Canadian Journal of Policy Research* 2, 3 (Autumn 2001), pp. 95-101: www.isuma.net/v02n03/blancquaert/blancquaert_e.pdf. (Accessed: November 24, 2004.)

[138] National Research Council of Canada, *Report of the Expert Roundtable on Heath Technology Assessment and Health System Adoption of Biotechnological Innovations* (unpublished report prepared for the Canadian Biotechnology Advisory Committee, April 26, 2004).

[139] See: www.nice.org.uk. (Accessed: June 30, 2004.) Established in England and Wales in 1999 to provide guidance to the National Health Service (NHS) on the use of selected new and established technologies, NICE promotes:

- the faster uptake of clinically and cost effective treatments;
- more equitable access to treatments (new or existing) of proven clinical and cost effectiveness;
- better use of resources in the NHS by focusing resources on treatments which achieve the most health gain in relation to NHS expenditures; and
- the longer-term interest of the NHS in developing innovative treatments for the future.

with a common currency of effectiveness to inform and assist decision-making about treatment and care at all levels — national, local and individual. NICE is asked to look at particular drugs and devices where the availability of the drug or device varies across England and Wales, or where there is confusion or uncertainty over its value. To end this uncertainty, NICE makes a national decision on its use. Since January 2002, the NHS has been legally obliged to provide funding and resources for medicines and treatments recommended for adoption by NICE, as part of its technology appraisals program.

In Canada, CCOHTA has developed a Common Drug Review Program that may serve as a model for evaluating a broader array of BHIs. In this model, reviews are carried out centrally, followed by appraisal by a panel of experts charged with developing recommendations. Panel recommendations are then evaluated by individual jurisdictions within their own circumstances (e.g., health needs, budgets, other services, etc.) to arrive at decisions on technology adoption and funding.

The expanded approach to HTA described earlier is particularly appealing for biotechnology-based products and processes because, if appropriately designed, it could provide decision-makers with multidisciplinary analyses of the broader system and social/ethical impacts of adopting complex new technology.[140] This requires assessment teams that include health practitioners, policy-makers, epidemiologists, economists, human health resource specialists, health system administrators, researchers, ethicists, counselors and consumers. Within each of these areas of expertise, there is a need for ongoing specialized training to keep pace with new developments in basic science, clinical practice, social and behavioural sciences, implementation studies, and research on public engagement. International collaboration could be particularly helpful in meeting these needs by reducing duplication of effort and sharing expertise.

Priority setting is currently uncoordinated among jurisdictions facing similar pressures with respect to particular technologies. Consequently, it would be sensible to provide a central focus for coordinating HTA activities in such cases. CCOHTA, because of its national and international networks, is well placed to perform this role along with its other activities, including those supporting horizon scanning for the early identification of emerging drugs and technologies that are likely to have a significant impact on health care systems.[141]

[140] Ibid.

[141] CCOHTA conducts the Canadian Emerging Technologies Assessment Program (CETAP), which includes advising decision-makers about significant new developments through brief "Alerts" and, as evidence builds, through in-depth, peer-reviewed “Issues in Emerging Health Technologies” bulletins. See: www.ccohta.ca. (Accessed: September 6, 2004.)

Recommendation 6

In order to ensure that HTA is developed sufficiently to provide the comprehensive evaluations required for decision-making on the adoption of beneficial BHIs, we recommend that the federal, provincial and territorial governments, in the context of their current efforts to develop and implement a comprehensive Canada-wide strategy on HTA, put a priority on the following key actions:

- Extend the existing models of Canada-wide HTA (e.g., Common Drug Review) to assessing a wider array of biotechnology-based health innovations (products, processes and tools).
- Complement HTA with an appraisal of broader social, ethical, economic and health system impact factors by a body composed of experts equipped to assess such factors (e.g., a National Biotechnology Appraisal Committee linked to the Health Council of Canada).[142]
- Establish a rapid response mechanism to provide conditional assessments that meet urgent decision needs and that incorporate commitments to follow-on full assessments.[143]
- Mount coordinated field trials on a demonstration basis when there is insufficient HTA evidence available to determine the direct and indirect impacts of adopting a biotechnology-based health innovation.
- Develop comprehensive mechanisms for assessing the efficacy, safety and health system impacts of innovations after they have been introduced in the community, and for supporting research on methods to facilitate such assessments.
- Establish programs to maintain the capacity and expertise of the HTA system to respond to emerging needs and opportunities (e.g., effective horizon scanning). Promote capacity sharing domestically and internationally to increase quality and efficiency, and to reduce cost burdens (e.g., inter-regional or international agreements might be reached whereby specific regions or countries specialize in assessing particular types of technology).
- Develop a comprehensive communication strategy that provides balanced and objective information about assessment results (both positive and negative) to professionals, system managers and the public.

Enhancing the Impact of HTA

Uptake of HTAs by decision-makers is widely viewed as the Achilles heel of the process. So far, health technology assessments have had a marginal impact on resource allocation decisions. Assessment agencies have limited contact with decision-makers, planners, health care providers, and people who use health services. Moreover, decision-makers and planners have not made effective use of the assessment materials provided to them. Thus, decisions about purchasing new technology are too frequently made without knowing the effects on the health care system. Other factors limiting the

[142] Some believe that HTA should include the appraisal of social, ethical, economic and health system impact factors. For the purposes of this report, we use the tern "technology assessment" more narrowly to refer to the unbiased synthesis of scientific and technical evidence.

[143] Rapid response assessments should involve special efforts to canvass the broader HTA community in order to discover unpublished but relevant information.

impact of HTA include: the lack of integration of HTA data with other types of knowledge used by decision-makers; the lack of funding and incentives for HTA knowledge dissemination beyond traditional academic modalities; the impediment to dissemination because of the multi-jurisdictional nature of Canada's health care system; the lack of expertise within health care organizations related to HTA (lack of "receptor capacity"); and the absence of consumer involvement in HTA processes.[144] The latter involvement would impel HTA knowledge to be put in a form that is meaningful to consumers and, by extension, to decision-makers.

The foregoing challenges are not unique to HTA, but are features of many aspects of the organization, management and delivery of health care. The Canadian Health Services Research Foundation has implemented programs designed to build linkages and exchange mechanisms between researchers and policy-makers. This work could be the basis for efforts to improve the impact of HTAs, by expanding recognition of the value and use of HTA by decision-makers. The need to build linkages is clearly an issue that should be addressed in the development of the National Strategy on Health Technology Assessment.

Recommendation 7:

In order to support the adoption of beneficial BHIs by health care systems, we recommend that the federal, provincial and territorial governments commit themselves to the collaborative development and implementation of a comprehensive Canada-wide system that:

- Links experts in technology assessment and appraisal to experts and decision-makers involved in the organization, management and delivery of health services, and to the public — for example, through a network of researchers, HTA practitioners, knowledge brokers, health care practitioners and decision-makers engaged in setting priorities, synthesizing results, gathering data from national and international sources, and interpreting international findings in the Canadian context.
- Establishes incentives and removes or ameliorates impediments to applying technology assessment and appraisal in decision-making.
- Establishes standardized information systems and linked databases required to model the impacts of introducing BHIs on institutions or the health care system.
- Develops and disseminates educational materials related to technology assessment and appraisal, which are suitably customized for professionals, system managers and the public.
- Makes HTA results public in plain language documents, so that the public can meaningfully participate in the uptake process and make informed decisions about BHIs for personal purposes.

[144] In the U.K., consumers actually participate in setting the agendas for health technology assessment and appraisal. There, the definition of "consumers" includes patients and potential patients, caregivers, representatives of populations at special risk, and organizations that represent people that use health services. See: B. Hanley, *Involving the Public in NHS, Public Health and Social Care Research: Briefing Notes for Researchers* (second edition) (Eastleigh, England: INVOLVE, 2004): www.invo.org.uk/pdfs/Briefing%20Note%20Final.dat.pdf. (Accessed: November 24, 2004.)

3.2.4 Technology Adoption

Any discussion about the adoption of innovations by health care systems must start with an understanding of the larger context within which governments manage health care systems, and administrators make decisions concerning the services that will be provided. Spending on health care is already outpacing economic growth in most member countries of the Organisation for Economic Co-operation and Development, and Canada is no exception.[145] Given that bio-based health innovations (including new drugs) are major drivers of rising health expenditures,[146] and that more than 80% of Canadian and global investment in biotechnology research and development is focused on the health sector, it is not unreasonable to expect that both the number and complexity of biotechnology-based health innovations will increase.[147]

Demographic trends arising from an aging population indicate that the demand for health services will increase over time. The public is increasingly well informed about health matters (including via the Internet), and demanding timely, good quality health care. It can be expected that the public will generate steady pressure on governments to adopt new technologies that promise significant benefits. As indicated earlier in this report, these new technologies will increasingly be based on scientific advances in molecular and cellular biology.

Health care systems face difficult choices concerning the adoption and funding of these innovations, not only because of their technical complexity and impact on the organization of health care generally, but because of their ethical and social implications. Decision-makers must be equipped to make decisions about the adoption of BHI, which in some cases present special challenges such as:

- the ethically controversial nature of biotechnologies that involve or affect human reproduction, crossing of species barriers, genetic privacy, and the use of human embryos for therapeutic purposes;
- the development of highly efficient yet costly treatments for rare conditions, or for those targeted at increasingly small patient subgroups as a result of our ability to personalize treatment through advances in pharmacogenomics; and
- the pressure on decision-makers to adopt diagnostic or therapeutic innovations that address previously intractable clinical problems, before there have been full assessments of longer-term clinical effects and health system impacts.

The Commission on the Future of Health Care in Canada did not directly address the impact that biotechnology will have on the health care system. However, the Commission paid considerable attention to the issue of medical necessity, concluding that "the definition of what is considered medically necessary and covered under the [*Canada Health*] *Act* needs to be updated to reflect

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[145] Organisation for Economic Co-operation and Development, Health Policy Unit, *Health at a Glance: OECD Indicators 2003* (Paris: OECD, 2003). See also: Canadian Institute for Health Information, *Health Indicators 2003* (Ottawa: May 2003).

[146] Conference Board of Canada, *Making Innovation Happen: Prospects for Research-Intensive Pharmaceutical Firms in Canada* (Ottawa: 2002): www.conferenceboard.ca/Health/reports.htm. (Accessed: July 20, 2004.)

[147] The cost of pharmaceuticals has grown more than any other component of health care over the past two decades. The total drug expenditure rose by 500%, from $4 billion in 1985 to $18.1 billion in 2002 (16.2% of total health care spending), more than three times the growth rate of total spending on health care. Most of this increase in pharmaceutical spending has been funded privately. See: Canadian Institute for Health Information, *Drugs Expenditure in Canada, 1985–2002* (Ottawa: April, 2003).

therealities of our contemporary health care system."[148] Biotechnological innovation is one of these realities. Genomic medicine will change medical practice,[149] and governments must prepare now for the challenges that will accompany this shift.

Creating a Culture of Innovation and Collaboration

Currently, Canada's health care systems do not have a systematic approach to identify and finance new technologies, so that the best technologies are quickly integrated into the health system while ineffective or outmoded approaches are set aside or restricted in use. Practices vary between provinces, regional health care systems, hospitals, and health care practitioners. This diversity is not surprising given that there has been relatively little systematic study on how health technology is introduced — i.e., who decides what technology will be introduced and used, what criteria they use, what evidence is used or rejected, who is consulted, and how medical practitioners and the public are prepared or engaged.

The effectiveness of *ad hoc* approaches is questionable in the face of rapid technological development and growing public demand. Our health care systems need: (i) the capacity to systematically identify those technological innovations that are likely to improve health outcomes and/or the capacity to deliver high quality care; and (ii) the ability to shift from a culture of cost-containment and budgetary silos to one with the flexibility and innovative spirit necessary to maximize the deployment of effective innovations.

Limited budgets for health care are a reality. The potential for BHIs to substantially increase the scope for health interventions means that their adoption will have to be funded, to a considerable degree, by reallocating existing resources to new uses. Constraints on the ability of health administrators to reallocate funding from older approaches to new and preferred methods and technologies — or even to ensure that the most cost effective options are given preference — impedes the entry of new technologies. This creates a systemic bias against the introduction of new technologies that may limit timely access to the most cost effective diagnostic tools and treatments. As participants at the National Symposium on Health Technology Assessment and Genetic Policy noted: "the incremental build-up of technology does not provide for ways of retiring older technologies so we are left with a sediment that get thicker and thicker."

A second and related issue is the fact that even when a new technology can be shown to reduce overall costs, there may be resistance to its introduction due to what has been termed the "multiple pocket" phenomenon. For example, one of the most frequently cited challenges by health administrators is the rapid growth in the budget for drugs. Typically, debate on this issue does not take into account that pharmaceutical interventions may greatly improve the health of patients, or that patients may return to work and productive activity sooner thus benefiting society, or that considerable savings may accrue to the health system by avoiding other costs. The focus is on total drug costs. In part, this arises because the cost savings may be in different parts of the health budget (such as hospital beds or nursing services or surgery), while the drug budget that accrues the costs

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[148] Commission on the Future of Health Care in Canada, *Building on Values: The Future of Health Care in Canada.* [See note 74.]

[149] P. Hamet et al., "New Genetics and the Medical Curriculum," *Annals of the Royal College of Physicians and Surgeons of Canada* 35 (August 2002), pp. 299-302.

cannot either claim or gain access to the savings arising elsewhere. Moreover, some savings only appear over a period of time that is much longer than the budget cycle.

Experience shows that the uptake of medical innovations can sometimes be too rapid, in that some innovations may be widely used before studies have proven their effectiveness. It was only after electronic fetal monitoring of women in labour was widely used by obstetricians that studies showed it was actually harmful in low-risk pregnancies, and led to an increase in Caesarean sections and other procedures that put women at greater risk.[150] Despite this knowledge, it has been very difficult to reduce the use of fetal monitoring because it has become established medical practice. On the other hand, some innovations diffuse too slowly, and patients do not get the benefit of diagnostic procedures and treatments for which there is strong evidence of effectiveness. The latter issue has prompted officials in the United States to strike a task force to find ways to promote speedier access to safe and effective medical technologies.[151] The outcome of this effort may have implications for Canada's regulatory system (capacity and process), and affect public expectations about speed of access to innovations.

The challenges that decision-makers face are illustrated in the following examples. While the direct costs associated with the introduction of an innovation can be estimated with reasonable confidence, the indirect costs and economic benefit are much more difficult to assess.

- Provincial health ministries have recently faced a decision on whether to fund the drug "Fabrazyme," a treatment for Fabry's disease. This disease is characterized by strokes, heart disease and kidney failure prior to the age of 40, and caused by a gene mutation resulting in a deficiency in an enzyme involved in the metabolism of lipids. Treatment with Fabrazyme is estimated to cost $200,000 per patient per year. Although Fabry's disease is rare (only 75 people in Alberta have the disease), the $15 million per year that it will cost Alberta for this treatment is likely less that the cost of treating the consequences of the disease.
- Not all new biotechnology innovations are expensive; in fact, some are quite inexpensive. A genetic test for Factor V Leiden (a mutation that predisposes a person to clotting within blood vessels) costs only $20.[152] A positive result from this test may either increase health care costs, because it indicates the need for a lifetime of blood-thinning drugs, or reduce them, as the need to investigate and treat blood clots in the legs or lungs is avoided.
- A research group in Ontario examined the impact of genetic tests on health care costs.[153] In evaluating two tests, it was determined that there would be net savings of $500,000 a year in Ontario alone if only high-risk persons were tested, but there would be a net cost of $60 million if used in an unfocused screening program. Another test, for Alzheimer's disease, would increase net costs by $10–20 million. Even if the cost is borne by the individual rather than through Medicare, the use and targeting of genetic testing needs to be carefully managed because the adverse financial impact on the health care system of uncontrolled testing can be significant.[154]

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[150] G. Anderson, *Intrapartum Electronic Fetal Monitoring* (Ottawa: Canadian Task Force on Preventive Health Care, March 1994).

[151] U.S. Department of Health and Human Services. News Release (May 19, 2004).

[152] Brenda Wilson, University of Ottawa, personal communication.

[153] F. Miller et al., *Predictive Genetic Tests and Health Care Costs* (Toronto: Ministry of Health and Long-Term Care, January 2002).

[154] S. Morgan et al., "Predictive Genetic Tests and Health System Costs," *Canadian Medical Association Journal* 168 (April 15, 2003), pp. 989-991.

The challenges are not confined to issues of relative cost and benefit associated with technology innovations. The ethical and social issues that arise will be at least as difficult, and are likely to exert increased pressure on existing mechanisms that regulate or influence the entry of new products onto the Canadian market. The goal of ensuring access by Canadians to safe and effective health interventions will be compromised if these mechanisms do not have the capacity to adapt to new challenges. However, the fundamental challenge of public policy in this regard is the need for enhanced capacity — not merely to produce and absorb innovations, but also to guide the process of innovation in directions that will materially improve health.

It has been argued that, rather than viewing health innovations as a burden, they should be viewed as opportunities — not only to improve health but also to create an affordable health system.[155] [156] It is posited that linking Canada's health innovation and economic agendas would provide substantial benefits to both sectors. By using the collective purchasing power of Canada's single-payer health care system more effectively, increasing the proportion of Canada's investment capital devoted to the life sciences, and marketing Canadian innovations to other countries more successfully, we can repatriate jobs, improve the balance of payments and add billions of dollars annually to the Canadian economy. This concept has informed the work of Health Innovation Canada, which was referred to earlier in the section on Regulation and Commercialization.

Perhaps more than ever before, decision-makers will need to rely on organizations equipped to generate evidence of the system-wide impacts of bio-based innovations before these technologies are adopted and diffused. They will need to understand the social and ethical dimensions of adoption for widespread use. And they will need to move out of budgetary silos in the interests of incorporating beneficial innovations and removing existing, and perhaps longstanding, approaches from their health care portfolios. In other words, managers of health systems will need to become innovators themselves.

Learning More about Adopting Biotechnology-based Health Innovations

As noted previously, there is no systematic approach to ensuring that appropriate new technologies are identified and financed, in a manner that will ensure that the best technologies are quickly integrated into the health system and that outmoded approaches are set aside or restricted in use. The absence of a consensus on best practice in these matters makes it difficult to be prescriptive in offering advice on how to improve the identification and uptake of new beneficial technologies, as well as the rejection or removal of ineffective or unnecessarily costly medical technologies.

Health care administrators indicate that there are insufficient incentives in the system for advocating the introduction of supporting leading-edge technology, or for sensible experimentation to evaluate risks. By contrast, the penalties (especially unknown future cost commitments) for technology failure are extremely high. As a result, most hospitals, especially medium-sized and smaller hospitals, avoid adopting significant innovations that have not been previously tested and proven elsewhere. Further,

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[155] H. Friesen, "Presentation to Public Policy Forum Roundtable." [See note 106.]

[156] Life science investments comprise 12% of the capital markets in the U.S. but only 2% of those in Canada. A 1% shift of Canadian capital markets into life sciences would represent $10 billion in investment capital. See: "New Models for Investing in Innovation in Health" (background paper prepared for Public Policy Forum Roundtable, see note 106).

the absence of risk pooling and pilot testing mechanisms to fully assess the in situ impacts and effects of new medical technologies present a systemic bias against the adoption of new technologies.

A partnership between the Canadian Institutes of Health Research, Health Innovation Canada, the Canadian Health Services Research Foundation, CCOHTA and the Health Council of Canada could be created to identify the health care and public/population health objectives for which biotechnological applications should be pilot-tested. The pilot tests should include social and managerial innovations that enhance the capacity of the health system to reallocate limited resources among its areas of responsibility, in order to reflect optimum use in relation to clinical outcomes. This will be particularly important for applications such as pharmacogenomics, gene therapy and stem cell therapies, that involve considerable financial and managerial risks, and that may be controversial. The absence of mechanisms and incentives for creating constructive linkages between the health sector and Canadian entrepreneurs have made it difficult for health system managers to articulate their needs in a manner that would allow them to be converted into a "demand" from innovators — i.e., health system pull on innovation. If this could be done, it might be possible to attract the energies of innovators, including those in the private sector, to provide new products or services that meet specific health system needs. In our consultations, we learned that health system managers have a limited ability and no clear incentive to devote their time and resources to working with smaller- and medium-sized Canadian firms to increase their understanding of how their potential products or services must perform in order to be useful within the real world of the modern medical setting.[157] Correcting this deficiency requires the creation of linkages between health care institutions and Canadian innovators that connect health care system needs with private sector priorities, and are focused on improving and/or reducing the cost of health care services and stimulating the development of an innovative industry with strong export potential.

Our consultations identified the following key underpinnings of a health care system that is equipped for bio-based innovations (and health innovations generally):

- a more broadly based and deeply rooted culture of innovation among management, professionals and staff;
- effective change management methodologies and training to support new innovations;
- information systems and analytic capacity to evaluate innovative solutions;
- rigorous assessment of new technologies after implementation; and
- supportive financial management systems that facilitate funding of innovations in one area of practice with savings from another.

The public has a major influence on health care funding decisions. Mechanisms designed to provide objective information and seek the public's views on trade-offs they are willing to make, as well as on the acceptability of new innovations, will need to be incorporated into decision-making about technology adoption issues. Engaging the public in dialogue must be viewed as an integral component of the decision-making process, and public engagement must receive adequate resources to support meaningful results. Organized efforts to create a community of interest around citizen engagement in the health sector would assist in developing best practices and building/sustaining expertise in this

[157] National Research Council, Office of Technology Oversight, *Expert Panel on Bio-health Commercialization Challenges* (Ottawa: January 28, 2004).

area. In Canada, regrettably, the processes for public participation in this area are, in general, poorly developed and a concerted effort is required to repair this deficiency.

Recommendation 8:

We recommend that a body, sponsored by or involving the federal, provincial and territorial governments and other stakeholders (such as the newly formed Health Council of Canada), contribute to improvements in Canada's ability to adopt beneficial BHIs by:

- Sponsoring studies to systematically identify barriers to the adoption of BHIs by the health system, and make recommendations to remove or ameliorate the barriers.
- Addressing the challenge of how the health care system can deal with the adoption of BHIs for which assessments and appraisals are incomplete or unavailable — including by determining the desirability and feasibility of establishing mechanisms to provide conditional approval for adoption.
- Identifying best practices in Canada and abroad for public (consumer) engagement in all stages of technology appraisal and assessment, and promulgating goals, strategies and guidelines to implement them on a Canada-wide basis. Specific consideration should be given to including the use of appropriate engagement practices among the attributes evaluated in institutional performance reviews and/or in accrediting health care institutions.

3.3 Foundations of Success

As we considered the readiness of our systems for BHIs, it became clear that, in addition to specific initiatives related to research and development, regulation and commercialization, health technology assessment and technology adoption by the health system, successful policy-making must be enabled by certain general strategies pertaining to collaboration, capacity building, public participation, education and support for evidence-based decision-making

Collaboration

Optimizing the potential of biotechnology to contribute to improving the health of Canadians requires cross-jurisdictional mechanisms, networks and operational linkages among, for example:

- a variety of sectors, including health, the economy, agriculture and the environment;
- the federal and provincial/territorial governments in relation to all the key components of health innovation, including research, assessment, regulation, citizen engagement, and assimilation and uptake in health care and public health;
- the public and private sectors in order to provide the expertise and risk capital needed; and
- Canada, its G8 partners, and developing countries, in order to share knowledge and find ways to engage in international efforts that benefit all.

Capacity Development

There is an urgent need to build the depth and range of expertise required to meet the goals of public policies related to BHI.

Optimizing access to the health and quality-of-life benefits of BHI in a cost-effective and efficient way involves:

- educating health care professionals, administrators and analysts about biotechnology and health; and
- developing processes, structures and personnel within the health system to enable effective knowledge transfer and the uptake of BHI, both at the system level (knowledge brokers) and at the clinical practice level (mobilizing the potential of general practitioners and nurses to facilitate the assimilation of BHI and to complement the efforts of specialists [such as genetic counselors] in rapidly advancing fields).[158] [159] [160] [161]

Addressing and managing the potential challenges and hazards that may be associated with BHI, and ensuring the responsible and ethical use of BHI, involves:

- improving capacity for regulation and assessment through continuing education of existing personnel, and the training and recruitment of additional personnel; and
- broadening the range of disciplines involved in technology assessment and appraisal to ensure that both biological and social dimensions of BHIs are appropriately addressed.

Building and sustaining the scientific and managerial capacity to generate, adopt and assimilate beneficial BHIs involves:

- complementing current programs of single discipline-based training with enhanced opportunities for dual-track training of scientific and managerial personnel (e.g., MD/PhD and PhD/MBA programs);
- increased team-based training to break down disciplinary and professional barriers; and
- fostering a strong, sustained capacity for research and development, both in the life sciences and social sciences.

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[158] D.W. Glasspool et al., "Risk Assessment in Genetics: A Semi-qualitative Approach," in *Proceedings of the Tenth World Congress on Health and Medical Informatics* (Medinfo2001, September 2-5, 2001) (London, U.K.: 2001), pp. 459-463.

[159] L. Mann, "The New Genetics: the general practitioner and the 'new genetics'," *Medical Journal of Australia* 179 (2003), pp. 109-111.

[160] D. Shickle et al., "The genetics liaison nurse role as a means of education and supporting primary health care professionals," *Family Practice* 19 (2002), pp. 193-196.

[161] D. Donnai et al., "Genetic counselors could be based in genetic centres but be formally linked to general practice" (letter), *British Medical Journal* 321 (July 22, 2000), p. 240.

Public Participation

There are a variety of points in the development and adoption of BHIs at which public participation is needed to ensure that the public interest is adequately served. Such participation is likely to be most important and productive at two levels:

- in discussions and debates about the ethical and social issues associated with the evolution of the legislative and regulatory framework for BHIs; and,
- in the processes of technology assessment and appraisal leading to decisions about adopting BHIs at the local and provincial levels.

Canadians need reliable, clear information and an understanding of the nature of the issues involved if they are to participate knowledgeably in crafting public policy. The sources of that information clearly include not only governmental, institutional and voluntary agencies, but also the popular media.[162]

Ensuring that adequate time is allocated to genetics and biotechnology in primary and secondary schools is seen as helping to solve the problem for future generations. Educating adults is more challenging. The U.K. has recognized the need to tackle this issue and its Department of Health supports the Progress Educational Trust[163] to educate Britons about genetic issues. A recent U.K. government white paper has allocated an additional £200,000 to the Trust for this purpose.[164]

Education

Apart from education about biotechnology to support public participation in policy-making, strategies are needed to enhance knowledge about clinical applications of biotechnology among both health care providers and patients. Physicians and other health professionals involved in primary care should be a special focus of educational efforts in this regard so that investigations and treatments based on new and complex biotechnological advances are applied judiciously and with the consent of patients who are as duly informed.

It is worth noting that in the U.S., the Centers for Disease Control's strategic plan for genomics and health identified the education of public health professionals as a priority area for action.[165] In addition, the U.K. recently decided to set up a Genetics Education and Development Centre to educate health professionals, and has allocated resources to a number of educational initiatives.[166] At present, no large-scale national efforts along these lines exist in Canada.

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[162] I. Hargreaves et al., *Science and the Media: Towards a Better Map* (Swindon, England: Economic and Social Research Council, 2003).

[163] See: www.progress.org.uk. (Accessed: September 6, 2004.)

[164] United Kingdom Department of Health, *Our Inheritance, Our Future*, p. 76. [See note 66.]

[165] Centers for Disease Control and Prevention, *Translating Advances in Human Genetics into Public Health Action: A Strategic Plan* (October 1, 1997): www.cdc.gov/genomics/about/strategic.htm. (Accessed: July 20, 2004.)

[166] United Kingdom Department of Health, *Our Inheritance, Our Future*. [See note 66.]

In Canada, the "Geee! in Genome" exhibition is a bilingual, national public education project that is designed to educate Canadians about genomics and its relevance to nature and human life. It also highlights the contributions of Canadian scientists working in the field, paying particular tribute to the late Dr. Michael Smith, a Nobel laureate. The project was launched on April 25, 2003, the 50th anniversary of the first published scientific description of the DNA double-helix structure. The exhibition is currently on a cross-Canada tour.[167]

Support for Evidence-based Decision-Making

Given a commitment to evidence-based decision-making at all levels, it is essential that the data and resources required for this function be adequately developed to support optimum data management, record linkage, and the development and incorporation of appropriate performance measures.

[167] See: www.nature.ca/exhibits/genome_e.cfm. (Accessed: July 20, 2004.)

Concluding Observations

In our statement to the Innovation Summit in 2002, we noted that transformative technologies like biotechnology bring fundamental changes to societies and thus hold important implications for all Canadian regions, communities and sectors.[168] In no sphere is this likely to be more evident than in BHI. The development and beneficial application of health-related biotechnology must therefore be a central element in the articulation and implementation of Canada's overall Innovation Strategy.

Our analysis of the role of biotechnology in health innovation clearly supports our view that "policies and programs seeking to promote successful and sustainable innovation in the broadest sense must focus not only on the technical aspects of innovation but also on fostering the social and institutional transformations necessary to realize the full social and economic benefits of technological advances and to manage the challenges, pressures and uncertainties."[169]

We believe that implementation of the recommendations in this report will assist the federal government and its provincial and territorial partners in:

- addressing the development of biotechnology in a manner that reflects the values of Canadians, protects the environment, ensures sustainability, and builds social cohesion and consensus;
- achieving a fair distribution of benefits including greater equality of access to useful products and services for all Canadians; and
- nurturing our intellectual and entrepreneurial resources, thereby strengthening our economic independence and sovereignty, boosting employment, stimulating greater productivity, and increasing our standard of living.

Identifying and successfully introducing BHI requires the involvement of all sectors of Canadian society in a process of institutional transformation. The transformations may involve changes in how existing institutions — both within and outside government — are organized and perform their functions; the development of new organizations; or the development of partnerships, alliances and networks among institutions and organizations. The institutional transformations fall into two categories: those that focus on social and economic development (e.g., education, training, research, knowledge transfer, the search for best practices, risk capital supply, staying abreast of scientific and technological advances, and new approaches to enhancing access to benefits); and those that focus on regulation (e.g., risk assessment, management and communication; protection of human health, animal health, and the environment; and respect for core social values). The transformation will inevitably involve striking a sustainable balance between competing objectives and social values.

[168] Canadian Biotechnology Advisory Committee, "Biotechnology and Canadian Innovation: Statement on the Occasion of the National Summit on Innovation and Learning" (November 18-19, 2002): www.cbac-cccb.gc.ca/epic/internet/incbac-cccb.nsf/en/h_ah00036e.html. (Accessed: November 24, 2004.)

[169] Ibid.

Annex 1
Abbreviations and Acronyms

AETMIS	Agence d'évaluation des technologies des modes d'intervention en santé
BDDA	Biotechnology Drug Development Accelerator
BHI	Biotechnology-based Health Innovation
BMCC	Biotechnology Ministerial Coordinating Committee – Government of Canada
CBAC	Canadian Biotechnology Advisory Committee
CBI	Canadian Bio-processing Initiative
CCAC	Canadian Council on Animal Care
CCOHTA	Canadian Coordinating Office for Health Technology Assessment
CIHR	Canadian Institutes of Health Research
DNA	Deoxyribonucleic acid
HIC	Health Innovation Canada
HTA	Health Technology Assessment
IDF	Innovation Development Fund
IP	Intellectual Property
IRAP	Industrial Research Assistance Program of the National Research Council of Canada
NCEHR	National Council of Ethics in Human Research
NHS	National Health Service of the U.K.
NICE	The U.K. National Institute for Clinical Excellence
NRC	National Research Council of Canada
PCBs	Polychlorinated biphenyls
PMPRB	Patent Medicine Prices Review Board – Government of Canada
R&D	Research and Development
TPC	Technology Partnerships Canada – Government of Canada

Annex 2
Glossary of Terms

ALS (Lou Gehrig's Disease)
Also called Lou Gehrig's disease, amyotrophic lateral sclerosis (ALS) is a progressive, fatal neurological disease that belongs to a class of disorders known as motor neuron diseases. ALS occurs when specific nerve cells in the brain and spinal cord that control voluntary movement gradually degenerate.

Bioinformatics
The science of managing and analyzing biological data using advanced computing techniques. Bioinformatics is especially important in analyzing genomic research data.

Biopharmaceuticals
Biopharmaceuticals is concerned with pharmacologically active substances derived from or related to the use of living organisms or their components.

Bioremediation
The use of biological organisms, such as plants or microbes, to aid in removing hazardous substances in the environment.

Biosensor
Device in which powerful recognition systems of biological chemicals (enzymes, antibodies) are coupled to microelectronics to enable low-level detection of substances such as sugars and proteins in body fluids, pollutants in water, and gases in air.

Biotechnology
A body of technical knowledge about living organisms or their constituent parts. Applied biotechnology includes those aspects of biotechnology that are used to make products and drive processes that serve social, scientific or economic purposes.

BSE (Bovine spongiform encephalopathy)
A progressive neurological disorder of cattle that results from infection by an unconventional transmissible agent. The nature of the transmissible agent is unknown. Currently, the most accepted theory is that the agent is a modified form of a normal cell surface component known as prion protein. The pathogenic form of the protein is both less soluble and more resistant to enzyme degradation than the normal form.

Commercialization
Commercialization by the private sector is the predominant avenue through which new technology is made available for use in the health system. Bringing biotechnology products to market is a complex, expensive and time-consuming process.

Diagnostic
A product used to diagnose a disease or medical condition. Both monoclonal antibodies and DNA probes are useful diagnostic products.

Deoxyribonucleic acid (DNA)
The molecule that carries the genetic information for most living systems. The DNA molecule consists of four bases (adenine, cytosine, guanine, and thymine) and a sugar-phosphate backbone, arranged in two connected strands to form a double helix.

DNA bank
A collection of genetic information, whether in the form of samples or data, extracted from blood samples or other human tissue.

Downstream processing
The stages of processing that take place after the fermentation or bioconversion stage; includes separation, purification, and packaging of the product.

Down Syndrome
A developmental disability, due to trisomy of chromosome 21.

Epigenetics
Commonly defined as the study of heritable changes in gene function that occur without a change in the DNA sequence.

Eugenics
The study of improving a species by artificial selection, eugenics usually refers to the selective breeding of humans.

Gene therapy
An experimental procedure aimed at replacing, manipulating, or supplementing nonfunctional or misfunctioning genes with healthy genes.

Genetic counseling
Provides patients and their families with education and information about genetic-related conditions and helps them make informed decisions.

Genetic discrimination
Prejudice against those who have or are likely to develop an inherited disorder.

Genetic engineering
The process of changing the genetic makeup of one organism by transferring DNA from another organism. Also known as ***recombinant DNA technology***.

Genetic medicine
Malfunctioning genes have been linked with a thousand disorders, ranging from heart disease, diabetes and asthma to cancer, obesity and Alzheimer's. Doctors hope to use the human genome to

devise medicines that block the working of a flawed gene, thus causing a disease to be stopped or reversed.

Genetic patents
Involves granting the right or title to genes, gene variations, or identifiable portions of sequenced genetic material to an individual or organization.

Genetic predisposition
Susceptibility to a genetic disease. May or may not result in actual development of the disease.

Genetic privacy
The right to restrict what people are allowed to know about you, and the confidentiality of your genetic information once it has been collected and stored.

Genetic testing
Analyzing an individual's genetic material to determine predisposition to a particular health condition or to confirm a diagnosis of genetic disease.

Genomics
The study of genes and their function.

Herd immunity
If enough people in a community are immunized against certain diseases, then it is more difficult for that disease to get passed between those who are not immunized. Herd immunity does not apply to all diseases because they are not all passed on from person to person. For example, tetanus can only be caught from spores in the ground.

Huntington's Disease
A progressive disorder involving degeneration of nerve cells in the brain. This disease is inherited as a single faulty gene on chromosome 4.

Immunotherapy
Treatment to stimulate or restore the ability of the immune system to fight infections and other diseases. Also known as biological therapy, biotherapy, or biological response modifier (BRM) therapy.

Informed consent
An individual willingly agrees to participate in an activity after first being advised of the risks and benefits.

Innovation chain
The process whereby a product is developed, from concept to commercialization, and eventually attains market entry.

Knowledge transfer
The transfer of research-based knowledge from the research community to the community of potential users.

Molecular biology
The study of the structure, function and makeup of biologically important molecules.

Nanotechnology
Research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1-100 nanometer range. Nanotechnology, or what could more specifically be termed "**molecular nanotechnology"** or "**molecular manufacturing**," is the anticipated ability to inexpensively fabricate complex devices, both large and small, with precise control over the arrangement of the individual atoms that constitute the device.

Orphan diseases
Diseases and conditions, such as Huntington's Disease and ALS (Lou Gehrig's disease), which affect such small numbers of individuals that the diseases and conditions are considered rare. See also ***Huntington's Disease*** and ***ALS***.

Patent
The exclusive right to make, use and sell an invention, and to prevent others from doing so without permission.

Pharmacogenetics/pharmacogenomics
Pharmacogenetics is the study of how particular genes influence the responses of organisms to drugs.

Pharmacogenomics is the study of the genomes of organisms to identify genes and their variants that are or may be involved in variable responses to drugs, or that are associated with abnormal metabolic processes that may be appropriate targets for new therapeutic drug development.

It should be noted that the terms pharmacogenetics and pharmacogenomics are sometimes used interchangeably.

Population genetics
The study of variation in genes among a group of individuals.

Protein engineering
The creation of synthetic proteins designed to carry out specific tasks.

Proteomics
The study of the full set of proteins encoded by a genome.

Recombinant DNA technology
See Genetic engineering.

Regulation
Regulation in its broadest sense is equated with governing. It is a principle, rule or condition that governs the behaviour of citizens or enterprises. In this way, regulation is used by governments, in combination with other instruments such as taxation, program delivery and services, to achieve public

policy objectives. Regulation encompasses a range of instruments that include formal rules, such as statutes, and less formal instruments, such as guidelines and standards.

SARS (Severe Acute Respiratory Syndrome)

A viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV).

Technology transfer

The process of transferring scientific findings from research laboratories to the commercial sector.

Annex 3
Major Canadian Work Underway in the Area of Biotechnology and Health Innovation

I. Key Organizations Undertaking Biotechnology and Health Innovation Research and Development

ORGANIZATION	DESCRIPTION
The Advanced Foods and Materials Network of Centres of Excellence (AFMNet)[170] www.afmnet.ca[171]	The ***Advanced Foods and Materials Network*** (AFMNet) brings together natural scientists, engineers, health researchers, social scientists, and lawyers to work on various facets of food and bio-material advances in a manner that is unique in its field. AFMNet aims to create the next generation of multidisciplinary scientists and researchers who will be able to contribute to large projects where their expertise combines with that of many others to advance the research. AFMNet addresses three broad themes: the structure, dynamics, and function of foods and bio-materials; functional foods and nutraceuticals; and economics, environment, and society issues (such as regulations and consumer attitudes and perceptions). Potential outcomes of AFMNet research include reduction in diet-related diseases; improved healing through better wound dressings; improved food quality by better controlling texture, flavour, and colour; improved food safety through the control of biofilms in foods and processing equipment; and increased public confidence in the food supply by creating the necessary knowledge to help develop and define regulations and laws.
The Canadian Genetic Diseases Network of Centres of Excellence (CGDN) www.cgdn.ca	When the ***Canadian Genetic Diseases Network*** (CGDN) was created, no other organization in Canada focused on medical genetics. As interest in this subject grew, other organizations began to fund research. CGDN's network approach, however, remains unique in providing opportunities for leading geneticists to collaborate and in helping to accelerate rates of discovery. CGDN has been associated with the discovery of more human disease genes (over 50) than any other non-profit organization in the world. To combat the perpetual shortage of highly qualified personnel in the field, CGDN is taking a proactive role in training genetic scientists in leading-edge technology as well as

[170] The Networks of Centres of Excellence Program (nce.nserc.ca) is funded by the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council (NSERC) and the Social Sciences and Humanities Research Council. Twenty networks, in a range of areas, are currently funded through this program.

[171] All websites were accessed on September 23, 2004.

ORGANIZATION	DESCRIPTION
	encouraging young Canadians to enter science. CGDN's Canadian Bioinformatics Workshops series has made a significant contribution to increasing the number of trained computational biologists in Canada. Interest in the series has been profound, as evidenced by the 172 students who completed workshops in 2002-03, and the bursaries provided by the Burroughs-Wellcome Fund.
The Stem Cell Network of Centres of Excellence www.stemcellnetwork.ca	The ***Stem Cell Network*** is a unique collaboration of ethicists, lawyers, biologists, bioengineers and clinicians dedicated to finding cures for some of society's most devastating diseases, including Parkinson's, Type 1 diabetes, stroke, hemophilia, and cardiac and ocular diseases. Its research program addresses four broad issues in bringing stem cell-based therapies to the clinic: how stem cells work at the cellular and molecular level; how to generate sufficient numbers of stem cells for clinical use; identifying the clinical protocols that will allow treatments to be effective; and examining the overarching legal, ethical and commercial issues that permeate this field. Beyond conducting research, the Network has a responsibility to inform, and it puts tremendous effort into making both the science and the ethical issues accessible to parliamentarians and the public. In its short existence, the Stem Cell Network has already emerged as Canada's most important voice in providing expertise to people seeking information, thanks in part to its website — a dedicated outreach vehicle that logs over 75,000 hits a month. Individual researchers also play a key role: almost 20% of them appeared as expert witnesses during the committee stages of Bill C-13, the *Assisted Human Reproduction Act*.
Canadian Bacterial Diseases Network of Centres of Excellence (CBDN) www.cbdn.ca	The ***Canadian Bacterial Diseases Network*** research covers a broad range of bacterial disease under three themes: vaccines and preventatives, therapeutics, and diagnostics. This research has had an impact on both the health of Canadians and the vitality of the Canadian economy. CBDN's science program is also dedicated to the training of highly qualified personnel (HQP). The Network has extended the training of its young scientists into new dimensions that bear directly on the promotion of university-industry linkages. These are Intellectual Practices (IP) training, Good Laboratory Practices (GLP) courses, and industry interactions. The latest initiative is the creation of an IP Primer – a research and training tool. The scientific discoveries of the researchers in CBDN are the basis for solutions and new technologies that can be transferred from academia to industry. CBDN is partnered with a not-for-profit facilitator company, the Canadian Microbiology Consortium Inc. (CMCI), providing a network-wide standard interface for these commercialization activities.
Canadian Arthritis Network of Centres of Excellence (CAN) www.arthritisnetwork.ca	The ***Canadian Arthritis Network*** (CAN) undertakes research in the following areas: genetics, inflammation, cellular and molecular biology, bioengineering for joint reconstruction, diagnostics and therapeutics, and methodologies and outcomes. The Network supports trainees with funding and programs, such as training rotations, that expose them to leading Canadian and international academic arthritis researchers. These opportunities stimulate fresh ideas, career development, and a desire to remain in Canada at the cutting edge. Consumer involvement is a unique feature of the Network. Consumers want relief from the pain, fatigue and symptoms of arthritis. CAN's Consumer Advisory Council actively participates in decision-making on all CAN committees as well as the review process for funding research and training. Its participation reminds the scientists that their work is not only about a disease, but is also about people.

ORGANIZATION	DESCRIPTION
Canadian Network of Centres of Excellence for Vaccines and Immunotherapeutics (CANVAC) www.canvac.ca	The ***Canadian Network of Centres of Excellence for Vaccines and Immunotherapeutics*** (CANVAC) has chosen to focus initially on cancer, HIV, and hepatitis C virus (HCV) infections because they are life-threatening, chronic diseases, for which there is a sound rationale for vaccines and/or immune-based therapies. CANVAC's research program has been rationalized to expedite translation of basic discoveries into clinical trials. The program focuses on six major themes: HIV vaccines; therapeutic HCV vaccines; breast and prostate cancer vaccines; the social sciences as they relate to vaccination; biology of dendritic cells (used as vaccine candidates); and immune monitoring to evaluate immune responses in vaccinated volunteers. CANVAC researchers have now completed a clinical trial with a melanoma vaccine and are currently analyzing the data. Another trial, sponsored by the Ontario Cancer Research Network, on a breast cancer vaccine is underway. Research is also moving forward on a prostate cancer vaccine, further to the identification of promising new candidate antigens. Additionally, the very first vaccine-based, investigator-driven therapeutic trial on HIV in Canada will shortly take place in collaboration with industry and the Canadian HIV Trials Network. Here, the goal is to restore and strengthen the immune system in HIV-infected, immunocompromised patients. In combination with antiretroviral therapy, vaccination may help patients control the replication of the virus and benefit from a drug holiday. CANVAC is currently a reactive network. With its industrial partners, ultra-modern laboratories and broad spectrum of knowledge, it is ideally positioned to become a centre of vaccine development for emerging viruses. That preparedness was tested and proven with the SARS epidemic. Indeed, CANVAC participates in a national effort, led by the CIHR Institute of Infection and Immunity, against the virus and opened up its state-of-the-art facilities to monitor individual immune responses to the infection and to develop candidate vaccines.
Canadian Stroke Network of Centres of Excellence (CSN) www.canadianstrokenetwork.ca	Currently, there are few funding mechanisms in Canada for large-scale collaborative projects in stroke research. With its breadth of expertise and access to partners, the ***Canadian Stroke Network of Centres of Excellence*** (CSN) is in an ideal position to help make Canada a strong contributor in advancing knowledge about stroke disease and management. To meet this challenge, CSN has been gradually evolving its research program toward collaborations, where applicable, and toward research that will lead to tangible social or economic benefits. For example, the Registry of the CSN is the world's largest and most comprehensive database on stroke patients. To date, information has been gathered on more than 9,000 patients in 21 hospitals across the country. The information includes how long it took them to reach hospital, how quickly they were treated, how soon they were seen by rehabilitation specialists, and whether different kinds of care affected the consequences. A number of projects and queries are now arising from the data (e.g., policy-makers are using it to find out how Ontario's Co-ordinated Stroke Strategy can implement changes in the way stroke patients are handled). Eventually the Network hopes to feed data straight back to the hospitals so they can evaluate their effectiveness using up-to-the-minute information. In partnership with the Stem Cell Network, CIHR's Institute of Neurosciences, Mental Health and Addiction, and the Institute of Circulatory and Respiratory Health, investigation is beginning on how stem cells from adult skin and bone marrow can be reliably transformed into functioning brain cells. The project will also examine the brain's ability to repair itself by recruiting stem cells from functioning areas to help repair damaged ones. This project holds exceptional promise for stroke victims.

ORGANIZATION	DESCRIPTION
Protein Engineering Network of Centres of Excellence (PENCE) www.pence.ca	The recent successful sequencing of the SARS genome by the Michael Smith B.C. Genome Sciences Centre and Health Canada has shown Canada to be a world leader in SARS research. The ***Protein Engineering Network of Centres of Excellence*** (PENCE) is fast-tracking seven national projects that will study the structure and function of SARS proteins. The aim is to facilitate short-term, high-impact research that may identify validated targets for therapies, lead compounds and vaccines. PENCE is also actively participating in a national consortium developed to pool the knowledge and resources of Health Canada, the Canadian Institutes of Health Research, PENCE, and the Canadian Network for Vaccines and Immunotherapeutics (referenced above). In a different vein, a molecular sensing technology under development by PENCE spinoff company Sensium Technologies Inc. may one day help Canadians live longer. The technology detects interactions between DNA, carbohydrates, proteins, peptides and other small molecules. It is anticipated that the technology will be used by researchers to diagnose and identify those proteins that may be good drug targets. Sensium has a worldwide patent on the biosensor. Since 2001, PENCE has shifted its focus from protein engineering to also include proteomics – the study of the structure, changes, function, and location and activity of all the proteins in a cell, at each stage of its development. Estimates put the number of proteins manufactured by the human body at six, possibly even seven, figures. Through the development and support of the Canadian Proteomics Initiative (CPI) annual conference, PENCE brings together proteomics researchers from across the country to share information and data that may lead to new protein products, services and technologies.
National Research Council Biotechnology Program www.nrc-cnrc.gc.ca/randd/areas/biotechnology_e.html	The ***National Research Council*** (NRC) is the premier biotechnology research agency of the Canadian federal government. Six institutes deliver the ***NRC Biotechnology Program***, [including the Institute for Marine Biology (NRC-IMB), the Institute for Biological Sciences (NRC-IBS), the Institute for Biodiagnostics (NRC-IBD), the Biotechnology Research Institute (NRC-BRI), the Plant Biotechnology Institute (NRC-PBI) and the Institute for Nutrisciences and Health (NRC-INH). The Steacie Institute for Molecular Sciences (NRC-SIMS) supports the program with specific basic research. The Biotechnology Program is a founding member of Genome Canada and contributes to Canadian innovation in genomics through the NRC ***Genomics and Health Initiative*** (GHI). The GHI is the NRC's first large-scale horizontal research program – managed across the National Research Council's major biotechnology institutes.) Several other NRC institutes, including the Steacie Institute for Molecular Sciences (NRC-SIMS), the Institute for Information Technology (NRC-IIT), and the Integrated Manufacturing Technology Institute (NRC-IMTI) are also involved in GHI programs. The GHI complements major research efforts underway through Genome Canada, the Canadian Institutes for Health Research, and other federal government departments. Through the GHI, the NRC is advancing fundamental and applied technical research in areas such as the diagnosis of disease, aquaculture, human pathogens, agricultural crop enhancement, environmental remediation of pollution, cancer, and neurobiology.
National Research Council – Institute for Biological Sciences www.ibs-isb.nrc-cnrc.gc.ca	The ***National Research Council – Institute for Biological Sciences*** (NRC – IBS) conducts innovative research in neurobiology and immunochemistry of importance to the health and pharmaceutical sectors. NRC-IBS carries out its research programs with partners in industry, universities, hospitals, and other R&D organizations. NRC-IBS research focuses on: ▪ neurodegenerative diseases, such as stroke, Alzheimer's, and Parkinson's disease; ▪ vaccines and immunotherapies against infectious diseases; and ▪ therapeutic cancer vaccines.

ORGANIZATION	DESCRIPTION
	NRC-IBS encompasses two major research programs. The *Neurobiology Program* develops applications related to therapies for neurodegenerative disorders through its six research groups: Cerebrovascular Research, Experimental Stroke, Neurogenomics, Neurogenesis and Brain Repair, Molecular Signaling, and Receptors and Ion Channels. The *Immunochemistry Program* conducts molecular-level research, through a multidisciplinary team, that leads to the development of novel vaccines and immunotherapeutics. These are pursued through the Bioanalysis, Carbohydrate-Protein Systems, Vaccine Design, Infections and Immunity, Immunobiology, Molecular Pathogenesis, and Pathogen Genomics research groups.
National Research Council – Institute for Biodiagnostics www.ibd.nrc-cnrc.gc.ca	The ***National Research Council – Institute for Biodiagnostics*** (NRC-IBD) conducts research and develops leading-edge instrument-based, non-invasive medical diagnostic technologies. The Institute performs its research in partnership with medical schools, universities, other research organizations and industry to foster socio-economic development through R&D and commercialization of its advanced medical devices. NRC-IBD has five core research groups: The *Biosystems Group* uses non-invasive investigative techniques, such as magnetic resonance (MR) and infrared (IR) spectroscopy, and is primarily focused on cancer, heart disease and infectious diseases. The *Informatics Group* develops and adapts methods to analyze and monitor complex biomedical data and helps bring the resulting software products to market. The two *Magnetic Resonance Technology Groups* develop magnetic resonance techniques and instruments to diagnose human disease, and create protocols to apply these techniques to solve medical and biological problems. The *Spectroscopy Group* uses optical methods, including the development of infrared imaging, to improve diagnostic capabilities in the health care of Canadians.
National Research Council – Biotechnology Research Institute www.irb-bri.cnrc-nrc.gc.ca	The ***National Research Council - Biotechnology Research Institute (NRC-BRI)*** promotes, assists and performs leading-edge R&D in biochemical engineering and molecular level biology, which is closely linked to the needs of industries in the pharmaceutical and natural resources sectors. The NRC-BRI Research Program has three sectors: health, environment and bioprocess. The *Pharmaceutical Biotechnology* sector is active in the development of new strategies for the treatment of cancer and infectious diseases, such as research at the molecular level, the use of receptors and signal transduction, and the use of proteases and protease regulation. The *Environment* sector's work is centred on prevention and pollution control, including technology and process development; identification and behaviour of pollutants; monitoring and ecotoxicological risk evaluation; green technologies and sustainable development; production of non-pollutant products; and exploration of ways to re-use organic wastes and turn them into value-added products. The *Bioprocess Platform* sector is engaged in the identification and integrated development of new bioprocesses; optimization of bioprocesses; scale up of fermentation processes to industrial levels; recovery and purification of biotechnology products; production of research materials; and training of industrial personnel.

II. ORGANIZATIONS/INITIATIVES/ACTIVITIES ADDRESSING SPECIFIC ISSUES IN BIOTECHNOLOGY AND HEALTH INNOVATION

ISSUES	ORGANIZATIONS/ INITIATIVES/ ACTIVITIES	DESCRIPTION
Genetic Information Databases (Biobanks)	**CARTaGENE** www.cartagene.qc.ca/en	The proposed ***CARTaGENE*** project would map genetic variation in a large reference population of Quebec. This information would allow large-scale medical, pharmacogenomic and public health studies, including association studies of common diseases or "protective" phenotypes, and lead to the discovery of new susceptibility genes. The overall aim of CARTaGENE would be to provide information for the best use of genetic knowledge and technology in the public health system.
	The Public Population Project in Genomics www.p3gconsortium.org	The ***Public Population Project in Genomics*** (P3G) is an international consortium whose main objective is to create a public, virtual genetic database that is accessible to researchers. P3G is comprised of three different but complementary projects: Quebec's CARTaGENE, Finland's study of twins (GenomEUtwin) involving eight countries, and Estonia's Genome Project. Genome Canada recently approved a commitment of $500,000 for the initiation of the operation of P3G.
	Canadian Institutes of Health Research (CIHR)[172] www.cihr-rsc.gc.ca/e/18542.html	The CIHR proposes to undertake a ***Canadian Lifelong Health Initiative*** (CLHI) which is intended to facilitate the establishment of a research program to conduct large multi-centered longitudinal cohort studies of Canadians. These studies will analyze the role and interaction of different genetic and environmental exposures involved in the human development and aging processes over the life course, the multi-factorial causes and evolution of common diseases, and the utilization of health care services. CLHI has an important ethical, legal and social component. With an advisory committee composed of 10 Canadian experts/scholars, CIHR is developing an ethical, legal and social framework to govern longitudinal types of research and research platform/biobanks created for multiple research uses. This work will inform similar research initiatives.
Genetic Information Databases (Biobanks)	**CARTaGENE** www.cartagene.qc.ca/en	The proposed ***CARTaGENE*** project would map genetic variation in a large reference population of Quebec. This information would allow large-scale medical, pharmacogenomic and public health studies, including association studies of common diseases or "protective" phenotypes, and lead to the discovery of new susceptibility genes. The overall aim of CARTaGENE would

[172] Federal research funding in the area of biotechnology is also provided by the Natural Sciences and Engineering Research Council of Canada (NSERC: www.nserc-crsng.gc.ca) and the Social Sciences and Humanities Research Council of Canada (SSHRC: www.sshrc.ca). NSERC's annual biotechnology expenditure of $50 million represents approximately 8% of NSERC's annual budget. NSERC funds all the major areas of biotechnology research, such as plant, animal and human health. Over the years, NSERC's investment in biotechnology R&D has resulted in numerous discoveries that have led to product and process innovations that are generating socio-economic wealth for the country. SSHRC invests approximately 2% of its annual core program budget in this area. SSHRC-funded research delivers innovative thinking about the human dimensions of biotechnology, including public health policy, administration and management; ethical, legal and social impacts of gene manipulation; intellectual property, political economy and innovation; biodiversity and sustainability; and globalization.

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		be to provide information for the best use of genetic knowledge and technology in the public health system.
Genetic Information Databases (Biobanks)	**The Public Population Project in Genomics** www.p3gconsortium.org	The ***Public Population Project in Genomics*** (P3G) is an international consortium whose main objective is to create a public, virtual genetic database that is accessible to researchers. P3G is comprised of three different but complementary projects: Quebec's CARTaGENE, Finland's study of twins (GenomEUtwin) involving eight countries, and Estonia's Genome Project. Genome Canada recently approved a commitment of $500,000 for the initiation of the operation of P3G.
Genetic Information Databases (Biobanks)	**Canadian Institutes of Health Research (CIHR)**[173] www.cihr-rsc.gc.ca/e/18542.html	The CIHR proposes to undertake a ***Canadian Lifelong Health Initiative*** (CLHI) which is intended to facilitate the establishment of a research program to conduct large multi-centered longitudinal cohort studies of Canadians. These studies will analyze the role and interaction of different genetic and environmental exposures involved in the human development and aging processes over the life course, the multi-factorial causes and evolution of common diseases, and the utilization of health care services. CLHI has an important ethical, legal and social component. With an advisory committee composed of 10 Canadian experts/scholars, CIHR is developing an ethical, legal and social framework to govern longitudinal types of research and research platform/biobanks created for multiple research uses. This work will inform similar research initiatives.
Genetic Information Databases (Biobanks)	**CIHR** www.cihr-irsc.gc.ca/e/16762.html	Through the Frontier Development Grant, CIHR's Institute of Circulatory and Respiratory Health is funding a research project entitled, ***Operational and Ethical Issues Associated with Banking Human Biological Materials***. The project will set out recommendations for a National Banking Consortium of circulatory, respiratory and blood-related tissues.

[173] Federal research funding in the area of biotechnology is also provided by the Natural Sciences and Engineering Research Council of Canada (NSERC: www.nserc-crsng.gc.ca) and the Social Sciences and Humanities Research Council of Canada (SSHRC: www.sshrc.ca). NSERC's annual biotechnology expenditure of $50 million represents approximately 8% of NSERC's annual budget. NSERC funds all the major areas of biotechnology research, such as plant, animal and human health. Over the years, NSERC's investment in biotechnology R&D has resulted in numerous discoveries that have led to product and process innovations that are generating socio-economic wealth for the country. SSHRC invests approximately 2% of its annual core program budget in this area. SSHRC-funded research delivers innovative thinking about the human dimensions of biotechnology, including public health policy, administration and management; ethical, legal and social impacts of gene manipulation; intellectual property, political economy and innovation; biodiversity and sustainability; and globalization.

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Genetic Information Databases (Biobanks)	***Mapping the Language of Research-Biobanks and Health Registries: From Traditional Biobanking to Research Biobanking*** www.humgen.umontreal.ca/en/projects2.cfm (see middle of web page)	This project is the result of an interdisciplinary collaboration between epidemiology and genetics with ethics, law and philosophy of science and involves researchers from seven different institutions in Norway, France, Portugal and the U.K. The aim of the project is to investigate some of the ethical, legal and social challenges raised by research biobanking in its different modern forms and formats. Besides analyzing current legislation, other forms of regulation, and public debates concerning biobanks in European and other relevant jurisdictions, the project also includes an "in-vivo" study of ethical, legal and social issues likely to emerge from two new genomics/functional genomics projects: Biohealth-Norway and Genomeutwin.
Managing Genetic Information: Privacy Issues	**CIHR** www.cihr-irsc.gc.ca/e/16344.html	In 2003, CIHR issued a Request for Applications entitled, ***Compelling Values: Privacy, Access to Data and Health Research***. The purpose of this funding is to support research initiatives that address issues related to collection, use and disclosure of personal information for health research purposes, with a view to improving the health of Canadians and ensuring a strengthened health care system, on the one hand, while respecting and protecting Canadians' right to privacy and confidentiality with respect to their personal information, on the other.
Managing Genetic Information: Privacy Issues	**CIHR** www.cihr-irsc.gc.ca/e/22085.html	CIHR, on the advice of its Privacy Advisory Committee, has developed draft ***Best Practice Guidelines*** for addressing privacy, confidentiality and security concerns in the design, conduct and evaluation of health research involving humans. A public consultation process to obtain feedback on the draft guidelines was held from March to September 2004. CIHR expects to publish the guidelines early in 2005.
Managing Genetic Information: Privacy Issues	**Department of Justice Canada Genetic Information and Privacy Working Group** www.bioportal.gc.ca/english/View.asp?x=524&mp=521	A Genetic Information and Privacy Working Group was created in the fall of 2001. Led by the Department of Justice Canada, the Working Group is taking a multidisciplinary and interdepartmental approach to policy considerations surrounding privacy and human rights, to anticipate and develop appropriate responses before problems surface. The Group has undertaken a research program to identify the challenges and to recommend any changes to federal laws, regulations, programs and policies that may be needed to address these concerns. To support its work, the Working Group commissioned public opinion research in March 2003 and in December 2003 on a range of genetic privacy issues, including: general familiarity and awareness of genetic information and privacy issues; willingness to undergo, and experience with, genetic testing; willingness to contribute genetic information to research; perceptions of the current and preferred governance models for privacy in connection with personal genetic information; and reaction to a series of possible governance measures to address genetic privacy issues.

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Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Genome Canada** www.genomecanada.ca	Genome Canada supports research projects aimed at studying and analyzing the ethical, environmental, economic, legal and social issues related to genomics research (GE^3LS). Genome Canada also holds an ***annual GE^3LS Symposium*** to bring together philosophers, lawyers, anthropologists, sociologists, geneticists, and many other scientists to discuss GE^3LS issues.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Genome Prairie GE^3LS project** www.genomeprairie.ca/research/gels.htm	The Genome Prairie GE^3LS project is composed of four interrelated sub-projects, each of which addresses one or more of the following research themes: 1. ***Genomics, Commercialization, Industry and Society*** examines commercialization strategies of industry players and how they influence and are influenced by public perceptions, market pressures, and the innovation cycle. 2. ***Genomics, Citizens, Information, and Social Values*** looks at government/institutional responses to the concerns of citizens, whether as individuals or as part of an organization. 3. ***Intellectual Property and Genomics*** is concerned with ethical, environmental, legal, and economic issues related to intellectual property development. Information on the four specific sub-projects can be found at the above-referenced website.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Genome Quebec GE^3LS project** www.genomequebec.com/GQprogrammeRecherche/projets/indexDetail.asp?id=c1p17&l=e	***Genomics in Society: Responsibilities and Rights*** is a multidisciplinary GE^3LS research project involving six universities in Quebec, on behalf of Genome Quebec's Genomics, Ethics/Environment, Law and Society (GELS) program. The project is supported by Genome Québec, Ministère de la Recherche, Science et Technologie, Quebec government and Genome Canada, with $375 million in federal funding. The project will analyze the rights and responsibilities of researchers, and address the issues of population research and professional accountability in the collection, use, transfer and protection of genetic information. It will explore a series of questions concerning genetic information and regional populations, communities and families. The project will have conceptual as well as infrastructure outcomes. At the conceptual level, the GELS team will analyze professional standards, including standards for basic scientists, as well as issues of cultural and religious diversity, and ethical and legal issues arising from the creation of biobanks. At the infrastructure level, the GELS team will create platforms of well-documented and easily accessible information drawn from a wide range of sources.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Genome British Columbia GE^3LS project** www.genomebc.ca/GBCScienceResearch/	The objective of Genome British Columbia's GE^3LS project, ***Democracy, Ethics and Genomics: Consultation, Deliberation and Modeling***, is to develop a defensible methodological framework within which government, industry and other parties can conduct defensible consultation processes. This project is supported by Genome British Columbia, as well as by Genome Canada. Led by Dr. Michael Burgess, Chair of Bioethics at the University of British Columbia's Centre for Applied Ethics, the project is designed to take advantage of the Centre faculty's diverse expertise by bringing together three

ISSUES	ORGANIZATIONS/ INITIATIVES/ ACTIVITIES	DESCRIPTION
	researchProjectsDetails.asp?id=c2p59	research streams — consultation, deliberation and computer-based modeling. The process, which will involve groups with no experience with genomics research, those with limited experience, and those with direct personal, political, professional or financial interests, including biotechnology companies, genome researchers and activists, is being done in collaboration with Canadian and international researchers and GE^3 LS components of Genome Prairie, the Ontario Genomics Institute, and Génome Quebec, as well as a private sector consultation company. Genome British Columbia also has in place an Ethics Advisory Committee, which identifies and assesses any GELS issues that may arise from funded projects, and promotes original thought regarding the GELS implications of genomics research in general.
Ethical/ Environmental/ Legal/Social issues (GE^{3}LS) Associated with Biotechnology	**Ontario Genomics Institute GE^{3}LS project** www.ontariogenomics.ca/gc/ogi/ethics/gelsIntro.asp?l=e	The Ontario Genomics Institute (OGI) project, the ***Canadian Program on Genomics and Global Health*** (CPGGH) analyzes the social implications of advances in genomics/biotechnology in order to identify problems associated with these advances at an early stage of their development. The program focuses on several areas: genomics policies of governments in developing countries; the use of plant vaccines, nutrients and drugs; ethical impacts of the introduction of genetically modified animals to the food system; and international and comparative perspectives on the regulation of genomics research. The project will address issues of intellectual property as well. The project is co-funded by the Ontario Research and Development Challenge Fund, Merck & Co., and GlaxoSmithKline, and through the Ontario Genomics Institute by Genome Canada ***Bridging the Emerging Genomics Divide*** addresses the issue of ensuring that the benefits of the unfolding revolution in health and nutrition genomics and biotechnology, which encompass health and agriculture, are available to all. The project will study the ethical strategies of multinational pharmaceutical and biotech companies and make recommendations for good practices. The project researchers will also be involved in developing ethical frameworks for genomics as applied to nutrition or "nutrigenomics." In addition, the team will study "enviropigs," which produce manure that contains less phosphorus, making the pigs more environmentally friendly. They will also look at ethics, consumer concerns, public reaction and other related issues. A key component of the project is capacity building in developing countries. The project team plans to conduct five executive courses on genomics and public health policy where opinion leaders from academia, industry, NGOs, government and the media can meet and exchange views. Finally, the project will lay the ground for creation of a Commission on Genomics and Global Health. This project is co-funded by Genome Canada, the International Development Research Centre, Indian Council for Medical Research, Pan American Health Organization, World Health Organization (Eastern Mediterranean Regional Office), Keck Institute, National Institutes of Health, Merck and Co., the University of Toronto, and the University of Guelph. The OGI provides funding through a ***GE^{3}LS Support Program*** to provide GE^{3}LS-related assistance and support to OGI-based research projects.

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Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Quebec Network of Applied Genetic Medicine (RMGA) of the Fonds de la Recherche en Santé du Québec (FRSQ)** www.rmga.qc.ca/en/f_pub_enonces.htm#Énoncés	The Quebec Network of Applied Genetic Medicine (RMGA) of the Fonds de la Recherche en Santé du Québec (FRSQ), as the project manager of the proposed genetic map of the Quebec population (CARTaGENE), has developed a ***Statement of Principles on the Ethical Conduct of Human Genetic Research Involving Populations***. This framework seeks to direct and harmonize such large genetic studies where the population is a partner in the research. This Statement is to be interpreted consistent with the RMGA's previous ***Statement of Principles: Human Genome Research (2000) on DNA Sampling and Banking in Individuals and Families***.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Centre de recherche en droit public (Public Law Research Centre) (Université du Montréal)** www.crdp.umontreal.ca/en/recherche/axes.php	The broad streams of the Centre's present research are on the interface between law and new technologies (life science technologies, information technologies) and on theory of law and social change. With respect to life science technologies, the scope of this area of research is constantly widening and now covers health care facility law, pharmaceutical law, new technologies and biotechnology law, biodiversity and environmental law, as well as several multidisciplinary approaches drawing particularly on sociology and ethics. Information on projects can be found at the above-referenced website.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Health Law Institute (University of Alberta)** www.law.ualberta.ca/centres/hli/research.html	The Institute conducts research on current issues in health law, and in response to significant developments in legislation, case law, provincial and federal policy, and new medical technologies. The topics researched by Institute personnel are extremely varied, including such topics as ethical and legal issues of biotechnology, questions of health care policy/reform, assisted suicide and euthanasia, personal directives, confidentiality and the handling of health information, consent to medical treatment, the legal status of the fetus, the fiduciary obligations of health care providers, and HIV/AIDS and the law.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**CIHR Institute of Genetics** www.cihr-irsc.gc.ca/e/19529.html	In order to build research capacity and promote original work into the ethical, legal and social issues relevant to population-based genetic research, the Institute of Genetics, Institute of Aging, Institute of Aboriginal Peoples Health, Institute of Human Development, Child and Youth Health, and Institute of Population and Public Health, and the CIHR Ethics Office have developed a strategic initiative (***Facing our Future: Human Genetics, Ethics, Law and Society***) to investigate the ethical, legal and social issues relevant to the study of gene-environment interactions in human populations. This request for applications is in support of CIHR's cross-cutting initiative, the ***Canadian Lifelong Health Initiative*** (referenced earlier in this inventory), which is intended to facilitate the establishment of a research program to conduct large multi-centred longitudinal cohort studies of Canadians. The purpose of this Request for Applications (RFA) is to provide operating funds in support of initiatives in order to address ethical, legal and social issues relevant to the design and conduct of population-based genetic epidemiological research (including implications for future studies in Canada), while building research capacity in this field by providing an opportunity for new investigators to develop and demonstrate their independence in initiating and conducting health research. The Institute of Genetics has established an ***Ethical, Legal and Social Issues Priority and Planning Committee*** to inform the Institute about

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		ethical, legal and social perspectives. The Committee's mandate is to identify ethical, legal and social research priorities and objectives; foster interdisciplinary communication and research partnerships among researchers in all disciplines including, but not limited to, social scientists, humanists, legal scholars, economists, basic and clinical scientists; and facilitate the growth of training and research in the Canadian GELS community including knowledge transfer to health care professionals, researchers and the general public.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**CIHR**	Through its ICE (Interdisciplinary Capacity Enhancement) Teams Grant Program, CIHR is funding two projects. One project is entitled, ***GeneSens: Translating genetic discoveries into appropriate health policy and services*** (Principal Investigator is Brenda Wilson, University of Ottawa). This program is concerned with the evaluation of the effectiveness and efficiency of emerging technologies and their implementation in practice and the assessment of different models of organizing genetics health services — such evaluations are designed to address questions of utility and acceptability from a societal as well as a technical perspective. The project research team brings together research expertise and approaches from a broad range of disciplines. Its focus is on identifying and prioritizing the most important research questions, using rigorous research methods to answer them, and communicating what is learnt in effective ways with various stakeholder groups, including citizens, users of health care, providers of health care, and those who make resource allocation decisions. Current activities include examining public perspectives on the appropriate use of genetic testing within the Canadian health care system, evaluating the effectiveness of approaches to enhancing the ability of family physicians to use emerging genetic technologies, assessing the need for psychosocial services in genetics, and developing outcome measures for routine use in genetics health services. The second project is entitled, ***Research Program to Support Health Policy in Genetics, Concerned with Quality, Efficiency and Social Welfare.*** (Renaldo Battista, McGill University.) This project is designed to contribute to health and genetic policies by creating a knowledge network that will bring together academics, genetic counselors, and government representatives. Utilizing interdisciplinary research, the goal of this network is to answer questions relating to policy-making in the field of genetics. The three main areas of research are genetics and health services, genetics and public health, and genetics and public relations.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**CIHR** www.cihr-irsc.gc.ca/e/19783.html	In December 2003, the CIHR issued a Request for Applications (RFA) on ***Addressing Health Care and Health Policy Challenges of New Genetic Opportunities***. The purpose of this RFA is to provide operating grant funds in support of research projects, the results of which will better equip health care providers, administrators and policy-makers to improve the health of populations and strengthen the health care system in Canada in the face of the rapid growth in new technologies and understandings associated with the "genetics era." The partners involved in this initiative include CIHR's Institute of Genetics, Institute of Health Services and Policy Research, and Institute of Population and Public Health, the Canadian Coordinating Office for Health Technology Assessment, the Heart and Stroke

ISSUES	ORGANIZATIONS/ INITIATIVES/ ACTIVITIES	DESCRIPTION
		Foundation, and the Federal/Provincial/ Territorial Task Group on Genomics and Health. Results of this RFA are anticipated to be announced in November 2004.
Ethical/ Environmental/ Legal/Social issues (GE^3LS) Associated with Biotechnology	**Government of Newfoundland and Labrador**	Newfoundland and Labrador has commissioned a report on the regulation of commercial genetic research conducted there. The report recommends the establishment of a mechanism (a Standing Committee on Human Genetic Research) to ensure appropriate benefit sharing agreements are in place before genetic studies with commercial potential are approved.
Accountability, Oversight & Norms for Research Ethics Review	**CIHR** www.cihr-irsc.gc.ca/e/16445.html www.cihr-irsc.gc.ca/e/24201.html	CIHR is funding a research project entitled, ***The Function of Academic Research Ethics Boards (REBs) in Governing Privacy, Confidentiality, and Security Issues in Studies Using Personal Health Information***. The long-range goal of this research is to improve the consistency in how REBs handle issues of privacy and confidentiality in two types of studies: (1) those involving the secondary use of personal information for health research, and (2) those involving the development of prospective registries and biobanks. The objectives of this study are: (1) to document the ways in which REBs vary in their handling of privacy, confidentiality, and information security issues when reviewing research protocols involving administrative or clinical records, registries, biobanks, or secondary use of biological samples, (2) to identify "best practices" and common challenges in the field, (3) to ascertain the concerns of REB chairs around oversight of the protection of personal information and the ability of REBs to address them effectively, and (4) to develop a data collection instrument that will provide a common set of questions that REBs can use with regard to privacy, confidentiality, and data security. CIHR is funding several other operating grants related to governance issues: ***1) Towards the Ethical Governance of Canadian Health Rresearch Involving Humans: Principles, Policies, Practices and Outcomes; 2) Monitoring of Medical Research Protocols in Research Involving Humans: Development, Implementation and Evaluation of a Proposed Model; 3) Risks to Participants Undergoing Qualitative Interviews: Perspectives of Researchers and Research Ethics Boards; and 4) Ethics Evaluation for Biomedical Research in Canada: An Evaluative and Prospective Study for a Type of Governance at the Service of Deliberative Democracy***. Also, a Priority Announcement launched in June of 2004 signals that governance of ethics in research involving humans is an important need for enabling health research in Canada.
Accountability, Oversight & Norms for Research Ethics Review	**Interagency Advisory Panel on Research Ethics (PRE)** www.pre.ethics.gc.ca/english/index.cfm	PRE is a body of external experts established in November 2001 by the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada, and the Social Sciences and Humanities Research Council of Canada, to advise them on the development and evolution of their joint research ethics policy, the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS) (www.pre.ethics.gc.ca/english/ policystatement/ policystatement.cfm). More than 80 universities or colleges, Health Canada and other government entities across Canada have formally adopted or apply the TCPS. For those institutions, research involving humans – including living human participants,

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		human remains, tissues, and biological fluids – undergoes prospective ethics review by an interdisciplinary research ethics board consistent with TCPS norms. PRE's independent and multi-disciplinary advice is intended to promote high standards of ethical conduct, advance the protection of human research participants, and enhance accountability in research ethics. PRE's advisory and policy development functions mean that it has no role in oversight, regulatory or enforcement matters. PRE's current projects include: ▪ incorporating CIHR stem cell guidelines and Bill-6 norms into the TCPS; ▪ studying recommendations from the Olivieri reports for the clinical trials provisions of the TCPS; ▪ participating in the CIHR Privacy Best Practices initiative; ▪ launching PRE's on-line TCPS tutorial; ▪ revising TCPS norms for research involving aboriginal peoples; ▪ participating in the national dialogue on governance systems for research involving humans (www.pre.ethics.gc.ca/english/publicationsandreports/publicationsandreports.cfm); ▪ updating definitional and procedural dimensions of ethics review of research; and ▪ monitoring emerging technologies or policy initiatives — e.g., biobanking, nanotechnology, the Health Canada/CIHR National Placebo Initiative — which may have implications for the TCPS.
Accountability, Oversight & Norms for Research Ethics Review	**Government of Newfoundland and Labrador**	Newfoundland and Labrador is introducing legislation to establish a Provincial Health Research Ethics Board that will ensure that all human health research conducted in the province — with a particular emphasis on genetic research — is subject to local review and ongoing monitoring. The impetus for this initiative was concern regarding research institutions from outside Newfoundland and Labrador that had collected genetic samples, family records, and health information that were subsequently stored elsewhere. The protocol includes materials transfer agreements designed to maintain some control over genetic samples that are sent outside the province.
Accountability, Oversight & Norms for Research Ethics Review	**National Council on Ethics in Human Research (NCEHR)** www.ncehr-cnerh.org	The ***National Council on Ethics in Human Research*** (NCEHR) is dedicated to advancing the protection of human participants in research and fulfills its mandate through a variety of education programs. These programs include NCEHR's system of educational site visits to research institutions, during which trained NCEHR volunteer surveyors provide a confidential assessment of an institution's human research protection program and identify areas for improvement. Health Canada, the Canadian Institutes of Health Research, and the Royal College of Physicians and Surgeons of Canada are long-time NCEHR funding partners. Pressure from the research community for an appropriate system of accreditation has been mounting. Note also that a system of accreditation of human research protection programs was endorsed in a recent report on pharmaceutical issues by the House of Commons Standing Committee on Health. In response, NCEHR recently established a new ***Task Force for the Development of an Accreditation System for Human Research Protection Programs***. The Task Force will: ▪ establish a mechanism for the development of standards of accreditation informed by TCPS and other policies and regulations governing human research in Canada;

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		▪ propose detailed operational models for the accreditation process; ▪ propose an appropriate model for the operation of the accrediting entity; ▪ identify the essential prerequisites for the success of an accreditation system; and ▪ report on the feasibility of operating pilot studies on one or more operational models. NCEHR anticipates that the accreditation program could be initiated in about two years. The Task Force plans to work closely and collaboratively with a range of interested organizations, including the Canadian Association of Research Ethics Boards.
Commercial-ization and Biotechnology	**Health Innovation Canada (HI Canada) proposal**	Conceived as an arm's length organization, ***HI Canada*** is being led by Dr. Aubrey Tingle, President/CEO of the Michael Smith Foundation for Health Research and Dr. Henry Friesen, Chairman of Genome Canada's board of directors. This initiative is designed to leverage the health care dollars spent to ensure there is a holistic stewardship of the publicly funded health system assets that should be positioned both to improve health and increase wealth. Dr. Friesen noted that the magnitude of health expenditures over the next decade in Canada will be $1.5 trillion. HI Canada would champion the creation of an opportunities fund that is capable of effecting a cultural change in the health system that would serve as a catalyst for "developing a globally competitive health industries/products/services sector that matches in quality and effectiveness the best in the world." At this point in HI Canada's evolution, emphasis is being placed on assessing areas requiring action, coordination and assistance before governance issues are resolved. One potential model would feature decentralized units with a centralized support mechanism and funding to foster linkages and achieve economies of scale. Critical mass would be achieved by creating and supporting a series of linked innovation networks, leading to an innovation infrastructure and economic development rooted in research. HI Canada is distinguished from previous health commercialization proposals by its scope, which encompasses the complete health care system.
Commercial-ization and Biotechnology	**Innovation Canada** www.i-can.ca	***Innovation Canada*** (I-CAN) is a proposed network of organizations that provide specialized facilities and expertise for prototyping, product development and commercialization. The I-CAN network proposes to integrate publicly supported infrastructure and specialized expertise into a seamless network accessible from anywhere in Canada to help improve small- and medium-enterprise (SME) product development and performance. The concept for this network has been developed in response to the need for a collaborative national innovation network aimed a strengthening the capacity of individual firms (especially SMEs) by making publicly supported facilities and expertise accessible across Canada so they can create products and services which are globally competitive – in summary, to step up Canada's efforts in technology commercialization. A series of six workshops were held across Canada in May and June — Ottawa, Toronto, Montreal, Winnipeg, Calgary and Edmonton — where over 150 SMEs, along with several intermediary organizations (between industry and government) were engaged to provide input to the concept. Overall, the feedback has been positive with a clear indication that there is a need to be filled. The next step is to develop a detailed business case for the network

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		that will involve the Alberta Research Council, other provincial and industrial research organizations, as well as key intermediary organizations in the design and development of the network. The network is already taking steps to influence the federal innovation agenda by requesting that provincial not-for-profit research organizations be eligible for federal granting programs such as the Natural Sciences and Engineering Research Council.
Commercial-ization and Biotechnology	**Canadian Biosciences Commercialization Institute (CBCI) proposal**	The ***Canadian Biosciences Commercialization Institute*** (CBCI) sees two main problems in the commercialization of biotechnology in Canada: the usual problems of early-stage companies, exacerbated by the length of time it takes to go from proof-of-concept to actual revenues in this field, and the lack of larger Canadian firms that can act as lodestars for the juniors. "We grow guppies for foreign sharks," says CBCI Chairman Harry Swain, a former Deputy Minister of Industry Canada. If Canada is to capture the benefits of its remarkable and successful investment in R&D, the structure of the Canadian biotech industry has to change. The proposal is for a $100 million “venture loan” from the federal government, to be matched by $100 million in private equity. Investments would be targeted at early, proof-of-concept stage firms, and at consolidation to improve sustainability. Market mechanisms are relied on to encourage investee firms to stay in Canada.
Commercial-ization and Biotechnology	**Biotechnology Drug Development Accelerator (BDDA) proposal, led by MDS Inc.**	The ***Biotechnology Drug Development Accelerator*** proposal is based on the observation that investors in biotechnology firms tend to select a single compound for development and, if this fails, the business often fails leaving other potential compounds or applications unexploited. It is estimated that between 600 and 1,000 compounds are not being developed because of this practice. The BDDA concept would use specific evaluation criteria to identify promising compounds and then buy the intellectual property from the company. In exchange, the company would receive cash and buy-back rights in the event that the compound successfully passes through the approval processes. Canadian contact research organizations (CROs) would develop the compounds and propose to finance the work through the creation of a large fund cost-shared by the private and public sectors, with the public sector contribution achieved through the extension of third-party flow-through-share financing mechanisms or direct government investment.
Commercial-ization and Biotechnology	**Centre for Biopharmaceutical Manufacturing - Canadian Bioprocessing Initiative** www.centrebiopharm.ca (under construction)	Formed by the Ottawa Life Sciences Council, the ***Centre for Biopharmaceutical Manufacturing*** (CBM) will be a public-private partnership (P3), with two thirds of its funding to come from the private sector. Its vision includes a $125 million current Good Manufacturing Practices (cGMP)-compliant pilot facility proposed to be located in Ottawa at the Greenbelt Research Farm. Conceptual designs for the facility are almost complete and formation of the P3 structure is a top priority of CBM’s second year. The cGMP Pilot Facility will manufacture clinical materials for biopharmaceuticals completing Phase I and Phase II clinical trials, across the major technology platforms —mammalian cell, microbial fermentation, viral, and transgenic systems. In addition, CBM will train and certify specialists in bioprocessing and cGMP, spearhead standards development in the bioprocessing field, and provide third party verification of regulatory guidance and third party validation of SOPs.

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		CBM's key mandate will be as a "steward" of our biopharmaceutical manufacturing industry. Its first major effort is the Canadian Bioprocessing Initiative — the development of a stakeholder-driven, national strategy for biopharmaceutical manufacturing that ensures we capture, within Canada, the economic impact of our world-class capabilities in biopharmaceutical discovery by addressing a market failure in the drug commercialization process. That effort includes over 75 stakeholders from industry, academia, government and NGOs, across five provinces. To be released in the fall of 2004, the national strategy will advance recommendations in training, research, regulatory foresighting, cGMP capacity, and international collaboration.
Regulation and Biotechnology	**External Advisory Committee on Smart Regulation** www.smartregulation.gc.ca	The ***External Advisory Committee on Smart Regulation*** was created in May 2003 to provide an external perspective on a regulatory strategy for Canada as well as specific regulatory issues. The Committee was given a three-part mandate: 1. to develop a regulatory strategy designed for the 21st century; 2. to identify priority sectors and areas requiring regulatory reform in order for Canada to have a strategic advantage; and 3. to review and provide an external perspective on current issues identified by departments and stakeholders. The regulatory issues related to biotechnology/life sciences are one of the key areas addressed under the second element of the Committee's 12 to 15 month mandate. The Committee released its report entitled, *Smart Regulation: A Regulatory Strategy for Canada,* in September 2004.
Regulation and Biotechnology	**Therapeutic Access Strategy**	In response to the Government of Canada's commitments in the 2002 Speech from the Throne, 2003 Budget ($190 million over five years), and 2000 and 2003 First Ministers' Meeting Accords and stakeholder input, Health Canada has developed a ***Therapeutics Access Strategy*** *(TAS)*. The objectives of TAS are to: ▪ improve timeliness and transparency of regulatory review; ▪ provide greater vigilance around safety issues once products have been marketed; and ▪ contribute to the cost effectiveness and sustainability of the health care system. The TAS system aims to achieve internationally comparable review times: 180 days for priority submissions (300 days for non-priority submissions) on 90% of conventional pharmaceuticals within three years. It will take four years to reach similar milestones for biologics and genetic therapies.
Health Technology Assessment (HTA)	**Canadian Coordinating Office for Health Technology Assessment (CCOHTA)** www.ccohta.ca/entry_e.html	The ***Canadian Coordinating Office for Health Technology Assessment*** is an independent, not-for-profit organization funded by Canadian federal, provincial and territorial governments. *CCOHTA's mission is to provide timely, relevant and rigorously derived evidence-based information to decision-makers and support for the decision-making process*. As a pan-Canadian organization, CCOHTA facilitates information exchange, resource pooling and the coordination of priorities for health technology assessments. CCOHTA supports informed decisions about drugs, medical devices and health systems through three programs: ▪ ***Health Technology Assessment*** evaluates the effectiveness, cost-effectiveness and impact, both on patient health and on the health care

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		system, of health technologies and their use. The program produces a diverse range of products, including: reports on comprehensive, peer-reviewed assessments of health technologies (drug, device or health system), and on issues in emerging health technologies; web-based information about emerging technologies; and preliminary summaries and appraisals of existing technologies. ▪ ***Common Drug Review*** (CDR) reviews new drugs for potential coverage by participating publicly funded federal, provincial and territorial drug benefit plans in Canada. ▪ ***Canadian Optimal Medication Prescribing and Utilization Service*** (COMPUS) collects, evaluates and distributes best practices information, strategies and tools on drug prescribing and use. ***The Canadian Emerging Technologies Assessment Program*** (CETAP) alerts decision- makers to upcoming drugs, devices and systems that are likely to have a significant impact on the delivery of health care in Canada. The available clinical evidence, costs and safety implications are highlighted in a brief, evidence-based format.
Health Technology Assessment (HTA)	**Alberta Heritage Foundation for Medical Research (AHFMR)** www.ahfmr.ab.ca/programs.html	***Alberta's Health Technology Assessment Program*** has been established under the Health Research Collaboration Agreement between the Alberta Heritage Foundation for Medical Research and the Alberta Health Ministry since 1995. The HTA unit undertakes assessments in response to requests from Alberta Health, health regions, health care providers, and organizations. Requests for assessments should be related to health technologies that are likely to be of significance to Alberta health care. The unit may also initiate assessments when it becomes aware of important health technology issues. The unit is a member of the International Network of Agencies for Health Technology Assessment. The unit produces a number of different reports in response to the needs of its clients: (1) full HTA reports which are externally reviewed; (2) TechNotes which are produced in two to three months in response to requests which are time sensitive — these may be externally reviewed; (3) Information papers — examining in detail an issue in the diffusion of emerging technologies; (4) HTA Initiatives — publications produced with a view to improving the use of HTA in the Alberta health care system; and (5) joint reports conducted in collaboration with sister agencies from around the world. The unit also produces a newsletter that can be viewed on the Internet. The unit offers a six-month HTA professional development opportunity for individuals interested in gaining experience in HTA. Eight individuals have completed the program — four from Alberta and four from countries outside of Canada. The program was recently reviewed and found to be very useful to the individuals undertaking it and to sponsoring organizations. An ambassador program is currently being piloted with the Calgary Health Region centred on chronic pain management programs. The program is attempting to identify effective strategies for disseminating HTA. The unit also works in collaboration with the Office of Innovation and Technology at the Capital Health Region.

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Health Technology Assessment (HTA)	**Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) (Quebec)** www.aetmis.gouv.qc.ca	The mission of the ***Agence d'évaluation des technologies et des modes d'intervention en santé*** is to contribute to improving the Quebec health-care system and to participate in the implementation of the Quebec government's scientific policy. To accomplish this, the Agency advises and supports the Minister of Health and Social Services as well as the decision-makers in the health care system, in matters concerning the assessment of health services and technologies. The Agency makes recommendations based on scientific reports assessing the introduction, diffusion and use of health technologies, including technical aids for disabled persons, as well as the modes of providing and organizing services. The assessments take into account many factors, such as efficacy, safety and efficiency, as well as ethical, social, organizational and economic implications.
Health Technology Assessment (HTA)	**Ontario Health Technology Advisory Committee (OHTAC)** www.health.gov.on.ca/english/providers/program/mas/ohtac_about.html **Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care** www.health.gov.on.ca/english/providers/program/mas/mas_mn.html	The ***Ontario Health Technology Advisory Committee*** (OHTAC) was announced in October 2003. OHTAC is comprised of Ontario stakeholder representatives and experts, and provides advice to the Ministry of Health and Long-Term Care regarding the uptake and diffusion of new health technologies in Ontario. OHTAC recommendations are based on evidence of effectiveness of patient outcomes, economic and human resource considerations, societal impact, regulatory and ethical considerations, and medical expertise regarding the introduction of new health technologies into health services in Ontario. This process is intended to maximize opportunities for the people of Ontario to have equal access to new effective technologies, underpinned by careful analysis. The Committee reviews prioritized new health technologies as requested by hospitals, community-based health services and any other potential purchaser of health technology for the delivery of health care services in Ontario through an application process. Technology assessments and reviews are prepared for OHTAC by the Medical Advisory Secretariat, (MAS) of the Ontario Ministry of Health and Long-Term Care. MAS staff present the results of assessments and reviews, and recommend options to OHTAC monthly. OHTAC may recommend adoption of the technology, with or without utilization guidelines, or that the technology not be adopted. With respect to the latter, OHTAC may request that MAS review the status of the technology periodically to update the assessment for OHTAC's reconsideration based on any new findings. OHTAC may also recommend the conduct of a field evaluation and/or human factors testing if the quality of evidence is insufficient for it to advise the Ministry of Health to commit to a long-term investment but the technology looks promising nevertheless. OHTAC recommendations regarding new health technologies are made public 60 days after they are made to the Deputy Minister of the Ontario Ministry of Health and Long-Term Care. The review by the MAS is also made public 60 days following the making of recommendations by OHTAC.

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Health Technology Assessment (HTA)	**Canadian Health Technology Strategy**	The 2003 First Ministers' Accord on Health Care Renewal directed health ministers to develop, by September 2004, a comprehensive strategy for technology assessment that assesses the impact of new technology and provides advice on how to maximize its effective utilization in the future. The Federal, Provincial and Territorial Advisory Committee on Information and Emerging Technologies (ACIET) was given responsibility for developing this strategy.
Patenting of Biological Material	**Genome Prairie** www.genomeprairie.ca	One of the projects under Genome Prairie's GE^{3}LS program is entitled, ***Creating, Managing and Commercially Exploiting Intellectual Property.*** This project is designed to examine the impact and management of intellectual property. Examples of other project initiatives include: ***Examining Evolutionary Public Sector Business Models – The National Research Council (NRC)/Plant Biotechnology Institute (PBI)***: This survey and qualitative research project was initiated in the summer of 2003. Individuals targeted for interviewing are those that have a longstanding past or current employment/contractual arrangement with the NRC-PBI. This work is designed to highlight the evolutionary role of the NRC-PBI in the regional community over the past two decades and will examine the organization's changing role in facilitating collaborative projects, its evolving IP strategies as well its role in the commercialization process. Results will be presented and published during 2004. ***Survey of IP Management in Genome Canada Projects, 2003-04***: The project is designed to determine past, current, and anticipated relationships related to research and commercialization involving the Genome Prairie research projects and personnel. It is also designed to shed light on the three stages in project development focusing on search costs, negotiation costs and ongoing costs. Additionally, questions will serve to highlight projects' intellectual property strategies and the costs incurred in the search, negotiation and monitoring of intellectual property rights, and to outline commercialization strategies (if any). Other projects that did not receive approval will also be surveyed in order to obtain a complete picture of developmental costs for the Prairie region. Interviews of principal investigators of Prairie Genome projects have been administered and a preliminary analysis of the results has been conducted. Further surveys will be administered over the following months with final analysis conducted by year-end 2004.
Patenting of Biological Material	**Centre for Intellectual Property Policy (McGill University)** www.cipp.mcgill.ca/en/projects.php	The ***Centre for Intellectual Property Policy*** recently obtained a $3 million grant from the Social Sciences and Humanities Research Council of Canada (SSHRC). The grant funds a transdisciplinary research project that will critically examine existing intellectual property regimes relating to biotechnological innovation in the health and agricultural sectors. During its four-year term, the project will suggest ways to improve current patent regimes as well as to propose other alternative methods to encourage innovation for the betterment of Canada and other nations. In doing so, the project brings major Canadian and foreign researchers in over a dozen disciplines together with partner agencies, governmental bodies, industry representatives, and research institutions from around the world.

Annex 4
CBAC's Research and Consultation Process on Biotechnology and Health Innovation

In 2002, the Canadian Biotechnology Advisory Committee, under the overarching theme of *Biotechnology in Canadian Society*, initiated an examination of the role of biotechnology in health innovation, and the implications of recent and prospective developments for Canadian public policy.

Work on this complex and multifaceted issue spanned two years, as outlined below.

In the fall of 2002, CBAC released a statement on the occasion of the National Summit on Innovation and Learning in November 2002. The statement committed CBAC to providing advice to federal ministers on short-term issues and opportunities associated with biotechnological innovation, as well as on pathways for longer-term institutional transformation (see Annex 5 - CBAC Publications and Commissioned Research).

As part of the project, CBAC met with biotechnology representatives from industry, academia, the research community, government (both federal and provincial), the OECD, and non-governmental organizations, to garner input on a range of biotechnology and health innovation issues. As background for these meetings, several research papers and technical reports were prepared by experts in the field.

In March 2003, CBAC hosted a two-day workshop in Gatineau, Quebec, facilitated by the National Research Council's Office of Science and Technology Foresight (NRC-OSTF). Participants from government, academia, research and industry sectors, and non-government organizations were in attendance. The workshop had five substantive themes: Commercialization, Research & Development, Public Health, Regulation, and Health Care. Reports were prepared on each theme in addition to an overall workshop report (see Annex 5 - CBAC Publications and Commissioned Research). A report on potential future developments in biotechnology and health to the year 2015 was also developed by the NRC-OSTF.

In the late spring and early summer of 2003, based on the aforementioned meetings and workshops, a discussion paper was developed, which was reviewed by a number of individuals from government, federal agencies, academia and private citizens.

The discussion paper was published on the CBAC website in May 2004 for public comment, both on the issues identified in the paper and the proposed strategic directions. In addition, CBAC requested feedback from experts on the policy implications of the proposed strategic directions.

CBAC also commissioned public opinion research on biotechnology and health issues. This research included focus groups in Halifax, Montreal, Toronto and Vancouver. The results of this research, conducted in November and December, 2003, were reported in February 2004 (see Annex 5 – CBAC Publications and Commissioned Research).

An expert roundtable was convened in April, 2004 to discuss the role of technology assessment of health-related biotechnologies and how these biotechnologies are adopted by the health care system. Participants were drawn from government (federal and provincial), government agencies, academia, health care associations, and non-governmental organizations.

Annex 5
CBAC Publications and Commissioned Research

CBAC Publications

(Note: URLs are provided for documents that are electronically available.)

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COMMISSIONED RESEARCH

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National Research Council of Canada Office of Science and Technology Foresight, *Towards a Sustainable Health Care System: Capturing the Commercial Potential of Bio-Health Innovations*, prepared for the Canadian Biotechnology Secretariat (Canada's Bio-Health Innovation and Stewardship Foresight Project 2004), Ottawa, April 2004.

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