Health Canada Santé Canada

Review of the Health Canada Blood Safety Program (BSP)

Final Report

Presented to:

Health Canada

Departmental Audit and Evaluation Committee

on October 2, 2003

Canada

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Review of Health Canada's Blood Safety Program
Preface / Evaluator's Note

Purpose

The purpose of this note is to provide the reader of this review with further context around the rationale for this review, the information contained in the review report, and the further work being undertaken by the Department to build on and clarify the findings in this report.

Background

The final report of the Commission of Inquiry into the Blood System in Canada, known as the Krever Report, was released in 1997. It included recommendations aimed at strengthening Health Canada's blood regulatory program and public health programs through enhanced blood surveillance. As a result, additional funding was provided to Health Canada to ensure that the following two critical objectives of the Health Canada Blood Safety Program (HCBSP) were met:

- to protect the people of Canada against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and
- to be on par, in general, with blood regulatory and surveillance programs in other leading industrialized nations, such as the United Kingdom, Australia and Germany.

One of the conditions of this funding was that Health Canada return in 2001-2002 with a review of the funding needed to sustain the Program. This review, conducted by Goss Gilroy Inc., between July 2001 and July 2002, was intended to provide information on initial implementation of the enhanced programming.

The specific objectives of the review were to:

- assess the extent to which the program has improved its capabilities and whether there are still gaps to be filled;
- be able to report to Cabinet on progress made against HCBSP goals and objectives and planned activities set as part of its 1998 Accountability Framework;
- assess the extent to which the program would be able to provide the benchmarks for decision-making based on concrete evidence of program achievements and outcomes; and
- review the necessary funding required for the sustainability of the HCBSP activities.

The Approach

The methodology of this review (described in further detail in the report) involved: document review, extensive interviews with several internal stakeholders and a few external stakeholders, as well as a review of selected literature.

- A key focus of the consultant's work was a detailed assessment of activities undertaken by the Department against the Program's 1998 accountability framework. Extensive information was gathered through a review of program documentation and key informant interviews. As a result, the study was successful in meeting the objective of documenting progress made in implementing enhanced programming.
- The review met with more limited success around the original objectives of assessing program gaps and future funding requirements. In this area, the findings presented are largely the perspectives of internal stakeholders gathered by the reviewers. Readers are cautioned that this information does not represent a complete or comprehensive evaluative analysis of gaps in programming or financial requirements.
- External stakeholder opinions regarding the Department's activities were also gathered. It should be noted that in some cases individual opinions are presented, and that these are not necessarily representative of the general opinion of all stakeholders.

As the activities of Health Canada constitute just one component of the Blood Safety system in Canada, other reviews that have been completed or are underway will also inform decision making regarding maximizing the effectiveness of the System as a whole. Examples of such initiatives include:

- Program reviews and audits of Canadian Blood Services and HemaQuebec, and;
- Reviews of the role, mandate, and composition of the Expert Advisory Committee on Blood Regulation, as well as the National Blood Safety Council
- Conclusions and recommendations from conferences, such as that held in November 2002, entitled "Renewing Canada's Commitment - A Blood System for the 21st Century"
- Reports of the Office of the Auditor General on both the regulatory and surveillance programs.

Building on this review

Health Canada has begun work on developing a detailed action plan and future options for programming, building on the information presented in this review. This process, which includes a detailed resource review, is allowing for further consultation and stakeholder validation of future needs.

A number of initiatives are also underway to build a strong foundation for future performance reporting and evaluation of the Blood Safety Program, which will need to focus more clearly on the outcome of program activities. A results-based management and accountability framework is being developed which will clearly articulate cause and effect linkages, and include key measures of performance that when implemented will support future Program monitoring and evaluation.

Prepared by:
Departmental Program Evaluation Division, Health Canada
May 2003

EXECUTIVE SUMMARY

Management Response to Goss Gilroy Inc. Review of the Health Canada Blood Safety Program

The Health Canada Blood Safety Program manages risks to the blood supply through blood transfusions; transplantation of tissues, organs, cells or xenografts; use of blood products; and the use of semen for assisted conception. The objectives of the program, as stated in 1998 are: (1) To protect Canadians against current and emerging health threats from the therapeutic use of blood, tissues and organs as well as xenotransplantation and; (2) To be on par with, or exceed, the blood regulatory and surveillance programs in other leading industrialized countries.

The two key components of the program are surveillance and regulation. The surveillance program monitors the nature, incidence and prevalence of blood-borne infections, investigates potential threats to the blood system, conducts risk assessments and research, and recommends risk management actions. The regulation component of the program is responsible for developing regulatory frameworks, setting standards, ensuring compliance, conducting regulatory research, and taking action to minimize risks to public health and safety.

In 1998, the Government of Canada committed $25M per year ongoing to strengthen Health Canada's Blood Safety Program. This investment was directed principally to the surveillance of blood borne pathogens and to regulatory activities for blood and blood products. These surveillance and regulatory activities were the Government's response to the recommendations of Justice Horace Krever's inquiry into the safety of the blood system in Canada.

The Government has made significant progress in collaboration with its partners to ensure the safety of the blood system and to meet objectives of the blood safety program. In 2001-2002, a review of the program was conducted (under contract) by an independent consulting firm, Goss Gilroy Inc. The review concluded that the program "has made considerable progress towards achieving the objectives articulated in the 1998 Action Plan developed in response to the Krever Inquiry," and that as a result "the level of safety of the Canadian blood safety system has improved". Health Canada supports this overall conclusion.

Health Canada has developed a Management Response in the form of a table (attached) to address the key conclusions highlighted in the Goss Gilroy Report, along with the current status, and associated targeted actions.

Outstanding Gaps & Management Practices Issues

Health Canada's Blood Safety Program is a complex and horizontal program requiring extensive coordination between organizational units and across branches; hence management of the program is a collective responsibility.

Within Canada's blood system, responsibility is shared among the Federal, Provincial and Territorial governments, and the Blood Operators. These relationships must be maintained, and information must be shared between organizations, in order to ensure continued safety. Provinces and Territories have significant costs associated with participation in the system, and the sustainability of their involvement over the long term was a concern raised by the review of the program. This concern relates to the capacity of Provincial and Territorial governments to fully participate, with respect to both surveillance activities and the development and implementation of regulatory frameworks.

National standards and regulatory frameworks under development will give attention to the collection, manufacture and distribution of blood, cells, tissues and organs, and products derived from them, wherever they occur. Activities undertaken within hospitals must become more fully integrated into the regulatory platform of Health Canada, which currently lacks a presence in the hospital environment. Health Canada is initiating a cost-benefit analysis (with Goss Gilroy Inc.) on adherence to the standards, and will be working in close collaboration with Provincial and Territorial governments in order to complete this. The regulatory frameworks will be supported by clear, innovative, flexible and uniform safety standards, and improved ability to address emerging issues in a timely manner.

Next Steps

Health Canada aims to enhance both direct communication (including research into public disclosure of health risks) and involvement with the public as the blood safety program evolves. This would include capturing the opinions and views of stakeholders such as patient advocacy groups (the Anemia Institute, for example).

Even while dealing successfully with existing issues, the blood safety program continues to face new challenges. These new challenges include: new infectious disease threats, for example, West Nile Virus; changes to the blood supply system; the increasing use of cells, tissues, and organs; and the need to move to an integrated national surveillance system. Health Canada program officials have undertaken a preliminary assessment of the additional resources required to address gaps in the program, and intends to develop a detailed management response and action plan to address emerging and future needs identified by the review of the program, with special attention to the management functions and processes that need to be strengthened within the current scope of the program. In addition, Health Canada plans to develop options for the future of the program that will address the gaps identified in the review.

Health Canada's Management Response to Goss Gilroy Inc. Review of the Health Canada Blood Safety Program
March 2003

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
Potential resource gaps for both the surveillance and the regulatory program . Resource constraints may have a negative impact on Health Canada's ability to deliver a national surveillance program, as there is a high degree of risk that the partnerships and collaborations built with different groups (e.g., public health organizations and practitioners, voluntary organizations, academic researchers, etc.) may be negatively affected.	Health Canada program officials have undertaken a preliminary assessment of the additional resources required to address gaps in the program, and intend to develop a detailed action plan to address emerging and future needs identified by the review of the program. Health Canada has made progress in increasing collaboration with public groups (the Anemia Institute for Research and Education, for example).	Health Canada plans to develop options for the future of the program which include proposals for strategic enrichments to address the gaps identified in the review. Health Canada aims to enhance involvement with the public as the blood safety program evolves. This would include capturing the opinions and views of stakeholders such as patient advocacy groups (the Anemia Institute, for example).	Spring 2003	Julia Hill, Director General, Biologics and Genetic Therapies Directorate (BGTD), Health Products and Food Branch (HPFB) Dr. Howard Njoo Director General, Centre for Infectious Disease Prevention and Control (CIDPC), Population and Public Health Branch (PPHB)

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
The financial costs borne by the provincial and territorial authorities for their participation in the national blood safety system both through their funding of blood operators and their participation in surveillance activities are significant. Health Canada will have to consider the future costs and negotiate with the provinces/territories who pays what.	Health Canada's Blood Safety Program serves to ensure the safety of the blood supply. Safety considerations come before costs. The development of new regulatory frameworks will address the collection, manufacture and distribution of blood, cells, tissues, organs, and products derived from them, wherever they occur. Health Canada entered into an agreement with the Canadian Standards Association for the further development of draft standards for blood and for cells, tissues and organs. Canadian Standards Association Technical Committees for blood and for cells, tissues and organs have been established to review the draft standards (including a review of public comments) and approve them. In addition, Health Canada is currently undertaking a resource review. Key to that resource review will be to ensure that P/T participation in surveillance systems and P/T needs are considered in future resource scenarios. Health Canada is committed to P/T cost-sharing, and the current system has developed a shared responsibility with our P/T partners. Health Canada further acknowledges that the relationships established with our partners may be compromised with the insufficient allocation of resources. Adequate consideration needs to be given to the financial implications for our external partners in order to ensure the success of our surveillance programs.	In accordance with the Federal Regulatory Process Management Standards, Health Canada is initiating a cost-benefit analysis on adherence to the standards, and will be working in close collaboration with provincial and territorial governments in order to complete this. The purpose of this analysis is to insure not only that benefits exceed costs, but that regulatory effort is being expended where it will do the most good. The resource review which is currently being undertaken will ensure that provincial and territorial participation in surveillance systems and that provincial and territorial needs are considered in all future resource scenarios.	2005.	Laura Reinhard Director, Centre for Policy and Regulatory Affairs, BGTD, HPFB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
Hospitals (and other private organizations) are important players in the distribution and administration of blood and blood components. An increase in the hospital sector's collection activities, although previously anticipated, has not yet occurred. Hospitals are subject to the current regulations; however, they are presently being applied only to the blood system operators. This remains one of the key gaps in the overall Canadian blood system. Health Canada is currently developing a new regulatory framework for blood safety, which will be based on the *Blood Safety Standards* and will address hospitals' activities in distribution, administration and collection. However, current practices for enforcement and compliance with the standards will need to be reviewed taking into account the limited resources available to Health Canada.	The development of new regulatory frameworks will address the collection, manufacture and distribution of blood, cells, tissues, organs, and products derived from them, wherever they occur. This includes activities undertaken within hospitals. Health Canada further agrees that hospital-based surveillance centres should be expanded, and that there is a gap in the surveillance of the transmission of blood-borne pathogens in cells, tissues, and organs. The blood-borne pathogen surveillance network would be significantly enhanced with the inclusion of hospital-based surveillance, which provides direct access to patient pools. In order to effectively respond to new and/or emerging threats, it is essential that we obtain data in a timely manner. The inclusion of hospital-based surveillance brings us much closer to obtaining relevant data in real-time, significantly cutting response times for problem identification and resolution or containment.	In accordance with the Federal Regulatory Process Management Standards, Health Canada is initiating a cost-benefit analysis on adherence to the standards, which will include the costs to Health Canada to enforce compliance and will be working in close collaboration with provincial and territorial governments in order to complete this. The purpose of this analysis is to ensure not only that benefits exceed costs, but that regulatory effort is being expended where it will do the most good. Health Canada will continue to develop and expand blood-borne pathogen surveillance to hospitals and transplantation centres.	Ongoing	Laura Reinhard Director, Centre for Policy and Regulatory Affairs, BGTD, HPFB Dr. Antonio Giulivi, Director, Health Care Acquired Infections, CIDPC, PPHB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
Many new establishments will also be involved in the tissues, organs, and xenotransplantation systems. These growing fields and new scientific and technological developments will tax the existing regulatory system at Health Canada and impact on the Department's ability to carry out its regulatory role with the existing resources especially using the current approaches and processes for enforcement and compliance.	Health Canada is in the process of developing new regulatory frameworks for blood, cells, tissues and organs, and will include a comprehensive cost-benefit analysis for adherence to standards. This will be used to assist in the development of the new regulatory framework. Health Canada recognizes that there are gaps in the surveillance of the transmission of blood-borne pathogens in cells, tissues, and organs. Health Canada is currently planning to prepare for the long-term sustainability of the Health Canada Blood Safety Program, and the safety of the blood supply will include considerations to develop new surveillance systems to monitor these novel routes for identifiable disease transmission.	In accordance with the Federal Regulatory Process Management Standards, Health Canada is initiating a cost-benefit analysis on adherence to the standards, which will include the costs to Health Canada to enforce compliance, and will be working in close collaboration with provincial and territorial governments in order to complete this. The purpose of this analysis is to ensure not only that benefits exceed costs, but that regulatory effort is being expended where it will do the most good. Health Canada will develop proposals to expand cell, tissue and organ surveillance.	Ongoing	Laura Reinhard Director, Centre for Policy and Regulatory Affairs, BGTD, HPFB Dr. Antonio Giulivi, Director, Health Care Acquired Infections, CIDPC, PPHB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
The complexity of the Blood Safety Program represents a challenge as a horizontal program. At the organizational level, responsibilities and accountabilities for the Blood Safety Program are spread across two branches and many organizational units within Health Canada. As a result, there is a need to strengthen management information and horizontal management to ensure adequate monitoring, tracking and reporting of expenditures and results in comparison to the 1998 Action Plan. This is in part because no one organizational unit was charged with the overall responsibility/accountability for the program.	The Health Canada Blood Safety Program is a complex and horizontal program involving extensive coordination between organizational units and across branches, requiring management of the program to be a collective responsibility. Health Canada uses the Decision Making Framework as a systematic and structured approach to identifying and assessing risks and making decisions to set the best course of action when faced with uncertainty. Beginning in the fall of 2001, connectors were put in place to manage risks effectively and efficiently. Risk Management Committees chaired at the Directorate, Branch and Department level provide a forum for different units to engage in dialogue and joint decision-making using a proactive and transparent approach. Health Canada completed a survey of horizontal management needs for blood related activities within the Department. Following this, it was decided that the coordination responsibility of the Health Canada CanBlood Safety ada	Health Canada will formalize this agreement between branches outlining coordination roles and responsibilities for blood related activities.	Fall 2003.	Julia Hill, Director General, BGTD, HPFB Dr. Howard Njoo Director General, CIDPC, PPHB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
	Blood Safety Program will be jointly shared between the Biologics and Genetic Therapies Directorate (BGTD) and the Centre for Infectious Disease Prevention and Control (CIDPC). Within BGTD, the required functional role to support coordination has been built into the Associate Director General's roles and responsibilities. BGTD has recruited Dr. Elwyn Griffith to provide the needed skills this position entails; and within CIDPC, the corresponding responsibility will rest with the Director of Health Care Acquired Infections, Dr. Antonio Giulivi.			
The actions stipulated in the 1998 Action Plan were not necessarily adhered to. Many of the activities/actions required were changed over time, primarily because of changing needs, or inappropriate specification of requirements in 1998. As the changes were not always documented, it is difficult to determine the extent to which the intent of the original action plan was actually met. In future programs, tracking should be improved.	Health Canada agrees that tracking of the Blood Safety Program needs to be improved. Many action plan items from the 1998 Action Plan involved interaction with partners and stakeholders; and the form and manner of the implementation of those action items evolved as partners and stakeholders were consulted. The current status of this is that while Health Canada has not documented all changes to the strategic direction of the program, the overall conclusions of the evaluation indicate that the Blood Safety Program has made considerable progress toward achieving the objectives articulated in the 1998 Action Plan.	As stated above, a functional role to support primary coordination responsibility of the Blood Safety Program has been assigned to the new Associate Director General of BGTD. Health Canada plans to formalize an agreement between branches concerning roles and responsibilities as they relate to coordination of the Blood Safety Program.	Fall 2003.	Julia Hill, Director General, BGTD, HPFB Dr. Howard Njoo Director General, CIDPC, PPHB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
There were limited performance baseline indicators available to measure progress in the safety of the blood system. Future work on the Health Canada Blood Safety Program Evaluation Framework will have to ensure that indicators are further refined and agreed upon to facilitate future reporting for the program.	There has been a corporate initiative to start a meaningful central collection of data (i.e., performance indicators). The development of performance indicators is necessary for the ongoing evaluation and monitoring of the Blood Safety Program. Ongoing performance evaluation will allow for the identification of strengthens and weaknesses associated with the program. This will initially be implemented at a fairly low level this year and will be built upon in the future. In addition, there is a current evaluation initiative underway in PPHB, to evaluate the Health Canada Blood Safety Program, which will examine performance indicators, and the overall evaluation initiative will target surveillance systems.	A number of activities are currently underway to strengthen the evaluation of the Health Canada Blood Safety Program, and include the following initiatives: 1. An Evaluation Framework for Health Canada's Blood Safety Program is under development with guidance from Consulting and Audit Canada. 2. A specific evaluation of the Health Canada Blood Safety Grant and Contribution Program. This grant and contribution program supports provincial and territorial transfusion and transplantation adverse event surveillance activities. 3. An evaluation initiative in PPHB for surveillance systems and the development of evaluation frameworks for surveillance systems, including blood-borne pathogen surveillance.	 Ongoing Spring 2003 Ongoing	Dr. David Mowat Director General, Centre for Surveillance Coordination, PPHB Julia Hill, Director General, BGTD, HPFB Dr. Howard Njoo Director General, CIDPC, PPHB

Outstanding Program Issues/Gaps				
Evaluation Conclusions:	**Program Response: Current Status**	**Program Response: Action Required**	**Due Date for Completion**	**Contact Persons**
Many of the Health Canada Blood Safety Program investments are costly and have long-term financial and regulatory implications. To our knowledge there has not been an external review by an expert panel to ensure the cost-effectiveness and appropriateness of activities undertaken.	Health Canada agrees that an external review by external panels or an international review by expert panels would be useful. The expertise required to do this type of work is not readily available, but the program would be willing to ask external expertise to undertake such an exercise in the future.	Once Health Canada's evaluation exercise is complete, Health Canada will investigate the possibility for an external review with international comparisons.	Ongoing	Julia Hill, Director General, BGTD, HPFB Dr. Howard Njoo Director General, CIDPC, PPHB

Health Canada Santé Canada

Review of the Health Canada Blood Safety Program (BSP)

Final Report

Prepared by:
Goss Gilroy Inc.
Management Consultants

Presented to:

Departmental Program Evaluation Division
Applied Research and Analysis Directorate
Information, Analysis and Connectivity Branch

July 9, 2002

Canada

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EXECUTIVE SUMMARY

Review of the Health Canada Blood Safety Program

Health Canada has a primary role in protecting the health and safety of Canadians at the national level; however, it is but one component of a complex system of health protection, which includes among others, various levels of government agencies, the health care and medical professions, the academic and health science research and development communities, manufacturers, importers, consumer groups and individual Canadians.

The final report of the Commission of Inquiry into the Blood System in Canada (Krever Report) released in November 1997 included recommendations aimed at strengthening Health Canada's blood regulatory program and public health programs through enhanced blood surveillance.

In response to the Krever Report, additional funding was provided to Health Canada to ensure that the following two critical objectives of the Health Canada Blood Safety Program (HCPSB) were met:

- to protect the people of Canada against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and
- to be on par, in general, with blood regulatory and surveillance programs in other leading industrialized nations, such as the United Kingdom, Australia and Germany.

Health Canada was to return in 2001-2002 with a review of the program and the funding needed to sustain the program starting in 2003-04.

The Review of the Health Canada Blood Safety Program (HCPSB) had the following major objectives:

- to assess the extent to which the program has improved its capabilities and whether there are still gaps to be filled;
- to be able to report to Cabinet on progress made against HCBSP goals and objectives and planned activities set as part of its 1998 Accountability Framework;
- to assess the extent to which the program would be able to provide the benchmarks for decision-making based on concrete evidence of program achievements and outcomes; and
- to review the necessary funding required for the sustainability of the HCBSP activities.

Responsibilities and accountabilities for the Blood Safety Program(BSP) at Health Canada are diffused across two different branches and many organizational units. The Regulatory Program is carried out principally by the *Health Products and Food Branch*. Three directorates are involved with the BSP within this Branch: the *Biologics and Genetics Therapies Directorate*, the *Therapeutics Products Directorate*, and the *Inspectorate.* The Surveillance Program is carried out principally by the *Centre for Infectious Disease Prevention and Control* and the *National Microbiology Laboratory* of the *Population and Public Health Branch.*

The following goals were set for the Regulatory Program:

- the enhancement of blood regulatory expertise to address emerging new blood technologies and blood substitutes;
- the enhancement of the blood inspection/compliance function to meet increasing demands;
- the development of more effective post-market surveillance, including voluntary reporting by health practioners; and
- generally supporting the transition to the new blood system.

In 1998, the Surveillance and Epidemiology in Transfusions (SET) Working Group, established by Health Canada, developed a plan and designed a program for a comprehensive blood surveillance system for Canada. Further to the SET report, the following goals were established for the Blood Surveillance Program:

- To develop linkages with public-health information systems in order to strengthen public health responses to blood-borne pathogen threats;
- To develop linkages with appropriate partner organizations so that the statistical databases integration of the Laboratory Centre for Disease Control (now called the Centre for Infectious Disease Prevention and Control) can be implemented;
- To develop analytic and response capacities within the Centre by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action;
- To establish coordinated research thrusts into new potential blood-borne threats, including prion diseases such as the human form of “mad-cow disease” known as variant Creutzfeldt-Jakob Disease (vCJD); and
- To establish a national surveillance system to determine the risk of infectious and non-infectious adverse events following administration of blood and/or blood products.
- Review methodologies included extensive document review, interviews with key internal and external stakeholders, a focussed literature review and the development of case studies.

Conclusions

Progress Towards Goals and Objectives

We concluded, based on the results of the study, that:

- The Health Canada Blood Safety Program has made considerable progress towards achieving the objectives articulated in the 1998 Action Plan developed in response to the Krever Inquiry and provided as a basis for funding improvements to the Blood Safety Program;
- As a result, the level of safety of the Canadian blood system has improved. The actions taken by Health Canada, as well as other players within the blood system, have contributed to this improvement. In most areas, Canada is meeting international standards for blood safety through the introduction of new standards, guidelines, deferral policies, diagnostics tests and research activities;
- With respect to whether the system is fully integrated, the existence of two major blood operators (CBS and Héma-Québec) does not impact on the overall integrity of the system as it was unified through the regulatory activities carried out by Health Canada; and,
- Given the many other players in the Canadian blood system (including provincial health authorities, hospitals, academic researchers, voluntary organizations, health practitioners, National Blood Safety Council, expert committees, etc.) that must contribute to ensuring the overall safety of the blood supply in Canada, one cannot say that a fully integrated national surveillance system is yet a reality in Canada.

We concluded that on the ***regulatory side***, Health Canada has:

- Expanded its regulatory functions and increased its capacity to carry out inspections/investigation activities of the two major blood operators - Héma-Québec and the Canadian Blood Services - who are responsible for the collection and the distribution of blood and blood products in Québec and Canada;
- Initiated the development, in close consultation with a wide range of stakeholders involved in the Canadian blood safety system, of a new regulatory framework for blood, which will use the *National Blood Standards* as a basis;
- Carried out a number of other regulatory activities in order to meet other pressing demands in the field of biologics, including amendments to the regulatory requirements for plasmapheresis; amendments to the Semen Regulations; and the initiation of a new framework for Cells, Tissues and Organs;
- Taken a more pro-active response, erring on the side of safety, to potential threats to the blood supply in the case of both classical Creutzfeldt-Jakob Disease and its variant form;

- Carried out more effective pre-market activity and post-market surveillance including the conduct of health hazards assessments and evaluations; and
- Developed the *Canadian Adverse Drug Reaction Information System* (CADRIS), a database that will capture adverse drug reactions from both manufacturers (where it is mandatory) and the hospitals (where it is voluntary and not regulated at the present).

We concluded that on the *surveillance side*, a number of activities were undertaken by Health Canada to put in place elements of a national surveillance system:

- Investments were made to support both epidemiological research and scientific research and development in major areas. Both types of research are important to sustain surveillance activities and ensure the safety of the blood supply and the health of Canadians;
- Surveillance activities are being carried out for the following critical areas: retroviruses (including HIV/AIDS, Simian foamy virus, etc.), prions, hepatitis , emerging blood-borne pathogens, and transfusion transmitted injuries;
- Surveillance activities through many different mechanisms including: health events monitoring and alert; routine surveillance; enhanced surveillance in six sentinel sites; surveillance for new or re-emerging blood-borne pathogens, including mutants of known pathogens; targeted surveillance carried out jointly with the Bureau of HIV/AIDS, Correctional Services, First Nations and Inuit Health Boards; and numerous special studies; and,
- A pilot project by Health Canada's Centre for Infectious Disease Prevention and Control Surveillance Program - the *Transfusion Transmitted Injury Surveillance System* (TISS), which integrates an active surveillance of infectious diseases and adverse transfusion-related incidences (ATRs), including errors in the administering of transfusions.

Outstanding Program Issues/Gaps

We concluded that there a number of outstanding program issues/gaps:

- Health Canada officials are concerned that there will be funding gaps for both the Surveillance and the Regulatory programs. Resource constraints may have a negative impact on Health Canada's ability to deliver a national surveillance program, as there is a high degree of risk that the partnerships and collaborations built with different groups (public health organizations and practitioners, voluntary organizations, academic researchers, etc.) may be negatively affected.

- The financial costs borne by the provincial and territorial authorities for their participation in the national blood safety system both through their funding of blood operators and their participation in surveillance activities are significant. Health Canada will have to consider the future costs and negotiate with the provinces/territories who pays what.
- Hospitals (and other private organizations) are important players in the distribution and administration of blood and blood components. An increase in the hospital sector's collection activities, although previously anticipated, has not yet occurred. Hospitals are subject to the current regulations; however, they are presently being applied only to the blood system operators. This remains one of the key gaps in the overall Canadian blood system. Health Canada is currently developing a new regulatory framework for blood safety, which will be based on the *Blood Safety Standards* and will address hospitals' activities in distribution, administration and collection. However, current practices for enforcement and compliance with the standards will need to be reviewed taking into account the limited resources available to Health Canada.
- In addition, many new establishments will also be involved in the tissues, organs, and xenotransplantation systems. These growing fields and new scientific and technological developments will tax the existing regulatory system at Health Canada and impact on the Department's ability to carry out its regulatory role with the existing resources especially using the current approaches and processes for enforcement and compliance.

Management Practices Issues

Finally, we concluded that there were a number of areas that can be strengthened in Health Canada's management practices related to the Blood Safety Program:

- The complexity of the Blood Safety Program represents a challenge as a horizontal program. At the organizational level, responsibilities and accountabilities for the Blood Safety Program are spread across two branches and many organizational units within Health Canada. As a result, there is a need to strengthen management information and horizontal management to ensure adequate monitoring, tracking and reporting of expenditures and results in comparison to the 1998 Action Plan. This is in part because no one organizational unit was charged with the overall responsibility/accountability for the program;
- The Actions stipulated in the 1998 Action Plan were not necessarily adhered to. Many of the activities/actions required were changed over time, primarily because of changing needs, or inappropriate specification of requirements in 1998. As the changes were not always documented, it is difficult to determine the extent to which the intent of the original action plan was actually met. In future programs, tracking should be improved;

- There were limited performance baseline indicators available to measure progress in the safety of the blood system. Future work on the HCBSP Evaluation Framework will have to ensure that indicators are further refined and agreed upon to facilitate future reporting for the program; and,
- Finally, many of the BSP investments are costly and have long-term financial and regulatory implications. To our knowledge there has not been an external review by an expert panel to ensure the cost-effectiveness and appropriateness of activities undertaken.

Future Requirement

This review provides an assessment of accomplishments in the Blood Safety Program and future needs and gaps. There is a need for Health Canada to build on this review and to make a further assessment of remaining gaps and future resource requirements for the BSP.

1.0 INTRODUCTION

In Canada, "risk management and the responsibility for improving and maintaining health is one shared by individuals, communities, industry and all levels of government. Health Canada has a primary role in protecting the health and safety of Canadians at the national level; however, it is but one component of a complex system of health protection, which includes among others, various levels of government agencies, the health care and medical professions, the academic and health science research and development communities, manufacturers, importers, consumer groups and individual Canadians."[1]

The objectives of the Health Canada Blood Safety Program (HCBSP) are two-fold:

- to protect the people of Canada against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and
- to be on par, in general, with blood regulatory and surveillance programs in other leading industrialized nations, such as the United Kingdom, Australia and Germany.

Health Canada's surveillance and regulatory activities monitor and mitigate the risks associated with the collection and transfusion of blood, and under Health Canada's precautionary principle several activities have been advanced toward the use of tissues, organs and xenografts.

Other major players in the Canadian Blood Safety Program include individual blood donors, blood collection agencies/operators, health care providers, provincial and territorial governments, non-government organizations and voluntary agencies contributing to the surveillance of diseases.

The HCBSP operates with the assistance of Expert Committees, Expert Working Groups and Advisory Committees.

On June 2, 1998, Cabinet Ministers endorsed the Memorandum to Cabinet entitled: *Strengthening Health Canada's Blood Safety Program* providing Health Canada with an additional $125 million over five years to establish strong regulatory and surveillance programs as recommended by Justice Krever. Cabinet also requested Health Canada to return in 2001-02 with a review of the program and of the funding needed to sustain Health Canada's Blood Safety Program (HCBSP). This study is considered to be an interim review. Health Canada also plans to conduct a final evaluation in 2003-2004 to determine the final costs for total implementation of these additional critical elements.

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[1] *The Health Canada Decision-Making Framework for Identifying, Assessing and Managing Health Risks*, August 2000.

1.1 Objectives of the Review

Goss Gilroy Inc. was given the contract to carry out the review, which had the following objectives:

- *to assess the extent to which the program has improved its capabilities and whether there are still gaps to be filled*;
- *to be able to report to Cabinet on progress made against the HCBSP goals and objectives and planned activities set as part of its 1998 Accountability Framework;*
- *to assess the extent to which the program would be able to provide the benchmarks for decision-making based on concrete evidence of program achievements and outcomes; and*
- *to review the necessary funding required for the sustainability of the HCBSP activities.*

A related objective was to validate the evaluation framework logic model and performance measurement framework developed as part of the HCBSP Evaluation Framework. A separate document was presented to Health Canada with the consultant's comments on the evaluation framework in January 2002.

This report presents the results of the mid-term review, with respect to the first four objectives. The study was carried out by a multi-disciplinary team, which included professionals with evaluation/review expertise as well as specialized health expertise. *(Note. While the $125 million included resources for Legal and Policy Coordination activities, this report focuses on the regulatory and surveillance activities as they comprised the bulk of allocated resources.*)

1.2 Structure of the Report

The report is structured as follows:

Section 1.0 introduces the report and provides an overview of the objectives of the review, the methodology and the limitations of the study;

Section 2.0 provides a brief historical context, an overview of the Health Canada Blood Safety Program and its objectives, and the current organizational structure;

Section 3.0 contains the findings (progress to date in developing strengthened capacities, resources utilized to date, gaps and future resource requirements and any issues raised by external stakeholders) for the regulatory program;

Section 4.0 contains the findings (progress to date in developing strengthened capacities, resources utilized to date, gaps and future resource requirements; and any issues raised by external stakeholders) for the surveillance program;

Section 5.0 contains the general conclusions with respect to the progress made against goals and major issues facing the HCBSP;

Appendix A contains a list of the documents reviewed;

Appendix B provides two lists of the persons interviewed during the course of the study– those interviewed during the planning phase and those interviewed during the second phase of the study;

Appendix C contains the study instruments;

Appendix D contains a synthesis of the information obtained during the document review and interviews on the activities carried out to strengthen the Health Canada regulatory and surveillance responsibilities. In addition, this appendix also includes identified gaps and/or future requirements; and

Appendix E provides the *1998 Accountability Framework - Strengthening Health Canada's Blood Regulatory and Surveillance Programs.*

1.3 Methodology

One major focus of the study was documenting the progress to date on meeting the goals, objectives and planned activities as set out in the accountability framework: ***Strengthening Health Canada's Blood Regulatory and Surveillance Program***, prepared as part of the 1998 Treasury Board submission. This described the general goals, objectives for both the blood regulatory and surveillance programs and the activities that would be undertaken by Health Canada to increase its capacities to deliver the Blood Safety Program. This document formed the basis of the response by Health Canada to the Krever Report. *It should be noted that, while the title of the document refers only to blood, the objectives and activities also relate to tissues, organs, xenografts and transplantation, for both the surveillance and regulatory programs.* Other related issues include the identification of any remaining gaps and reviewing the necessary funding to ensure the sustainability of the HCBSP activities.

The following approach was used in carrying out the study:

- In the *planning phase*, a total of 17 preliminary interviews were carried out with internal stakeholders and key documents on the program were reviewed, including memoranda to Cabinet, program plans, business plans and reports on activities, web-sites, etc. This led to the development of a methodology report and data collection instruments.

- In the *first phase of the study*, the preliminary findings from the document review, as well as background information gathered from key informants, were summarized in a draft report. The basis for reporting was the 1998 Accountability Framework.
- The following activities were carried out in the *second phase of the study*:
  - the preliminary information obtained in the first phase of the study was validated with all key internal stakeholders, and further analysis done on the basis of additional information provided to us by Health Canada;
  - thirty-six (36) Health Canada program personnel were interviewed either in person or through teleconference calls;[2]
  - Health Canada provided a list of 44 external stakeholders representing blood operators, manufacturers of blood products, representatives from provincial Ministries of Health, health care providers and volunteer organizations. Two of the forty-four individuals could not be reached; thirty-five persons were contacted by telephone and/or e-mail (and messages left at least twice). Only ten (10) returned our call and were willing to be interviewed; and,
  - a focussed literature review was carried out to support the development of three cases studies: Hepatitis C, variant Creutzfeldt-Jakob Disease (vCJD) and Simian Foamy Virus. These case studies were chosen in consultation with Health Canada and were considered representative of different aspects of the Blood Safety Program. Health Canada officials had also started work on a research paper related to research on the TT virus. They felt this case study was representative of another aspect of their work. It had been prepared using the same approach used by GGI, a focussed review of scientific literature and GGI agreed to include it in the report.

GGI faced four major challenges in carrying out the study. First, in order to cover all aspects of Health Canada's regulatory and surveillance programs, it was necessary to carry out a much larger number of internal interviews than originally anticipated. Second, program activities are carried out by two different branches and various divisions and/or centres within Health Canada. Third, the restructuring of Health Canada also created some difficulties with respect to following up on specific activities. Actual expenditures on specific blood safety program activities was not readily available. Fourth, the literature review was focussed on the three case studies. A more exhaustive approach was beyond the scope, budget and time frame for the study.

Appendix A provides a list of the key documents reviewed. **Appendix B** gives the lists of the internal and external stakeholders interviewed during both the planning and the second phase of the study; and, **Appendix C** contains the study instruments.

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[2] Note: After discussion with Health Canada personnel, it was decided that individual interviews would be held with HC personnel as opposed to holding internal working groups for both the regulatory and surveillance programs.

Limitations

In reading this report, the following limitations, or areas that were beyond our mandate and the scope of the review should be kept in mind:

First, this was not an evaluation of the Canadian Blood Safety System as a whole. Our study neither reviewed the role of other players in the system; e.g. operators, manufacturers of blood products, hospitals, research organizations, etc., nor examined the role of expert committees within the System (e.g. National Blood Safety Council, Expert Committees; internal HC committees) or their relationship with Health Canada.

Second, this was not a financial audit of the expenditures carried out by Health Canada for the implementation of the Blood Safety Program.

Third, mention will be made occasionally of regulatory issues related to tissues, organs and xenografts to the extent that these issues were raised by internal and external stakeholders and considered relevant to this study. Therefore, the focus of this report is essentially on the Blood Safety Program at Health Canada and the activities carried out to strengthen its regulatory and surveillance programs under the 1998 Accountability Framework.
Fourth, this review did not address the scientific basis or justification of R&D activities.

2.0 Health Canada's Blood Safety Program

This section provides a brief historical background with respect to the Blood System in Canada; and describes the objectives of the Health Canada Blood Safety Program, the key players in the system, the responses of Health Canada to the Krever enquiry and the resources allocated to the Program.

2.1 Background

2.1.1 The Blood Tragedy of the Late 70's and 80's

In the late 1970's and the 1980's, the Canadian national blood supply became contaminated with two infectious viruses: the human immuno-deficiency virus (HIV) which causes AIDS; and, the hepatitis C virus. Canadians were infected through the blood system by two principal means: after having received blood transfusions while in hospital; or, after using factor concentrates, blood products used to treat hemophilia, that were made from the pooled plasma of thousands of donors.

Delays in implementing safety measures related to testing blood and blood products for infectious diseases can have tragic consequences. As a result of delays in the introduction of tests to screen donated blood for the Human Immuno deficiency Virus (HIV), over 1,200 hemophiliacs and transfusion recipients became infected in the early 1980's. Similarly, between 1986 and 1990, approximately 16,000 Canadians (of which an estimated 6,600 have survived) were infected with the Hepatitis C virus (HCV) through blood transfusions when surrogate tests, which were introduced voluntarily in other countries (e.g. US) were not introduced into the Canadian system.

In the spring of 1993, the parliamentary Standing Committee on Health and Welfare, Social Affairs, Seniors, and the Status of Women submitted a report entitled: "Tragedy and Challenge: Canada's Blood System and HIV".One of the most important recommendations of this report was the call for a comprehensive review of the Canadian blood system, in the form of a public inquiry, to fully clarify the tragic events of the 1980's, to reaffirm public confidence in the system, and to ensure the Canadian blood system will be able to deal with future challenges as well as the myriad requirements of day to day operations.

2.1.2 The Krever Commission

Consequently, on October 3, 1993, Order in Council PC 1993-1879 was issued, which provided that a Commission, headed by Mr. Justice Horace Krever, be issued under Part I of the *Inquiries* Act. Justice Krever was appointed to:

> ***"review and report on the mandate, organisation, management, operations, financing, and regulation of all activities of the blood system in Canada, including the events surrounding the contamination of the blood system in Canada in the early 1980's."***

The Krever Commission was established in October 1993 to review the mandate, organization, management, operations, financing and regulation of all activities of the blood system in Canada.

Justice Krever issued two reports: an interim report in February 1995 , "on the safety of the blood system, with appropriate recommendations on actions that might be taken to address any current shortcomings"; and a final report in November 1997 "with recommendations on an efficient and effective blood system in Canada for the future."

While the Krever Commission was in progress, the players within the Canadian blood system, including federal and provincial governments, began working towards immediate changes to improve and safeguard Canada's blood supply. By mid-1996, guided in part by the February 1995 interim report which identified over 300 flaws in the system, many changes and improvements were in progress or already completed:

- plans and strategies to create a new blood agency were developed; the governing principles for a new and improved Canadian blood system: safety, accountability, integration of the system, and transparency were put in place;
- the requirement that the members of the operating Board of this new system be at arm's length from government was accepted;
- the roles and responsibilities of the provinces and the federal government were clarified. The fundamental role of the federal government being responsibility for regulation of blood, blood products and their supply and responsibility for national disease surveillance;
- work was started to create a more effective, coherent regulatory capacity and to ensure the development of a standards based framework for regulation;
- a closer working relationship between the federal government and the then operator of the blood system, the Red Cross was established;
- an Expert Advisory Committee on Blood Regulation was created to advise the federal government on issues related to blood and blood products; and,
- there was some strengthening of Health Canada's disease surveillance capacity related to blood and blood products.

The final report of the Commission of Inquiry of the Blood System in Canada was released in November 1997.

Of the fifty recommendations, 17 were targeted at "The Regulator: The Health Protection Branch".The findings of the Commission and its subsequent recommendations indicated that substantial additional efforts needed to be implemented to ensure that Canadians have a safe national blood system. These recommendations were aimed at strengthening Health Canada's blood regulatory program and public health programs through enhanced blood surveillance. The seventeen recommendations targeting Health Canada are summarized in **Exhibit 2.1** below.

Exhibit 2.1: The Seventeen Krever Recommendations Aimed at Health Canada

Recommendations 29 to 45:

- **It is recommended that there continue to be a bureau that is dedicated to the regulation of biological drugs, including blood components, blood products, and their substitutes.**
- **It is recommended that the Bureau of Biologics and Radiopharmaceuticals (BBR) adopt a policy of active, not passive, regulation of the national blood supply system.**
- **It is recommended that the BBR make decisions with respect to the safety of blood components and blood products independently of those made by manufacturers and distributors.**
- **It is recommended that the BBR accept manufacturers' or distributors' decisions to take actions that exceed the standards of safety set by the bureau.**
- **The federal Minister of Health appoint an advisory committee to assist the BBR in its assessment and management of risk.**
- **It is recommended that the decision making process of the BBR be open and accessible to the public.**
- **The Food and Drug Regulations be rewritten to make them intelligible.**
- **It is recommended that the Food and Drug Regulations be amended to give the Therapeutic Products Directorate the authority to order a manufacturer or a distributor to recall a drug.**
- **It is recommended that the Food and Drug Regulations be amended to contain regulations for the collection and processing of whole blood.**
- **It is recommended that the Food and Drug Regulations be amended to require that labels on biological drugs contain information about the risks or potential risks of infectious diseases associated with the use of the drug.**
- **It is recommended that the BBR communicate regulatory requirements to manufacturers and distributors of blood products and blood components in a formal and unambiguous manner.**
- **It is recommended that there be an active program of post-market surveillance for blood components and blood products.**
- **It is recommended that the BBR conduct frequent and thorough inspections of the operations of the national blood service.**
- **It is recommended that the BBR re-evaluate the safety of blood products on the market during its review of manufacturers' applications to renew their licences.**
- **It is recommended that the BBR be given sufficient resources to carry out its functions properly.**
- **It is recommended that Canada continue to participate in efforts to develop international harmonization in many aspects of drug licensing, but that it retain the duty and authority to make decisions about the products to be distributed in Canada.**
- **It is recommended that international audits of the BBR be conducted every five years.**

The federal government accepted Justice Krever's recommendations and made a commitment to "continue to take an aggressive leadership role in making Canada's national blood system second to none."

In March 1998, the Laboratory Centre for Disease Control (LCDC) of Health Canada created the Surveillance and Epidemiology in Transfusions (SET) Working Group to develop a plan and design a program for a comprehensive blood surveillance system for Canada. Membership in this group included staff of the LCDC, the Bureau of Biologics and Radiopharmaceuticals, provincial and territorial public health organizations, and experts in the areas of transfusion medicine and epidemiology. Based on their findings[3], the SET Working Group made thirteen recommendations with the primary objective that the federal, provincial and territorial governments establish a national surveillance system to determine the risk of infectious and non-infectious adverse events following administration of blood and/or blood products. They also recommended the establishment of a surveillance system for infectious diseases in the community which would involve tracking the emergence, modes of transmission, and spread of blood-borne infectious diseases; and finally the surveillance of blood donors to identify trends in donation patterns, risk factors and infectious disease markers.

Between 1995 and 1999, the structure of the blood system in Canada underwent considerable **change. Exhibit 2.2** below - Organizations involved in decision-making in 1995 and 1999[4] - provides an overview of the organizations involved in decision-making during these two periods.

Exhibit 2.2: Organizations Involved in Decision-Making in 1995 and 1999

1995	1999
Policy-makers	
Minister of Health Office *Regulator* Health Protection Branch →Drugs Directorate→Bureau of Biologics	Minister of Health Office *Regulator* Health Protection Branch→Therapeutic Products Programme→Bureau of Biologics and Radiopharmaceuticals*
Operators	
Canadian Red Cross	Canadian Blood Services Héma-Québec

[3] *The Surveillance and Epidemiology of Transfusions Working Group Final Report,* Chair: Dr. Steven Kleinman, February 28, 1999

[4] *A policy analysis of major decisions relating to Creutzfeldt-Jakob disease and the blood supply*, Kumanan Wilson & al, CMAJ. July 10, 2001; 165 (1)

Funder	
Provincial and Territorial governments through the Canadian Blood Agency	Provincial and territorial governments directly to respective operator
Manufacturer of Blood Products	
Bayer Inc.	Bayer Inc.
Consumer Groups	
Canadian Hemophilia Society had highest profile	Canadian Hemophilia Society had highest profile
Other	
Laboratory Centre for Disease Control (scientific arm of the Health Protection Branch - limited role in 1995)** No equivalent organization No equivalent organization	Laboratory Centre for Disease Control (scientific arm of the Health Protection Branch - important role in 1999)** National Blood Safety Council Bayer Advisory Council on Bioethics (independent agency provided evaluation of blood policy issues)

Source: *A policy analysis of major decisions relating to Creutzfeldt-Jakob Disease and the Blood Supply,* Kumanan Wilson & al, CMAJ, July 10, 2001; 165 (1)

* Health Canada underwent a major realignment in 2000, with the merger of health protection and promotion activities. The Therapeutic Products Directorate has been split into three groups - the Therapeutic Products Directorate, the Biologics and Genetic Therapies Directorate, and the Health Products and Food Branch Inspectorate. It should be noted that these units also have strong scientific capabilities.

** Now called the Centre for Infectious Disease Prevention and Control (CIDPC), Population and Public Health Branch.

In 1995, the Red Cross was the national operator responsible for collecting and distributing blood. It received funding from the Canadian Blood Agency, whose responsibility was to direct, coordinate and finance aspects of the blood system consistent with the objectives of the provinces and territories.

In September 1998, the new national blood authority, the Canadian Blood Services (CBS), started operations and received funding directly from the provinces and territories and, in turn, collected, tested, distributed blood products for all provinces and territories with the exception of Québec. It combined the operating and financing roles of the Red Cross and the former Canadian Blood Agency. Québec developed its own plan following the Gélineau Committee, and a new agency, Héma-Québec also started operations in September 1998.Both agencies are required to follow Health Canada regulations.

In November 1997, the federal Minister of Health established the *National Blood Safety Council* to advise him on blood-related matters within the responsibility of the federal government, particularly issues pertaining to blood regulation and national disease surveillance.

2.2 The Health Canada Blood Safety Program

In response to Justice Krever's recommendations, additional funding was provided to Health Canada to ensure that the following two critical objectives of the Blood Safety Program (BSP) were met:

- to protect the people of Canada against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and,
- to be on par, in general, with blood regulatory and surveillance programs in other leading industrialized nations, such as the United Kingdom, Australia and Germany.

Between 1995 and 1999, there were important changes within the regulatory authority. In 1999, the Drugs Directorate was renamed the Therapeutics Products Program due to the inclusion of medical device regulation in its mandate, and the Bureau of Biologics was now called the Bureau of Biologics and Radiopharmaceuticals, within the Therapeutic Products Program, under the Health Protection Branch. These units continued to be responsible for the regulation of blood and blood products.

Currently, the Health Canada BSP is delivered through both its regulatory and surveillance programs. In 2000-2001, Health Canada underwent a major realignment exercise. This report reflects the new structure, although it would be premature to evaluate any impact it could have on program effectiveness. It remains, however, that responsibilities and accountabilities for various aspects of the Blood Safety Program are now diffused across two different branches and many organizational units. A brief description of the organizational structure is provided below to set the overall context for the **review. Exhibit 2.3** provides an overview of the organizational units responsible for both the regulatory and surveillance programs at Health Canada.

Exhibit 2.3: Organizational Units - Regulatory and Surveillance Activities Health Canada Blood Safety Program

Regulatory Activities	Surveillance Activities
Health Products and Food Branch	**Population and Public Health Branch**
Biologics and Genetic Therapies Directorate • Centre for Policy and Regulatory Affairs • Biologics and Radiopharmaceuticals Evaluation Centre • Centre for Biologics Research **Therapeutics Products Directorate** • Bureau of Licensed Product Assessment • Medical Devices Bureau **Inspectorate**	**Centre for Infectious Disease Prevention and Control** • Blood-borne Pathogens Division, Bureau of Infectious Diseases **Bureau of HIV/AIDS, Sexually Transmitted Diseases and Tuberculosis** • Division of Retrovirus Surveillance • Division of HIV/AIDS Epidemiology and Surveillance • National HIV Laboratories **National Microbiology Laboratory** • National Laboratory for Host Genetics and Prion Diseases • National Laboratory for Viral Diagnostics

Overall, the Health Canada Blood Safety Program regulatory and surveillance responsibilities are with the Assistant Deputy Minister of the Health Products and Food Branch and the Assistant Deputy Minister of the Population and Public Health Branch respectively. Issues related to blood safety are identified through weekly meetings of individuals responsible for the various aspects of the blood safety program within the two branches. At the Departmental level, a risk management committee has been created and meets weekly as well. Any high priority issues related to the blood safety program can be brought to the attention of senior management through these channels.

2.2.1 Regulatory Program

Health Canada BSP ***regulatory responsibilities*** operate within the mandate established under the *Food and Drugs Act* and Regulations, Division 1A (Establishment Licences), Division 2(Good Manufacturing Practices), Division 4 (i.e. Schedule D Drugs) and various Health Canada guidelines and directives. Under the Food and Drugs Act, Health Canada regulates the collection of blood and the manufacturing of blood components, products derived from blood, which are sold in Canada. Health Canada sets national standards, defines the minimum procedural requirements for Canadian organizations that collect blood and manufacture blood components and licences the blood operators.

Within the regulatory program, the following general goals were established to support the overall objectives of the Blood Safety Program:

- enhance the breadth of Blood regulatory expertise to address emerging new blood technologies and blood substitutes;
- enhance the blood inspection and compliance function, which is expected to grow exponentially with the implementation of a separate blood system in Québec (Héma-Québec); and,
- perform more effective post-market surveillance, which will allow the regulator to develop information on risks, to take action to minimize these risks, and to provide this information to Canadians.

The regulatory program is carried out principally by the ***Health Products and Food Branch*** (HPFB).The mandate of the Branch is to promote good nutrition and informed use of drugs, food, medical devices and natural health products, and to maximize the safety and efficacy of human and veterinary drugs, food, natural health products, medical devices, biologics and related biotechnology products. The Branch plays a key role in managing the risks associated with the use of these products. To this end, it is involved in the enforcement of federal legislation that sets standards for quality, health and safety, conditions for sale and the prevention of fraud and diversion from legitimate uses.

Three directorates are involved with the Blood Safety Program within this Branch:

- *Biologics and Genetic Therapies Directorate* is responsible for the majority of the regulatory activities related to blood, blood products, tissues, organs, xenografts, and semen for assisted conception. As of September 1, 2001, the Directorate has been reorganized into three Centres: Centre for Policy and Regulatory Affairs; Centre for Biologics Evaluation and the Centre for Biologics Research. Regulatory activities include: review of License Applications and Amendments; Establishment Licensing for blood operations; lead role in inspection activities; investigations; review and analysis of Adverse Transfusion Reports; policy development; and, issuance of guidance documents and directives to blood establishments;
- The *Therapeutics Products Directorate* where two bureaus support the regulatory activities: Bureau of Licensed Product Assessment (BLPA) and Medical Devices Bureau (BMD); and,
- The *Inspectorate* which delivers a national compliance and enforcement program for all products under the mandate of the Branch. This is done through industry inspection, product investigation, establishment licensing and regulated laboratory functions. The Inspectorate delivers a national program using legislation , policy, science, communication and education, and regional operations as the foundation for all compliance and enforcement activities.

The organization of the BSP regulatory functions in these three directorates combines the scientific and technical expertise, and the administrative and public policy expertise both of which are needed for strong and effective leadership on the regulatory side. Enforcement and compliance were separated out from both directorates and now report directly to the ADM. Post-market surveillance is also a function that is needed by both directorates with the potential for overlap and the need for collaboration with another Branch, the Centre for Infectious Disease Prevention and Control (CIDPC) of the Population and Public Health Branch.[5]

2.2.2 Surveillance Program

The ***Centre for Infectious Disease Prevention and Control (CIDPC)*** and the ***National Microbiology Laboratory of the Population and Public Health Branch*** are responsible for implementing the BSP's ***surveillance activities*** aimed at strengthening public health programs through enhanced blood-borne surveillance activities.

The CIDPC's Director General (DG) manages the overall surveillance activities of the HCBSP. This is achieved through the work and collaboration between: i) ***the blood-borne Pathogens Division in the Bureau of Infectious Diseases; ii)*** the ***Division of HIV/AIDS*** and the ***Division of Retrovirus Surveillance in the Bureau of HIV/AIDS, STDs and TB; iii)*** the ***National HIV Laboratories;*** iv) the ***National Microbiology Laboratory.***
In brief:

- The *Bureau of Infectious Diseases (BID)* and its *Blood-borne Pathogens Division (BBPD)* are responsible for: the creation of a national blood surveillance system based on a voluntary post-market surveillance system; an active surveillance of infectious diseases and adverse transfusion related incidences (ATRs) which includes errors related to a transfusion; a donor database; the conduct of public health surveillance investigations; risk assessment; risk management and risk communication of blood safety and injuries including hepatitis, other blood-borne pathogens, and prions.
- The *Bureau of HIV/AIDS, STDs and TB* and its *Division of Retrovirus Surveillance (DRS)*, the *Division of HIV/AIDS Epidemiology and Surveillance* and the *National HIV Laboratories* are responsible for: maintaining and improving the quality of national HIV and AIDS surveillance data via the creation of a nationwide network of provincial field surveillance officers; establishing an integrated surveillance system for HIV and AIDS, and emerging retroviruses, and collaborating with provincial and territorial partners on targeted epidemiological studies; enhancing Bureau lab capacity for the identification of new HIV strains and HIV drug resistance surveillance; the

[5] Sources: Notes of the National Blood Safety Council Meeting, February 15, 2001

development of new lab tools for the detection of retroviral contamination or infection; targeted surveillance risk assessment for emerging retroviruses; and, support to blood and tissue safety regulatory activities.

- The *National Microbiology Laboratory* is responsible for providing laboratory science, reference services and surveillance support in connection with infectious threats to blood safety other than retroviruses. Two of its Divisions - the *National Laboratory for Host Genetics and Prion Diseases-NML* and the *National Laboratory for Viral Diagnostics-NML* - are directly involved in and funded by the HCBSP. Specific activities include: development, validation and support for new and improved diagnostic tests (including those for novel agents such as prions); genetics, biochemistry and molecular epidemiology of disease transmission and expression; and, provision of expert consultations and information.[6]

2.2.3 Other Key Players

Along with the above, other key 'players' in the Blood Safety Program include:

- The Expert Advisory Committee on Blood Regulation provides Health Canada with ongoing and timely medical, scientific, ethical and communications advice on current and emerging issues concerning: the regulation of the Canadian blood system; the manufacture, distribution and use of blood, blood components and blood products; standards and procedures including prospects for international harmonization; developments in Canada and internationally; and, public disclosure of information. This Committee is supported through a coordinator with an internal working group made up of representatives from all groups involved in blood regulation or surveillance;
- The *National Blood Safety Council* provides advice to the Minister on blood-related matters within the purview of the Federal government, in particular, on issues related to blood regulation, availability issues, and infectious disease risks;
- *Provincial Ministries of Health* and hospital transfusion centres provide data to the CIDPC on infections related to transfusion and transplantation;
- The *Canadian Blood Services (CBS)* and *Héma-Québec* collect and test donor blood and distribute blood and blood products to hospitals and sites across Canada. In addition, they perform research into the blood supply and its utilization;
- *Hospitals* across Canada maintain transfusion services and acquire and process blood for autologous transfusions;

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[6] Health Canada Blood Safety Program, Evaluation Framework, Working Document, May 2001 pp8-9.

- *Interest groups* such as the Canadian Hemophilia Society, the Canadian AIDS Society and the Canadian Society of Transfusion Medicine serve as advocates on blood-related matters of concern;
- The *Canadian Food Inspection Agency's* role in food inspection and quarantine includes responsibilities for surveillance, prevention and control of animal diseases, including prion diseases and other diseases with the potential for transmission between animals and humans; and,
- *Connections to other societies and agencies*, including the U.S. Food and Drug Administration (FDA), National Institutes of Health (NIH) and Centres for Disease Prevention and Control (CDC), and the World Health Organization (WHO).

2.3 HCBSP Resources

Exhibit 2.4 below shows the HCBSP approved funding for fiscal years 1998/99 through 2002/03, including corporate and program support service charges. The total of $214 million and 250 fu ll-time equivalents (FTEs) reflects the following components:

- Initial A-base funding of $25 million and 36 FTEs;
- In December 1996, Cabinet approved an additional$20 million and 81 FTEs annual investment to improve blood safety (MC 96). Of this, $13 million annually was used commencing 1996-97 for initial improvements to the federal government's blood regulatory and surveillance programs. The annual $13 million was allocated as follows:
  - Regulatory: $2.5 million
  - Surveillance: $6.3 million
  - Blood system report and governance activities: $4.2 million

  Of the remaining $7 million, $5 million was allocated to the Canadian Blood Services (CBS) commencing in 2000-2001 and ongoing to support their research and development initiatives. The remaining $2 million remains in the fiscal framework commencing 2000-2001 and ongoing to address emerging priorities related to HC's safety responsibilities.[7]
- An additional $125 million and 133 FTEs over 5 years was announced in November 1998 (MC 98) to establish strong blood regulatory and surveillance programs within Health Canada. The allocation of the $125 million and FTEs are shown in the shaded areas of the following table, which summarizes the total funding and FTE allocation for the HCBSP.

[7] TB submission on, date stamped January 26, 2001, requesting TB approval for $2M annually, for 2000-01.

Exhibit 2.4: Summary of Planned HCBSP Resourcing

Activities	FY 98-99		FY 99-00		FY 00-01		FY 01-02		FY 02-03		Total	
	FTEs	$M	FTEs	$M	FTEs	$M	FTEs	$M	FTEs	$M	FTEs	$M
Initial A-base	**36**	**$4.8**	**36**	**$4.8**	**36**	**$4.8**	**36**	**$4.8**	**36**	**$4.8**	**36**	**$25**
1997 A-base Increase	**80.5**	**$13.0**	**80.5**	**$13.0**	**80.5**	**$13.0**	**80.5**	**$13.0**	**80.5**	**$13.0**	**80.5**	**$64**
A. Regulatory	31	$5.6	62	$10.5	73	$13.5	73	$12.9	73	$12.2	73	$55
B. Surveillance	36	$7.8	44	$13.4	46	$13.4	46	$10.0	46	$10.2	46	$54
C. Legal Support	6	$0.9	8	$1.0	9	$1.0	9	$1.0	9	$1.0	9	$5
D. Policy & Coordination Support	11	$3.2	11	$2.3	5	$1.7	5	$1.8	5	$1.6	5	$11
Total TB Submission	**84**	**$17.5**	**125**	**27.2**	**133**	**$29.6**	**133**	**$25.7**	**133**	**$25.0**	**133**	**$125**
Grand Total	**200.5**	**$35.3**	**241.5**	**$45.0**	**249.5**	**$47.4**	**249.5**	**$43.5**	**249.5**	**$42.8**	**249.5**	**$214**

Source: Health Canada Blood Safety Program, Evaluation Framework, May 2001

2.4 The Accountability Framework

The Accountability Framework: ***Strengthening Health Canada's Blood Regulatory and Surveillance Program***, prepared as part of the 1998 Treasury Board submission, described for the blood regulatory and surveillance programs, their general goals, the increased capacities needed for effective program delivery, the planned actions/results, and resources required to deliver these activities. A copy of the framework is provided in **Appendix E**. This action plan included fourteen (7 for regulatory and 7 for surveillance) specific requirements and corresponding activities/projects aimed at strengthening the regulatory and surveillance programs.

3.0 Blood Regulatory Program

This section provides a brief overview of the activities that were undertaken to strengthen Health Canada's regulatory activities and to deliver programs that will allow it to reach its long-term objectives. We also examine the overall resources applied to different activities, as well as identified gaps and future resource requirements are also examined. In addition, issues raised by external stakeholders with respect to the regulatory functions are briefly discussed.

3.1 Role of the Regulator and Program Goals

The Canadian blood regulator must have the resources to analyse information provided by the manufacturer and compare it to other information; to perform frequent and thorough inspections; to conduct research; to actively monitor products on the market; to develop regulations and policy; to manage emergency situations; and, to communicate and consult with consumers and other blood system stakeholders.

The focus of regulation in the past decade has been on blood. In addition to the change in the operator of the national blood supply system (CBS and Héma-Québec), privately owned blood banks and plasmapheresis centres are expected to enter the Canadian "blood market".Many hospital blood banks are now actively manufacturing blood and blood components, and are positioned to change and expand. These new organizations will require federal oversight and education on federal regulatory requirements.

The Regulator performs various activities to ensure blood components and plasma-derived products meet high standards of safety, quality and efficacy, not only when new products enter the market, but throughout their life cycle. Such activities include issuance of guidance documents to industry and modifications to *Food and Drug Act and* Regulations. One such guidance document entitled "*Guidance on the Manufacture of Human Plasma-Derived Products - Viral Safety Evaluation*" has been posted on the HC web-site in July 2001 with a request for comments from stakeholders. The comments have been received and an updated Guidance document will be promulgated later in 2002.

As well, in 1996 new regulations entitled "*Processing and Distribution of Semen for Assisted Conception Regulation"* were added under the Food and Drugs Act. These regulations provide a framework for minimizing the risk of disease transmission through donor semen use in assisted conception. An independent Expert Working Group established by Health Canada has drafted Standards for Blood Safety. Work has also been done to draft the Canadian General Standard on the Safety of Cells, Tissues and Organs for Transplantation and Assisted Reproduction and five subset standards for individual tissues and organ types. As well the regulatory requirements applicable to human plasma collected by plasmapheresis are being amended.

These new developments post-Krever pose new regulatory challenges for Health Canada.

General goals established for the Blood Regulatory Program[8] include the enhancement of blood regulatory expertise to address emerging new blood technologies and blood substitutes; the enhancement of the blood inspection/compliance function to meet increasing demands; the development of a more effective post-market surveillance, including encouragement of voluntary reporting by health practitioners; and, generally supporting the transition to the new blood system.

Seven specific requirements and corresponding activities/projects aimed at strengthening the regulatory program were outlined in the 1998 Accountability Framework:

- ***Capacity to conduct compliance and enforcement activities*** - hospitals currently manufacturing blood and blood components, new sites in the proposed separate Quebec blood supply system, tissue and organ facilities and establishments processing, distributing and/or importing donor semen for use in assisted conception (semen establishments) must be inspected to assess their compliance with the applicable regulatory requirements.
- ***Capacity to conduct pre-market and post-market reviews*** - this involves the licence issuing function of the regulatory program. The staff are involved with the pre- and post-review of sites to ensure that the facilities and operation of blood product manufacturers, semen establishments, and tissue and organ transplantation centres including hospitals meet regulatory requirements applicable to their activities/products. This capacity also includes the pre-market and post-market review of medical devices used to ensure the safety of the blood supply system.
- ***Capacity to perform more effective post-market surveillance*** - this includes laboratory based analysis of blood and blood products, as well as monitoring adverse events resulting from the use of those products. This allows the regulator to develop information on risks, to take action to minimize these risks, and to provide this information to concerned Canadians.
- ***Capacity to perform regulatory research related to blood safety*** - this includes research activities in support of safety, quality and efficacy assessments of new types of products, assessments of new types of therapeutic approaches to medical treatments and benefit/risk analysis. This research supports the independence of the regulator and its ability to reach decisions separately from those of the manufacturer, as was recommended by Krever.
- ***Capacity to conduct regulatory policy development*** - this involves the development of a responsive and flexible regulatory approach, using extensive consultation. This is to be accomplished through the use of a standards-based regulatory framework.

[8] Accountability Framework: Strengthening Health Canada's Blood Regulatory and Surveillance Programs

- ***Capacity to respond immediately to threats to the blood supply*** - this involves activities such as crisis management planning, contingency planning and international monitoring.
- ***Capacity to provide an effective communications interface between regulator and stakeholders*** - this activity allows the program to respond to the demands of consumer-based organizations and other stakeholder groups to provide more information and to become more proactive.

Exhibit 3.1 below provides an overview of the linkages between the long term goals of the Regulatory Program and the capacities needed to support the attainment of these goals.

Exhibit 3.1: Goals and Capacity Development - Regulatory Program

Goals	Capacities
• enhancement of blood regulatory expertise	• capacity to conduct regulatory research related to blood safety • capacity to conduct regulatory policy development • capacity to respond to threats to the blood supply
• expansion of blood inspection/compliance function	• capacity to conduct compliance and enforcement activities
• effective post-market surveillance	• capacity to conduct pre and post-market reviews, including the capacity to conduct benefit-risk assessments of marketed blood products and timely access to new technologies • capacity to provide effective communication, including the capacity to provide effective risk management and communication of licensed product safety
• support transition to new blood system	• capacity to provide effective communications interface between regulator and stakeholders

3.2 Program Resources

Exhibit 3.2 below summarizes the HCBSP project plan for the expenditures by Directorate and Bureau distribution. It also provides information on the deductions for Corporate Services support, branch support, employee benefits and accommodation from the overall resources allocated by the 1998 MC for the support of enhanced regulatory activities. It should be noted that the financial management system reports on the basis of organizational units, and that many units may contribute to the strengthening of different

capacities and to the achievement of long-term goals. Health Canada staff also reported that actual expenditures on blood supply program activities are not generally available. This table shows the funds available for the various activities after the standard taxes, which account for between 30 and 40 percent of the total resources provided by the 1998 MC[9]:

- Branch support (about 7%) of gross
- Departmental corporate support (about 5% of gross)
- Employee Benefit Plan (about 20% of salaries)
- PWGSC Accommodation (about 13% of salaries)
- Branch Strategic Investment Fund (15% of salary and operating and EBP for HPFB in 2001-02 and assumed equal for 2002-03)

The table is based on what funding from HCBSP should have been available for the 1998-99 to 2000-2001 period and will be available for 2001-2002 and 2002-2003.According to Health Canada staff, one can assume that what is shown in the table also represents actual use of these funds. The financial information provided to us to date did not permit us to confirm or validate the actual moneys spent on the Blood Safety Program.

It should also be noted that according to Health Canada staff, the HCBSP resources within the Therapeutics Products Division; Bureau of Licensed Product Assessment for 2002-03 of $724 thousand represent 17 percent of their estimated expenditures of $4.2 Million. HCBSP funds for the Medical Devices Bureau funds for 2002-03 of $663 thousand represent 12 percent of their estimated expenditures of $5.7 Million.

Exhibit 3.2: Project Plan for Expenditures and Directorate and Bureau Distribution for Regulatory Activities

Activities	FY 98-99		FY 99-00		FY 00-01		FY 01-02		FY 02-03	
	FTEs	$M	FTEs	$M	FTEs	$M	FTEs	$M	FTEs	$M
A. Regulatory	31	$5.603	62	$10.471	73	$13.538	73	$12.893	73	$12.216
HPFB (Program Support)	4.3	$0.312	8.8	$0.557	6.2	$0.750	6.2	$0.715	0	$0
DG Office	1	$0.367	3	$0.806	4	$0.896	0	$0	0	$0
BBR	8	$1.526	24	$3.063	34	$4.528	33.5	$3.697	36.1	$3.675
BGTD							11	$1.701	11.6	$1.670
BCE	5	$0.793	9	$1.061	11	$1.676	12.5	$1.344	13.5	$1.332
BLPA	5	$0.513	5	$0.805	5	$0.805	5	$0.723	5.5	$0.778

[9] The 1998 MC states that all dollar amounts include corporate and program support service charges.

MDB	2	$0.202	6	$0.806	6	$0.806	6	$0.664	6.3	$0.713
BPC	6	$0.773	7	$0.868	8	$1.327	0	$0	0	$0
Corporate Support		$0.753		$1.105		$0.994		$0.858		$0.852
EBP @20% of salary		$0.373		$0.851		$1.064		$1.064		$1.064
PWGSC Accommodation		$0		$0.553		$0.692		$0.692		$0.692
HPFB Special Investment Fund								$1.434		$1.441
Actual Totals	31.3	$5.612	62.8	$10.475	74.2	$13.538	74.2	$12.892	73	$12.217
Delta (over) under	-0.3	($0.01)	-0.8	$0.0	-1.2	$0	-1.2	$0.0	0	$0

Source: Financial Information provided by HPF-TPP-OMS, 7 December 2001

Footnotes:
1) The Biologics and Genetic Therapies Directorate (BGTD) was created in April 1, 2001.Resources originally allocated to the DG Office and BPC were transferred to BGTD starting in 2001-2002.
2) In 2001-2002 the Health Products and Food Branch created a Branch Strategic Investment Fund (SIF). This replaced the Program Support component of the resources identified in the TB Submission. In 2001-2002 the SIF was equal to 15% of salary, operating and EBP. It is assumed that a SIF of 15% will exist in 2002-2003.

3.3 Progress to Date

This section describes the progress to date on strengthening Health Canada's regulatory capacity in response to the Krever recommendations and in meeting their long term goals and any issues raised by internal and external stakeholders. The information is based on document review as well as interviews with key internal and external stakeholders. The findings will be grouped along the following four major themes:

- overall enhancement of the blood regulatory expertise including: the capacity to conduct regulatory research related to blood safety and regulatory policy development and the capacity to respond to threats in the blood supply;
- expansion of the inspection and compliance function which is an essential and critical element of the regulator's role;
- effective post-market surveillance including the capacity to conduct pre-market and post-market reviews and to conduct more effective post-market surveillance; and,
- support provided to transition to the new blood system including increased transparency and communications with key stakeholders.

Appendix D provides a synthesis of the activities planned, outputs to date and specific gaps and resource requirements for each of the capacities identified in the 1998 Accountability Framework.

3.3.1 Enhancements to Health Canada's Blood Regulatory Expertise

Both the document review and the interviews with key stakeholders provide evidence of progress towards enhancing Health Canada's blood regulatory expertise through the conduct of regulatory research related to blood safety; e.g., the development of new techniques and/or approaches to meet new and emerging requirements and the ability to stay at the leading edge of new developments in the field; the capacity to develop appropriate regulations; and, the capacity to respond to new threats to the blood supply.

In the period 1989-1997, regulatory guidance and requirements for Canada's blood system were set out in correspondence with a single blood system operator, namely, the Canadian Red Cross Society (CRCS). With the transition of the blood system to two new operators in 1998, Health Canada needed to review all operations of the new Canadian Blood Services and Héma-Québec (HQ) to ensure compliance with regulations. Given that HQ had never before applied for an establishment (operating) license, developed standard operating procedures for their operating environment for regulatory review, or had knowledge of regulatory requirements for other aspects of their new operation, Health Canada was challenged to provide unprecedented regulatory guidance over a very short time frame to HQ to ensure that their separate operations could be safely begun with issuance of anew establishment license. The CBS operating environment inherited from CRCS also needed to be reviewed and an establishment license issued. Health Canada was able to ensure the transition to the new blood system.

A review of new techniques in the area of preparation of blood components by Health Canada scientific staff led to the development of position papers and issue analyses recommending that all blood components in Canada be leuko-reduced to enhance safety of components. This became a mandatory manufacturing requirement of blood system operators in 1998. As a result of this initiative, Health Canada estimates that 10, 000 Canadians annually will benefit from not suffering immune reactions as a consequence of blood transfusion.

Scientific staff within the former BBR (currently the Biologics and Radiopharmaceuticals Evaluation Centre or BREC) had reviewed developments with new testing methodologies for detection of infectious disease agents such as HIV and hepatitis C. As a result of this review, regulatory requirements were defined for industry to use nucleic acid testing (NAT) to test for a number of infectious disease agents including HIV as part of issuance of a notice of compliance to market a number of blood products in Canada. Health Canada also worked to establish independent NAT testing in BBR laboratories to validate a number of these tests and participated in international standardization of the testing methodologies. Arising out of this initiative, the BBR held many regulatory meetings with CBS and HQ, recommending that NAT technology be investigated as a test of record for testing of blood

and blood components. Working with the Medical Devices Bureau, Health Canada has reviewed and approved new NAT tests for both HIV and hepatitis C and put in place new molecular testing methodology within the blood system to allow the introduction of new, more sensitive tests for infectious agents that may prove a threat to the blood system.

During the review of the safety of the blood system over the period 1989-1999 it was evident that the level of automation within the blood system operating environment was not satisfactory and many information management systems needed Y2K "upgrading". Health Canada developed new guidelines for information management systems to be followed by blood operators and reviewed a large number of new IMS installations leading to a successful and problem free Y2K transition and compliance process.

As shown in **Exhibit 3.3** below, over the last years according to BGTD, there has been a significant increase in their workload regarding the regulation of blood establishments.

Exhibit 3.3: Workload Changes for BGTD

	Year 1997	Year 2001
Submissions received	47	124
Errors and accidents reported	358	2047
Post Donation Information reports	179	2343
Adverse Transfusion Reaction reports	49	170
Regular Annual Blood Inspections performed	20	20

Source: Health Canada - BGTD

Capacity to Perform Regulatory Research Related to Blood Safety (Requirement 4)

As stated in the Accountability Framework, "The research program supports the independence of the regulator and its ability to reach decisions separately from those of the manufacturer, as was recommended by Justice Krever." The strengthening of the regulatory research program through the addition of BSP resources has permitted the program to carry out a number of research activities aimed at ensuring the safety of Canada's blood supply.

For example:

- One factor of critical importance to the safety of transfusion is the elimination of the infectious agents associated with blood and blood products. It is important that Health Canada has the capability to assess new screening technologies and emerging new infectious agents which may threaten blood transfusion. Therefore, research is being conducted on the use of powerful physiological oxidants that neutralize retroviruses like HIV in blood and blood products.

- Research on the evaluation of novel systems for the expression of biotherapeutics and oral/edible vaccines is also being conducted, as products derived from recombinant DNA technology are replacing the more traditional blood products. Specifically, the use of plant (tobacco and rice) systems for the expression of biotherapeutics and oral/edible vaccines has been investigated. Related research continues to be conducted on blood transmissible infectious diseases, in particular new subunit vaccine development, which would enable oral delivery and mucosal immunization.
- Research on the development of *in vitro* methods for the evaluation of anticoagulant and fibrinolytic blood proteins has been conducted, with a view to modernizing these methods wherever possible. Similarly, research is supported on development of in vitro methods for evaluating the potential detrimental effects of biological products, including those derived from blood.
- The regulator has also participated in collaborative studies organized by European Pharmacopoiea on the standardization and calibration of clotting factors. This type of effort strengthens the international linkages of the BGTD, and allows for further exchange of scientific information in support of the regulatory program. Other examples of international linkages include membership on the WHO working group on Genome Amplification Techniques for the detection of viral contaminants in blood and blood products, and membership in the European Pharmacopoeia Expert Working Group on Gene Amplification Methods, resulting in a monograph being prepared to describe PCR-based methods for the detection of pathogens in products derived from blood or blood products.
- Laboratory work was conducted to investigate genetic variation in the Prp (prion) gene, in blood donors subsequently diagnosed with CJD. This work was part of a collaborative effort with the LCDC, as part of the National CJD Surveillance Program. Subsequently, all laboratory work on CJD was transferred to LCDC. The expertise continues to exist within the research centre, related to genetic screening.
- Research expertise has been brought to bear on the development of safety standards for xenotransplantation, with particular concern on the possible transmission of novel xenozoonotic infectious diseases.

Although staffing was often a difficult and lengthy process (due to many reasons including the federal government recruitment processes and uncompetitive salary scales) and the ability to recruit individuals with significant blood expertise was limited (e.g., limited availability of experts in the field); BGTD indicated that efforts were made to attract and retain staff as needed both on the scientific/research side and the policy development side despite these two major challenges.

For example, the hiring of two additional scientists allowed Health Canada to go forward with key projects, including research related to protein folding and prion disease; the interaction of antithrombin III with fibrinolytic proteins; and the characterization of the genetic polymorphism identified in a CJD patient sample as part of the international CJD surveillance study.

Health Canada program staff believe that the Blood Safety Program has also been able to maintain its position at the leading edge of methods development through it's participation in international collaborative studies with the European Pharmacopia OMCL Network (e.g. method for HIV screening by NAT; methodology for analysis of Factors II, IX, and X). Participation in these studies gives Health Canada access to the results of studies before they are published.

Internally, concerns were raised with respect to the need for additional staff (2 FTEs) to support the development of new technologies.

In addition, a few external stakeholders expressed concerns about some of the BSP approaches, as well as their cost benefits. For example: 1

- At least one of the external stakeholders expressed concerns about the test kits approved by Health Canada. The Committee responsible for reviewing the requirements for these kits has apparently not met in five years and concerns were raised with respect to how new products will be regulated in the future.
- Another external stakeholder expressed concerns with respect to the cost-effectiveness of the enhanced testing being done for HIV/AIDS; i.e., the P24 Antigen test and the NAT (nucleic acid test).Both tests are very expensive and this respondent felt that they were not more effective than other tests at identifying known blood-borne pathogens or else were identifying too many false positives.
- Another external stakeholder also raised concerns with respect to the excessively high costs associated with Health Canada directed safety testing by the Canadian Blood Services and the costs/benefits of alternate blood safety technologies. These costs impact highly on the provinces. The provincial and territorial governments have invested significant funds for the national blood provider, the Canadian Blood Services (CBS), and in Québec, Héma-Québec operations. Ontario, for example, contributes 51% of funding to support the activities of CBS, many safety related.

Capacity to Respond Immediately to Threats to the Blood Supply (Requirement 6)

A number of activities were carried out to increase Health Canada's ability to respond to potential threats to the blood supply. The emergency response manual was updated and related procedures used three times in the 1999-2000 period and reviews to ensure that the system was effective were conducted in two of the three situations. As well, two training sessions were conducted with all teams, plus a Validex exercise and simulations related to

Y2K, including blood scenarios. As stated earlier, issues related to blood safety are identified through weekly meetings of individuals responsible for the various aspects of the blood safety program within the two branches. At the Departmental level, a risk management committee has been created and meets weekly as well. Any high priority issues related to the blood safety program can be brought to the attention of senior management through these channels. In addition, BGTD has put in place a risk process manager, with responsibility for issue coordination and response to specific emergencies as they occur.

Creutzfeldt-Jakob Disease (CJD) is the first major challenge that the blood system has faced since the completion of the Krever enquiry in 1997.As a novel group of infectious diseases, prion diseases (also known as transmissible spongiform encephalopathies or TSEs) present challenges to the public health decision makers.

A mini-case study provides a brief overview/history of the actions taken by Health Canada and other stakeholders in response to potential threats from both (classical) cCJD and its (variant form) **vCJD. Exhibit 3.4** on the following pages summarizes the actions taken by Health Canada with respect to these potential threats, and the role played by both the regulatory and surveillance programs in the overall situation, with an emphasis on the policy decisions taken by Health Canada to protect the safety of the blood supply in Canada.

Exhibit 3.4: Policy Decisions Relating to Creutzfeldt-Jakob Disease and the Canadian Blood Supply

Policy Decisions - cCJD and vCJD and the Canadian Blood Supply

- **Classical Creutzfeldt-Jakob Disease (cCJD) was the first major challenge to the blood system since the completion of the Krever inquiry in 1997. Prion diseases (also known as transmissible spongiform encephalopathies, or TSEs) have been long recognized as rapidly progressing, fatal, potentially transmissible neurological syndromes found in both humans and animals.**
- **In 1994, the issue of potential blood supply infection with cCJD became a concern. The US Food and Drug Administration (FDA) developed a policy to withdraw cellular product donations from individuals with CJD. In Canada, the Red Cross, in conjunction with Bayer Inc., voluntarily decided to withdraw blood products connected with this donor and informed the Bureau of Biologics of their decision. The Bureau supported the voluntary nature of this recall, although it did not have an official policy available to guide decision-making on this issue. The immediate consequences of the recall were shortages of some blood products. On October 1995, the Health Protection Branch of Health Canada, announced its official policy on cCJD, supporting the blood recall and deferring donations from donors at risk of acquiring cCJD.**
- **In 1996 and 1986 respectively, the appearance in the United Kingdom of variant CJD (vCJD) and bovine spongiform encephalopathy (BSE) as novel prion diseases led to unprecedented challenges.**
- **As Health Canada was determining how to address the issue of vCJD, it was also considering a reversal of its policy on classical CJD. Scientific knowledge at that time suggested that cCJD did not constitute a serious threat to the blood supply. This rationale led to a policy decision by Health Canada in 1998 that recalls and withdrawals of blood were not indicated by virtue of those products being associated with donors found later to have developed cCJD.**

Policy Decisions - cCJD and vCJD and the Canadian Blood Supply

- **Current scientific knowledge has informed a different set of public policy decisions concerning blood safety in relation to vCJD. A number of compelling arguments suggest that it is necessary to consider the possibility of its being transmittable by blood. Arguments include: the wide exposure of human populations to an infective agent that causes prion disease in cattle and the possibility of a significant international epidemic of vCJD in future decades; inadequate experience with a new form of human prion disease and lack of knowledge it poses about threats to the biological safety of blood products; and sobering data concerning the distinctive pathobiology of vCJD and the possibility of its being transmissible by blood. Current knowledge lead to the conclusion that it would be best not to treat the threat to Canadian public health from blood borne transmission of vCJC as purely theoretical, but rather as a real and large enough threat to warrant deferral policies and intensified efforts in prion disease surveillance, prevention and research.**
- **In October 1998, Health Canada (Bureau of Biologics Research) asked the operators to evaluate the impact that a donor deferral policy would have on their respective supplies. In March 1999, both operators (CBS and Héma-Québec) presented the results of their surveys, but could not agree on a common position.**
- **In June 1999, Health Canada presented a draft proposal for donor deferral which was based on the risk assessment model developed by LCDC. It called for the deferral of blood donations from individuals with a six-month travel history to the UK between 1980 and 1996.As operators can exceed the standard of the regulator on these matters, Héma-Québec chose to proceed with a one-month policy. Both operators implemented their policies before the deadline of February 2000.**
- **In the year 2000, 2 new cases of vCJD were identified in France. Based on the LCDC risk assessment model, donor deferral was recommended. In August 2000, Health Canada announced that it would defer donations from individuals who had spent time in France (exclusive of french territories outside the European continent) amounting to a period of 6 months or more between 1980 and 1996 inclusive. Both Héma-Québec and CBS indicated they would follow this directive.**
- **In August 2001, a further decision was taken to defer donations from individuals who had spent 3 months or more in the UK or France since 1980, or had spent a cumulative total of 5 years or more in Western Europe outside France & the UK since 1980, as well as from individuals who had a blood transfusion in the UK since 1980.**

Sources:

A policy analysis of major decisions relating to Creutzfeldt-Jakob Disease and the blood supply, **Kumanan Wilson & al., CMAJ - July 10, 2001; 165(1)**

Prion Diseases, blood and the immune system: concerns and reality, **Adriano Aguzzi, Haematologica 2000,; 85:3-10**

Variant Creutzfeldt-Jakob Disease: a summary of current scientific knowledge in relation to public health, **Coulthart, M.B. & Cashman, N.R., CMAJ 2001; 165(1):51-8**

Open Forum on Variants of Creutzfeldt-Jakob Disease and Issues for the Blood System, **National Blood Safety Council Documents, May 6-7, 1999**

Donor Exclusion to Address Theoretical Risk of Transmission of variant CJD through the Blood Supply, **Health Canada, Directive D99-01, August 17, 1999**

Donor Exclusion to Address Theoretical Risk of Transmission of variant CJD through the Blood Supply, **Health Canada, Directive D2000-01. 30 August 2000**

Blood Deferral Policy - United Kingdom, France and Western Europe, **Health Canada, August 30,2001**

This case study demonstrates a greater degree of pro-activity with respect to Health Canada's ability to initiate a rapid response to ensure the safety of the blood supply through relevant policy decisions and informed decision-making. A risk-assessment model, and consultation with the major players (operators and consumer organizations)in the blood

system were important considerations. There was also evidence of increased collaboration between the regulatory and the surveillance programs within Health Canada. Although improvements to the system are always possible, these are positive steps overall in the moving overall towards a more transparent blood system.

3.3.2 Enhancement of the Inspection/Compliance Function

Capacity to Conduct Compliance and Enforcement Activities (Requirement 1)

A Branch level Inspectorate with responsibility for the inspection, investigation, most establishment licensing and related laboratory analysis functions for products regulated by the Health Products and Food Branch was created. The inspection of blood establishments is a shared responsibility between two Directorates namely the Biologic and Genetic Therapies Directorate who has the lead on these blood inspections and the Inspectorate. Additional resources were made available to hire more evaluators and specialists to conduct pre-market and post-market review activities within standard time frames and to increase compliance/enforcement activities.

For example, during the 1998-2000 period, the following compliance/enforcement activities were carried out:

- Thirty-nine (39) scheduled and 22 unannounced inspections of blood establishments were completed. The unannounced inspections were pursuant to a number of concerns, including those raised during the evaluation of submissions and those related to accidents/errors arising from new initiatives, e.g. the introduction of the leuco reduction process, which removes white cells (leucocytes) from blood products using filtration or apheresis.
- There was one joint inspection of a medical device manufacturer done by the Bureau of Biologics and Radiopharmaceuticals, the Inspectorate and the Medical Devices Bureau. This collaboration was viewed positively by Health Canada staff.
- Five (5) blood product manufacturers were evaluated on-site and 1 Canadian blood product manufacturer underwent a Mutual Recognition Agreement (MRA) inspection.

During the 1999-2001 period, the following compliance/enforcement activities were carried out:

- A national investigation was carried out of the 100 known semen establishments to assess their compliance with the applicable regulatory requirements of the Semen Regulations further to deficiencies brought to the attention of Health Canada, as well as a number of regional investigations.

- A national inspection program (November 1, 2001) of semen establishments (123 distributors including 14 processors and 21 importers) was implemented.

The current compliance/enforcement system is viewed as generally strong with a high level of standards being applied throughout the system by both internal and external respondents. However, mechanisms for product licensing have not yet been fully implemented and international harmonization will be critical in this area. One blood operator mentioned that they have had to use the Special Access Program (SAP) process to obtain Factor VIII[10] from a California manufacturing facility. It would save a lot of paperwork and reduce the time if Health Canada inspected this facility in order to grant it a licence.

However, concerns were raised, both internally and externally, with respect to the capabilities of Health Canada to expand its compliance and enforcement activities with respect to blood operators. New players (hospitals) are getting involved in the blood system, and many establishments will be involved in the tissues, organs, and xenotransplantation system. These growing fields and new developments will tax the existing system and concerns were expressed about Health Canada's ability to deliver these programs with the existing resources and current approaches.

One concern raised by blood operators and other external stakeholders was the length of the approval process even for minor changes to existing procedures; it would appear that the average rate of response is 90 days. This discourages the introduction of better processes or procedures to respond to new imperatives. A suggestion was made that the current approval process could be changed to reflect the approaches currently in place in the U.S. Federal Drug Administration whereby certain categories of changes are allowed to take place without FDA approval. Monitoring then occurs through the regular inspection program or an audit. This would give them the flexibility to revise operating guidelines and then have these revisions undergo the regular audit process. Many felt that the regulatory process was overly micro-managed. The difficulty Health Canada has experienced in recruiting staff with the appropriate blood expertise only compounds this problem.

Interviews with Health Canada staff indicated that, as no additional funds were received for activities related to compliance and enforcement of the Semen Regulations, five additional FTEs would be necessary to bring the scrutiny level of semen establishments to the same level as for blood establishments.

[10] Factor VIII is a protein in the blood which is involved the coagulation process. Factor VIII deficiency results in Hemophilia A.

Capacity to Provide an Effective Communications Interface Between Regulator and Stakeholders (Requirement 7)

One of the Krever recommendations addressed the need for increased transparency and communications with key stakeholders within the Canadian blood system. Overall, the external stakeholders interviewed felt that they had been consulted and kept informed with respect to major changes in regulations, standards and policies.

Examples of efforts to provide an effective communications interface between the regulator and the stakeholders include the following:

- the establishment of a Blood Consumers' Sounding Board composed of representatives of various interested consumer/user groups to provide feedback on proposed policy directions, new initiatives, etc.;
- the development of a strategy for increased transparency and public involvement;
- the development of a national public consultation strategy for xenotransplantation issues with consultations conducted from March to July2001; and,
- the development of various fact sheets and information kits for distribution to different groups of stakeholders.

There were also examples of increased collaborations between different divisions within Health Canada itself - for example, the Bureau of Biologics and Radiopharmaceuticals (BBR), and the Medical Devices Bureau, and the Centre for Infectious Disease and Control.

Provincial and territorial governments have invested significant funding for the national blood provider, CBS, and in Québec, Héma-Québec operations. Ontario, for example, has contributed 51% of funding to support the activities of the CBS, many safety related. CBS, in turn, has invested in several expensive technologies to improve blood safety, such as NAT testing, leuko depletion, and plasma solvent detergent processes.

> ***Overall, according to both internal and external stakeholders, the safety of the blood system appears to have improved as quality standards overall have been implemented at the provincial and territorial level.***

3.3.3 Effective Post Market-Surveillance

Capacities to Conduct Pre-market and Post-market Reviews and to Perform More Effective Post-market Surveillance (Requirements 2 and 3 respectively)

As stated earlier, the objective of performing more effective post-market surveillance was tied to the capacity to conduct pre-market and post-market reviews, as well as the capacity to perform more effective post-market surveillance. In the pre-market area, the regulations require that information be submitted for marketing new products, and also that establishments be licensed for their operations related to manufacturing, distributing, labelling, and testing activities. Under the Establishment License regulations, submission for Licence Amendments from the blood system operators are classified into three categories, based on the impact of the amendment to the safety of the product, safety of the donor and the recipient. **Exhibit 3.5** below shows the screening and review time allocated to blood submissions by category of risk. In addition, the number of Licence Amendment blood submissions received by the regulator is provided for 2001.

Exhibit 3.5: Time for Pre-market Assessments

Type	# of Licence Amendment Submissions (2001)	Screening Time	Review Time
Blood Category I (Low Risk)	51	10 days	Acceptable upon screening
Blood Category II (Minor Risk)	22	10 days	Defaults after 60 days
Blood Category II (Major Risk)	51	10 days	90 days

Source: Health Canada

The Medical Devices Bureau is responsible for regulating devices, including test kits, used by the operators of the blood system. In this area, there were a number of examples of more effective post-market surveillance taking place within Health Canada. These include:

- A number of post-market health hazard assessments and evaluations were carried out; e.g., the migration of plasticizers in blood bags, a new HIV variant, the use of CP2D as an anticoagulant by blood operators in Canada, the recall of typing trays by the Canadian Blood Services (CBS) and the use of expired p24 wash buffer concentrate by CBS.

- A scientific review is being carried out of the information sent by manufacturers for a number of products for licensing, including first Investigational Testing Application for blood screening assays using the NAT technology for detection of HCV and HIV, as well as first applications for an HIV test kit for point-of-care use.

Some internal respondents mentioned that although the pre-market surveillance is well established, post-market surveillance would need additional resources.

One critical element of any post-market surveillance system is the need for an information system (database) that captures adverse drug reactions from both the manufacturers (where it is mandatory) and the hospitals (where it is voluntary and not regulated at present).Health Canada has developed the ***Canadian Adverse Drug Reaction Information System*** (CADRIS) to capture data from both manufacturers and hospitals on adverse events (AEs) from therapeutic products (including blood products).CADRIS captures data on adverse reactions associated with the transfusion of blood products including albumin, immunoglobulins, Coagulation Factor concentrates, etc. However, it does not capture data on adverse incidents and this is felt to be an important gap. For example, a recent Canadian study of transfusion-related events and near-miss events during a 19-month period at Toronto's Sunnybrooke and Women's College Health Sciences Centre found that over half (58%) of the reported events and near-miss events were due to human error.[11]

Health Canada's Centre for Infectious Disease Prevention and Control Surveillance Program is currently carrying out a pilot project - the ***Transfusion Transmitted Injury Surveillance System*** (TTISS), which integrates an active surveillance of infectious diseases and adverse transfusion-related events which includes errors related to a transfusion.[12]This data is reported from the hospital level to both the Biologics and Genetic Therapies Directorate (BGTD) and the Centre for Infectious Disease Prevention and Control (CIDPC).The Bureau for Licensed Product Assessment (BLPA) within the Therapeutics Products Directorate (TPD) would like to use this information for signal generation of post-approval product safety issues with respect to blood and blood products.

A partnership arrangement is also being developed with the U.S. Food and Drug Administration (FDA) for a combined database on adverse reactions and events for therapeutic products, including biologics. This larger database would allow the analysis and dissemination of information on rare, but critical, adverse reactions. However, delays have been experienced in the finalization of this agreement.

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[11] *Reporting of Near-Miss Events for Transfusion Medicine: Improving Transfusion Safety,* J.L. Callum et al., Transfusion Practice, Volume 41, October 2001

[12] It should be noted that errors (ATRs) are not reported to BGTD, however, some potential errors, eg ABO incompatibility will be reported to CIDPC.

External stakeholders gave mixed reviews with respect to post-market surveillance activities. On the one hand, many felt that some progress had been made towards post-market surveillance and the reporting of adverse events, especially through networking activities and pilot projects, while others felt the system was still very passive, with no widespread awareness of the importance of reporting requirements and lack of follow-up when it does occur.

3.3.4 Transition to a New Blood System

Capacity to Conduct Regulatory Policy Development (Requirement 5)

There is significant public interest in the safety of biologics, which include blood and blood products, cells, tissues and organs of human or animal origin as well as vaccines and other biological drugs. There is a wide range of safety risks associated with biologics; yet, it is expected that there will be a significant growth in new biological products and therapies. These rapid developments require a regulatory regime that is up-to-date and responsive to change. Under the provisions of the Food and Drugs Act and Regulations, Health Canada is responsible for regulating biologics. The Department's objective is to ensure that biologics available to the people of Canada are safe, effective and of high quality.

In a recent report,[13] the Auditor General concluded that "the Department is taking a reasonable approach in developing and implementing frameworks and approaches for regulating different biologics ... (and) has adopted a proactive approach to identifying risks that could threaten the health and safety of Canadians in the area of biologics."
Health Canada has in the past followed a traditional approach with prescriptive regulations to regulate most biologics. However, in order to deal with emerging products and other technological advances in biologics, it is now moving towards adopting a standards-based regulatory approach for blood, tissues and organs, and xenografts. Under this approach, third-party standards development organizations develop standards with Health Canada and other interested parties.

A number of activities have been initiated, including the development of a new regulatory framework for blood, which will use blood standards as a basis. At the present time, the regulations are being applied only to the blood system operators; new players in the blood system - hospital blood establishments and private centres are not being subjected to the regulations. The future regulatory framework will comprise laws and regulations which outline the legal requirements to be met and also may be complemented by policies, directives and guidelines. Key elements may include clinical trials and pre-market requirements, licensing scheme, product safety standards, compliance and enforcement policy and post-market surveillance requirements.

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[13] *Report of the Auditor General - December 2000*, Health Canada - Regulatory Regime of Biologics, Chapter 26

The Therapeutic Products Directorate's Expert Working Group (EWG) on Blood Standards completed the first Draft Standards for Blood Safety in July 2000.These were posted and circulated for public comments with an extended 90-day period allowed for stakeholders to return their comments. A total of 1500 comments were received from 75 separate groups. Both the internal Health Canada Committees and the External Working Group reviewed the comments. Health Canada will consider the most effective and efficient way of integrating sections of these standards into the regulations. The Canadian Standards Association (CSA) will formalize the safety standards into National Standards and ensure that they meet the guidelines laid out by the Standards Council of Canada, the crown corporation responsible for standardization. The regulatory process is expected to be completed by the end of 2004.

In order to meet other pressing demands in the field of biologics, Health Canada has had to carry out a number of other regulatory activities which have created important and time consuming demands on staff that may have been unforeseen in 1998.These include:

- Xenotransplantation: In November 1997, Health Canada sponsored a *National Forum on Xenotransplantation - Clinical, Ethical, and Regulatory Issues*. In response to recommendations to develop safety standards that could be used to regulate xenografts if and when they are approved for use in Canada, Health Canada established an Expert Working Group and as a result of their work, released for public comment the draft Proposed Canadian Standard for Xenotransplantation. In response to recommendations identifying the need for public consultation, Health Canada developed a Public Involvement Plan for xenotransplantation and sponsored, in April 2000, a Planning Workshop to obtain input to the Plan. As a step toward implementing the Plan, Health Canada funded the Canadian Public Health Association to form a Public Advisory Group and to conduct a public consultation on xenotransplantation. Health Canada will develop a policy recommendation by the end of July 2002 on whether or not clinical trials involving xenotransplantation should be allowed to proceed.
- A Lot Release Program is being implemented in stages (enforceable under the MDR) and Health Canada is working towards the development of a policy and the corresponding Guidance Document for the Lot Release Program for Medical Devices.
- Plasmapheresis: Regulatory requirements applicable to human plasma collected by plasmapheresis are being amended.

- Semen Regulations were promulgated in June 1996 and amended in July and December 2000.[14]The experiences with the implementation of the Semen Regulations will provide useful knowledge about best practices that could be retained for the implementation of other biologics related regulations.
- Cells, Tissues and Organs Regulatory Framework: Health Canada will be proposing new regulations under the *Food and Drug Act* based on safety standards currently under development.(The General Standard on Safety of Cells, Tissues and Organs for Transplantation and Assisted Reproduction and its subset standards of specific organs and tissues, all other tissues and hematopoietic stem cells).Health Canada's Expert Working Group completed a draft of the standards and they have been transferred to the Canadian Standards Association who, in consultation with stakeholders, will formalize the standards and obtain Standards Council of Canada approval as National Standards. Other key elements of the regulatory framework include surveillance and adverse transfusion reporting and a compliance and enforcement strategy. The regulatory process is expected to be completed by December 2004.

3.4 Gaps and Future Needs

Interviews with internal stakeholders at Health Canada provided some information on existing gaps that need addressing in order to ensure the sustainability of the regulatory program over the long term. However, program management also indicated that the Regulatory Program was not ready to establish specific future requirements at this time. The gaps identified to date, through interviews with staff only, include the following:

- Additional resources will be needed for activities related to compliance and enforcement of the Semen Regulations. Staff estimated that 5 additional FTEs would be necessary to bring the scrutiny level of semen establishments to the same level as for blood establishments.
- A survey is being undertaken to determine the extent to which hospitals are becoming active players in the Canadian blood system. The introduction of the new Blood Standards expected in 2003 will impact on the responsibilities of Health Canada, particularly in the regulatory and inspection area. Increased resources will probably be needed to address this situation, but they remain undetermined at this time.

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[14] *"Guidance on Donor Semen Special Access Program: Alternative Test Requirements."*This document was developed in response to queries from physicians and patients regarding the alternative testing provisions outlined in subparagraph 20(1)(b)(ii) of the *Processing and Distribution of Semen for Assisted Conception Regulations* (Semen Regulations) which were promulgated on December 1, 2000.It provides guidance on alternative tests that will be considered acceptable by Health Canada within the context of the Donor Semen Special Access Program.

- Health Canada interviewees mentioned a lack of adequate resources for pre-market and post-market reviews of certain blood related products.
- Lack of capital funding for laboratory instruments is having a negative impact on progress in research and on the sustainability of the research programs already in place at Health Canada.
- The recruitment and retention of the needed expertise to carry out the regulatory program continues to be a significant challenge for Health Canada.

3.5 Other Issues

Although the major focus of the study was on documenting the progress made towards reaching the goals of the regulatory program, a number of other questions emerged from the interviews with internal Health Canada staff. These included questions with respect to baseline or performance data, international collaborations, access to external expertise when needed; cost effectiveness of the program and alternative mechanisms for delivery.

Baseline or Performance Data

Overall, staff felt that generally progress had been made with the additional dedicated resources and that the action plans that were developed addressed the basic concerns of the Krever enquiry. However, baseline data and performance information was not easily available. Information tended to be descriptive and there were many operational planning documents but few performance or activity reports. Some staff mentioned that there was a risk management process in place which allowed operational plans to be reassessed and priorities established. It was also difficult to establish performance baselines and outcomes for research with only output indicators such as the number of conferences attended, the number of publications, and the number of linkages to other regulatory agencies.
Our analysis indicated that there was a lack of available baseline performance information and readily available indicators to measure performance against the accountability framework and Health Canada's blood safety objectives.

International contacts and collaborations

Most of the groups had access to international expertise and participated in a number of international committees. Staff track changes in the international scene in their area of expertise, be they (the changes) development of policies, regulatory practice or scientific research and are also members of international groups and expert committees. This international networking allows them to stay at the leading edge of methods development, gives them access to studies before they are published and generally enhances Canada's credibility in the field.

Although international comparisons were not formally available, Health Canada staff felt that their participation in internationally recognized committees ensured that Canada was meeting international requirements, that Canada adopted best practices and that its system was recognized internationally. For example, Canada is at the forefront of blood safety with its stringent requirements for universal leuco reduction, vCJD and NAT testing.

Access to external expertise

Most groups felt they generally had access to external expertise as needed. However, researchers mentioned the importance of maintaining internal capabilities since external expertise, usually found in universities, was not always focussed on issues of concern to the regulators. Some staff mentioned that there is no national coordination of blood research in Canada at the moment.

Cost-effectiveness of programs and alternatives

Most internal respondents felt that Canada's system of hemo-vigilance was as good as that of other countries. However, it was a low-cost version of what existed in other countries such as the UK, France and the U.S. and that resource allocations allowed them to cover the basic minimum activities only. Some staff mentioned that it was critical to ensure stable A-base funding for current operations.

Internal and external respondents both felt that there was no alternative for Health Canada's role as the regulator of the Blood Safety System. The federal government must play a leadership role in this field.

3.6 Conclusions

Overall, Health Canada has expanded its regulatory functions to address the concerns raised by the Krever Commission.

3.6.1 Contribution of BSP Regulatory Activities

Based on the information obtained through document review and interviews with key informants, we concluded that the Blood Safety Program's regulatory activities have contributed to:

- **An Enhanced Regulatory Expertise**

Health Canada has enhanced its blood regulatory expertise by *enhancing the Department's capacity to: a) conduct regulatory research and b) respond immediately to threats to the blood supply*.

While there are still gaps with respect to recruiting the necessary scientists (transfusion physiology, stem cell research, xenotransplantation, purification systems) to support research, the necessary action plans have been put in place and it is felt that no additional resources beyond the allocated ones would be necessary for now. The key challenge will be to attract and retain the necessary expertise.

There was also evidence of a more pro-active response to potential threats to the blood supply in the case of both classical Creutzfeldt-Jakob disease (cCJD) and its variant form (vCJD).Erring on the side of safety, policy decisions were taken with respect to donor deferrals.

- **An Enhanced Inspection/Compliance Function**

The inspection/compliance function has been expanded through *an enhanced capacity to conduct compliance and enforcement activities and an enhanced capacity to provide more effective communications interface between regulator and* stakeholders. The current compliance/enforcement system is viewed by both internal and external respondents as generally strong with a high level of standards being applied throughout the system.

Although inspections were carried out prior to 1998, the function has been expanded to meet the demands of a new system where two blood operators share the responsibilities for the collection and distribution of blood and blood products in Québec and Canada. The major challenge it will face in the coming years is responding adequately to ensure the enforcement of regulations for the collection and distribution of blood by hospitals and other private sector firms. However, external stakeholders have expressed concerns with the lengthy approval process in place for even minor changes to operating procedures and suggested a different approach, closer to that of the Federal Drug Administration in the U.S. could be a viable alternative.

Compliance and enforcement activities in the area of semen use in assisted conception was a clear expansion of the function with the national investigation of the 100 known semen establishments (1999-2001) and the implementation of a national inspection programme of semen establishments (123 distributors including 14 processors and 21 importers).

There are a number of examples of efforts to improve the communications interface between regulator and stakeholders; e.g., the establishment of a Blood Consumers' Sounding Board and the development of a national public consultation strategy for xenotransplantation issues. Overall, the external stakeholders interviewed felt they had been consulted and kept informed with respect to major changes in regulations, standards and policies.

❑ **More Effective Post-market Surveillance**

There is strong evidence of efforts to improve Health Canada's *capacity to conduct pre-market and post-market reviews and to perform more effective post-market surveillance*, including the conduct of health hazard assessments and evaluations.

One critical element of any post-market surveillance system is the need for an information system (database) that captures adverse drug reactions from both manufacturers (where it is mandatory) and the hospitals (where it is voluntary and not regulated at present).To respond to this need, Health Canada has developed the ***Canadian Adverse Drug Reaction Information System*** (CADRIS).

❑ **The Transition to a New Blood System**

The BSP's regulatory activities have supported the transition to a new blood system by *enhancing the capacity of Health Canada to conduct regulatory policy development.* A number of activities have been initiated, including the development of a new regulatory framework for blood, which will use blood standards as a basis. As well, in order to meet other pressing demands, Health Canada has carried out a number of other regulatory activities, including a Lot Release Program for medical devices, amendments to the regulatory requirements for plasmapheris, amendments to the Semen Regulations, and the initiation of a new regulatory framework for Cells, Tissues and Organs.

3.6.2 Outstanding Issues

We concluded that there are two key issues facing the regulatory area of the Blood Safety Program:

- **The lack of regulatory power over hospitals**. The regulations are not presently applied to hospitals and this remains one of the key "gaps" in the overall blood system. Health Canada is currently developing a new regulatory framework for blood safety, which will be based on the *Blood Safety Standards* and will address hospitals' activities in distribution, administration and collection. However, current practices for enforcement and compliance with the standards will need to be reviewed taking into account the limited resources available to Health Canada; and
- **The high cost of implementing new standards and regulations and participating in extra surveillance activities.** Some external respondents have identified one critical issue for the Ministries of Public Health in the provinces and territories, the cost of implementing new standards and regulations and of participating in extra surveillance activities. They feel it would be important to consider fully the cost impacts of CBS voluntary/Health Canada-directed policy on the provinces and territories. The provinces and territories are already investing significant amounts of resources to contribute to the safety of the blood supply.

The incremental costs for funding programs and initiatives, such as the high costs associated with HC-directed safety testing by the CBS, are ultimately borne by the provinces and territories. They suggested that cost/benefit analyses of alternative blood safety technologies would be needed.

3.6.3 Future Requirements

Finally, we concluded that it was not possible to identify the financial requirements for the Blood Safety Program in future years. This was mainly due to the nature of the financial information provided to the study team to date and the inability of the Regulatory Program to identify specific future needs at this time.

4.0 Blood Surveillance Program

This section provides a brief overview of the activities that were undertaken to strengthen Health Canada's surveillance activities of the Canadian blood system and to deliver programs that will allow it to reach its long term goals. The overall resources applied to different activities, as well as identified gaps and future resource requirements are also examined. In addition, issues raised by external stakeholders with respect to the surveillance function are briefly discussed.

4.1 Surveillance Role of the Department

Under the *Department of Health Act*, the Minister of Health has responsibility for "investigation and research into public health, including the monitoring of diseases". Surveillance, both epidemiologic and laboratory, is the touchstone of risk assessment of the blood supply. Surveillance, when properly planned and executed, should provide an indication of the magnitude and importance of known transfusion-transmitted infections, an early warning of important deviations from the expected; and, a mechanism to rapidly explore potential problems.

According to the definition adopted by Health Canada, health surveillance is "the tracking and forecasting of any health event or health determinant through the ongoing collection of data, the integration, analysis and interpretation of those data into surveillance products and the dissemination of such products to those who need to know. Surveillance products are produced for a predetermined public health purpose or policy objective."

4.2 Blood Surveillance Program

The blood surveillance program is one of many programs that contribute to the fulfilment of Health Canada's role in monitoring and protecting the nation's health.

At Health Canada, the Blood Safety Surveillance System is based on two major components: Health Risk Science and Health Risk Policy Analysis. ***Health Risk Science*** provides the necessary scientific base for identifying risk factors in the donor population based on genetic, environmental and social and behavioural factors. Once these factors are identified, they are brought to the attention of the Regulators and Policy Makers who are responsible for setting the screening protocols for deferring or eliminating potential and actual blood donors. According to Health Canada, the blood screening system used by Héma-Québec and Canadian Blood Services (CBS) blocks 99% or more of the identified risks. All blood is tested post-donation, as well, for known pathogens.

The risk of transmission of many blood-borne pathogens has been reduced through stringent blood donor interviews and questionnaires, specific screening tests and the manufacturing processes for blood products. Changes in microbes, such as the emergence of new mutant strains of HIV or hepatitis viruses that are undetectable by current screening tests, require the reassessment of risk management practices and the development of new tests.

Once risk factors are identified, the information is transmitted to the ***Risk Policy Analysis function***, which develops, in conjunction with other stakeholders in the Blood System (operators, community, healthcare providers, manufacturers), an appropriate response and policy decision. The case study on (classical) cCJD and (variant) vCJD in section 3.0 provides one example of the decision-making process followed by Health Canada as the regulator responsible for the safety of the blood system in Canada.

Goals - Blood Surveillance Program

As mentioned previously, the Surveillance and Epidemiology in Transfusions (SET) Working Group developed a plan and designed a program for a comprehensive blood surveillance system. The primary objective was that the federal, provincial and territorial governments establish a national surveillance system to determine the risk of infectious and non-infectious adverse events following blood transfusion. The first was a development of a post-market surveillance program of blood and blood products that involves monitoring the effects and possible adverse events following administration of blood or blood products. They also recommended the establishment of a surveillance system for infectious diseases which would involve tracking the emergence, modes of transmission, and spread

of infectious diseases in the community; and finally the surveillance of blood donors to identify trends in donation patterns, risk factors and infectious disease markers. Further to the SET report, the following goals were established for the Blood Surveillance Program:[15]

- Develop linkages with public-health information systems in order to strengthen public health responses to blood-borne pathogen (BBP) threats;
- Develop linkages with appropriate partner organizations so that the statistical integration of Laboratory Centre for Disease Control (LCDC) databases can be implemented (linkages with Statistics Canada, provincial laboratories, hospitals, etc.);
- Develop analytic and response capacities within LCDC by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action; and
- Establish coordinated research thrusts into new potential blood-borne threats, including prion diseases such as the human form of "mad-cow" disease known as variant Creutzfeldt-Jakob Disease vCJD.

The action plan outlined in the 1998 Accountability Framework established seven specific requirements and corresponding activities/projects aimed at strengthening the surveillance program:

- *Capacity to create a blood surveillance system based on a mandated post-market surveillance and CBS data base management system* - the need for enhanced national and international surveillance was emphasized by the Krever report. Epidemiologic investigations must include the development of routine surveillance systems, the analysis of that data and the publication of results of that analysis in a timely fashion and within an HPB risk management framework, in collaboration with the surveillance framework established and operated by the regulator and by the Canadian Blood Services and Héma-Québec. Close federal, provincial and territorial partnership will be needed to bring about this enhanced capacity. This surveillance system will capture data on both infectious and non-infectious adverse events.
- *Capacity to conduct statistical analysis and risk assessment and management* - this involves the completion, in a comprehensive and timely fashion, of detailed analysis (risk assessment) conducted on all procedural changes, on unusual adverse reactions or suggested emerging pathogens. This process involves:
  - ***Risk identification and research*** on a) methods for the identification, prevention, treatment, education and control of diseases and/or risk factors; b) risk analysis, cost-benefit effectiveness analysis and feasibility analysis methods as they relate to

[15] Accountability Framework: Strengthening Health Canada's Blood Regulatory and Surveillance Programs

disease surveillance and control; c) risk factors and diseases themselves; d) new regulatory requirements, problem areas; and, d) the evaluation of health effects of regulations and programs;

- ***Risk assessment and surveillance*** of risk factors and disease (e.g. blood transfusions, blood-borne pathogens, etc.), incidence of diseases (e.g. Hepatitis C, HIV/AIDS, etc.) and their outcomes. Surveillance includes epidemiological investigations, and the collection, synthesis, analysis and interpretation of information on the presence, incidence and occurrence of risk factors and disease entities. The Surveillance component also includes retrospective evaluation of health effects of regulations and programs, and, in particular of those regulations and programs which are designed to reduce health risks and/or to improve health.
- ***Risk management and regulation*** includes health promotion, education, regulation (of industry, manufacturers, importers and operating agencies), and healthy public policy. Risk management also includes actions (e.g., blood donor deferral) taken by individuals in response to guidelines and regulations to avoid health risks. Preventive measures like blood and organ donor deferral, recall of contaminated blood products, disposal/destruction of unsafe blood products, etc. also come under risk management and regulation; and risk management ensures the safety of blood collection, blood transfusion, blood transportation, delivery and manufacturing.
- ***Capacity to study most vulnerable populations and to conduct outbreak investigations*** - this involves the conduct of special surveys and field studies to investigate potential pathogens or unusual infectious patterns not addressed by the current screening system and the enhancement of the national sentinel system for other blood borne pathogens.
- ***Capacity to provide BBP laboratory based epidemiological surveillance*** - develop the capacity to undertake intensified laboratory based surveillance for infectious diseases (HBV, HGV, HTLV, 1/11, Hepatitis, Herpes simplex virus, among other STDs).This will include, in collaboration with the provinces/territories, the development of an enhanced surveillance database and the provision of technical assistance by HC.
- ***Capacity to conduct public health investigation of emerging blood borne pathogens (BBPs)*** - includes the need to develop and adopt new methods to detect potential blood borne pathogens, e.g. molecular and serological detection methods, the provision of services to clients (provincial health laboratories and major hospital centres in Canada) for their detection; and improved response time.
- ***Capacity to conduct surveillance and laboratory investigation of prion disease*** - this will include the expansion of the current CJD surveillance system. One of the prion files is the one related to variant-CJD. Activities in this area will involve the development and maintenance of a neuropathology diagnostic reference centre, the implementation of new diagnostic tests; the provision of essential scientific core expertise in support of future/ongoing regulatory considerations; and the provision of full reference service for genetic diagnostics, etc.

- ***Capacity to link with public health information networks*** - this network would provide full support to provincial and territorial laboratories to create an effective link and cooperative and fair exchange of information between laboratories.

Exhibit 4.1 below shows the linkages between the goals of the program and the specific capacities that needed to be strengthened in the Blood Surveillance Program. In many cases, more than one capacity/activity contributes to the achievement of goals

Exhibit 4.1: Goals and Capacity Development - Surveillance Program

Goals of the Enhanced Blood Surveillance Program	Enhanced Capacities
Develop linkages with public health information systems in order to strengthen public health responses	• capacity to create a blood surveillance system (Transfusion Transmitted Injury Surveillance System, Public Health Infrastructure, Xenotransplantation surveillance) • capacity to link with public health information networks
Develop linkages with appropriate partner organizations so that the statistical integration of LCDC databases with other external databases can be implemented	• capacity to create a blood surveillance system • laboratory-based epidemiological surveillance
Develop analytic and response capacities within LCDC by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action.	• capacity to create a blood surveillance system • capacity to conduct statistical analysis and to assess and manage risk • develop the capacity to conduct surveillance and laboratory investigation of prion diseases
Establish coordinated research thrusts into new potential blood-borne threats, including prion diseases such as CJD.	• capacity to create a blood surveillance system • capacity to study most vulnerable populations and to conduct outbreak investigations • capacity to provide blood-borne pathogen laboratory-based epidemiological surveillance • capacity to conduct public health investigation of emerging blood borne pathogens • capacity to conduct surveillance and laboratory investigation of prion diseases

4.3 Planned Program Resources

Exhibit 4.2 below summarizes the Blood '98 resource allocations and actual resources received to date by surveillance capacity.

Exhibit 4.2: Summary of Blood '98 Resource Allocations and Actual Resources[16] Received to Date

Capacity	1998/98	1999/00	2000/01	2001/02	2002/03
1. Capacity to create a blood surveillance system based on mandated post-market surveillance and CBS Database Management System					
Allocated:	2 FTEs; $1.119M	4 FTEs; $2.344M	5 FTEs; $2.741M	5 FTEs; $2.594M	5 FTEs; $2.749M
Actual Received to Date:	2 FTEs; $0.973M	4 FTEs; $2.111M	5 FTEs; $2.391M	5 FTEs; $2.299M	5 FTEs; $2.443M
2. Capacity to conduct statistical analysis and risk assessment and management					
Allocated:	0 FTEs; $0.261M	2 FTEs; $0.755M	3 FTEs; $0.765M	3 FTEs; $0.758M	3 FTEs; $0.682M
Actual Received to Date:	0 FTEs; $0.243M	2 FTEs; $0.679M	3 FTEs; $0.619M	3 FTEs; $0.619M	3 FTEs; $0.564M
3. Capacity to study most vulnerable populations and to conduct outbreak investigations					
Allocated:	0 FTEs; $0.238M	1 FTE; $0.762M	1 FTE; $0.785M	1 FTE; $0.703M	1 FTE; $0.793M
Actual Received to Date:	0 FTEs; $0.221M	1 FTE; $0.685M	1 FTE; $0.704M	1 FTE; $0.636M	1 FTE; $0.636M
4. Capacity to provide Blood-borne pathogen (BBP) laboratory-based epidemiological surveillance:					
A. Retroviruses & STD					
Allocated:	5 FTEs; $1.612M	5 FTEs; $1.798M	5 FTEs; $2.386M	5 FTEs; $1.514M	5 FTEs; $0.655M
Actual Received to Date:	5 FTEs; $1.309M	5 FTEs; $1.309M	5 FTEs; $2.091M	5 FTEs; $1.309M	5 FTEs; $0.485M
B. Hepatitis					
Allocated:	5 FTEs; $0.794M	5 FTEs; $1.064M	5 FTES; $0.836M	5 FTEs; $0.878M	5 FTEs; $0.890M
Actual Received to Date:	5 FTEs; $0.572M	5 FTEs; $0.957M	5 FTEs; $0.671M	5 FTEs; $0.714M	5 FTEs; $0.725M
C. DNA Sequencing					
Allocated:	3 FTEs; $0.349M	3 FTEs; $0.606M	3 FTEs; $0.402M	3 FTEs; $0.458M	3 FTEs; $0.406M
Actual Received to Date:	3 FTEs; $0.219M	3 FTEs; $0.545M	3 FTEs; $0.307M	3 FTEs; $0.361M	3 FTEs; $0.363M

[16] Actuals are amounts received by the program after deductions for employee benefit plans and program/corporate supports.

Capacity	1998/98	1999/00	2000/01	2001/02	2002/03
5. Capacity to conduct public health investigation of emerging BBPs					
Allocated:	3 FTEs; $0.388M	3 FTEs; $0.880M	3 FTEs; $0.536M	3 FTEs; $0.659M	3 FTEs; $0.647M
Actual Received to Date:	3 FTEs; $0.255M	3 FTEs; $0.792M	3 FTEs; $0.4432M	3 FTEs; $0.432M	3 FTEs; $0.538M
6. Capacity to conduct surveillance and laboratory investigation of prion diseases					
A. Tanz Neuroscience, Neuropathology and Prion Diagnostic Research Centre					
B. Winnipeg Human and Animal Prion Reference Laboratory					
Allocated:	16 FTEs;$2.857M	19 FTEs; $4.887M	19 FTEs; $4.685M	19 FTEs; $2.145M	19 FTEs; $3.176M
Actual Received to Date:	5 FTEs; $1.381M	18 FTEs; $4.398M	18 FTEs; $3.986M	18 FTEs; $1.620M	18 FTEs; $2.578M
7. Capacity to link with public health networks					
Allocated:	2 FTEs; $0.220M	2 FTEs; $0.312M	2 FTEs; $0.248M	2 FTEs; $0.235M	2 FTEs; $0.238M
Actual Received to Date:	1 FTE; $0.184M	2 FTEs; $0..280M	2 FTEs; $0.189M	2 FTEs; $0.182M	2 FTEs; $0.182M
TOTAL					
Allocated:	**36 FTEs; $7.838M**	**44 FTEs; $13.408M**	**46 FTEs; $13.357M**	**46 FTEs; $9.944M**	**46 FTEs; $10.236M**
Actual Received to Date:	**24 FTEs; $5.357M**	**43 FTEs; $12.065M**	**45 FTEs; $11.39M**	**45 FTEs; $8.172M**	**45 FTEs; $8.514M**

Source: Director General's Office, Centre for Infectious Disease Prevention and Control, Health Canada, February 22, 2002.

Footnotes: 1) The amounts shown were allocated to programs; however, a more detailed level of analysis (i.e., tracking of actual expenditures on specific projects/ activities to the specific funding source) cannot be easily done using information readily available in the financial system.
2) Resources for capacities 1,2,3 and 5 are received by the Blood-born Pathogens Division, CIDPC.
3) Resources for capacity 4 are shared by the Bureau of HIV/AIDS, STD and TB, CIDPC and the National Laboratory for Viral Diagnostics, National Microbiological Laboratories (NML).
4) Resources for capacity 6 are shared between the Blood-borne Pathogens Division, the Bureau of Infectious Diseases and the National Laboratory for Host Genetics and Prion Diseases, NML.
5) Resources for capacity 7 are received by the National Laboratory for Viral Diagnostics, NML.

4.4 Progress to Date

The major goals of the Surveillance Program include the development of linkages with public health information systems and with appropriate partner organizations; the development of analytical response capacities within LCDC; and, the establishment of coordinated research thrusts into new potential blood-borne threats.

Appendix D contains a synthesis of the activities carried out to date to strengthen the Surveillance Program's capacities in different areas, outputs to date and current issues and gaps facing the Program.

This section highlights the key achievements and progress made with respect to the expansion of the blood surveillance system.

As part of the response to the Krever recommendations, laboratory capabilities for identification of blood-borne pathogens and reference services have been strengthened in major areas. Recent developments have focussed on building information systems in cooperation with the provinces that provide provincial and national adverse reporting for blood products. Surveillance is carried out in different ways. The following is a partial list of all the surveillance activities in the Blood Safety Program:

- health events monitoring and alert;
- routine surveillance: collection of data from Statistics Canada; CIHR, etc.;
- enhanced surveillance: there are 6 sentinel sites, Vancouver-Richmond, Calgary, Edmonton, Winnipeg, Ottawa and the province of New Brunswick. The first five sites are managed by the Regional Health Boards, while the Ministry of Health manages the site in New Brunswick. Each reported incident of HEP B and HEP C is investigated and the data analysed to estimate the incidence rate, the risk factors and transmission patterns;
- surveillance for new or re-emerging blood-borne pathogens including mutants of known pathogens. A network is being established by Health Canada in collaboration with health care providers and health professionals to maintain a rapid surveillance and risk assessment capacity for the identification of any such pathogens and for evaluation of their public health implication;
- targeted surveillance which is carried out jointly with the Bureau of HIV/AIDS, Correctional Services, First Nations, and Inuit Health Boards and targets special groups; e.g. prisoners, street youth, pregnant women (HEP B) and injection drug users;
- case surveillance: identification and notification of newly detected HIV infections and of AIDS diagnoses through collaboration with all Canadian provinces and territories;
- enhanced surveillance: specimens from newly diagnosed HIV positive individuals are monitored for strain and primary transmission of drug resistant mutants (B.C., Alberta, Saskatchewan, Manitoba, Ontario and Nova Scotia); and
- special studies , e.g. Hep B mutants study.

The following major surveillance areas covered by the Surveillance Program are: retroviruses (including HIV/AIDS and Simian foamy virus, etc.); prions; hepatitis; emerging blood-borne pathogens and transfusion transmitted injuries (TTIs).

4.4.1 Laboratory-based Epidemiological Program for HIV and Related Retroviral Diseases

The objective of this project is to develop and manage an intensive provincially-based blood-borne retrovirus and STD system. Following the development of MOUs with the provinces, a network of Field Surveillance Officers (FSOs) are in place in B.C., Alberta, Saskatchewan, Manitoba, Québec, Ontario and the Atlantic provinces. Co-supervised by both Health Canada and the provincial public health authorities, this collaborative network addresses current and emerging issues. This arrangement allows the Bureau, through its FSOs, partnership with the provinces and the territories at a level that allows input on case surveillance forms (data), database and data standards, and surveillance procedures and operations. This has resulted in the forging of new and comprehensive data linkages between national and provincial epidemiological and laboratory systems, providing timely and enhanced surveillance data while protecting privacy and confidentiality.

The Canadian Strain and Drug Resistance Program (CHSDRSP) was established to monitor the diversity of HIV strains (subtypes) in Canada.[17] Utilising the integrated surveillance approach between the provinces, territories and BHST, laboratory samples (serum from newly diagnosed HIV-positive individuals or plasma taken for the purpose of first viral load testing) and corresponding epidemiological data are sent via the FSOs from the Provincial Health Laboratories to the BHST. The results are then shared with the provinces and territories. This program allows the provinces/territories and BHST to mount effective, realtime and evidence-based public health interventions to emerging infectious disease threats. This program helps to improve HIV diagnostics and screening strategies, informs vaccine development, assesses HIV transmission patterns and HIV pathogenesis and progression of HIV-related diseases. There have been a number of preliminary reports and presentations at conferences and a formal report of data is expected in 2002.

The National HIV Laboratories HIV reference service programs provide a ancillary function to the BHST integrated surveillance system by providing information on HIV strains which prove difficult to detect by the testing algorithms currently used the provincial health laboratories and the Canadian Blood Services. Samples submitted to the HIV reference service program frequently include subtypes and recombinant viruses from regions of the world where new HIV strains may be evolving (i.e., Africa and Asia). These are samples which may not have been captured in other surveillance programs and represent the leading edge of new HIV strains within Canada.

The National HIV Laboratories maintain the capacity for HTLV diagnostics for samples submitted by Canadian provincial labs and the Canadian Blood Services. It has the most comprehensive ability in Canada to detect and type HTLV-I and HTLV-II by serologic or

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[17] *HIV Strain Surveillance in Canada*, HIV/AIDS Epi Update, Centre for Infectious Disease Prevention and Control, Health Canada, May 2001

genetic testing. Currently one activity that the NLHRS and the BHST is conducting in collaboration with its provincial stakeholder labs is the genetic subtyping of HTLV-I and HTLV-II strains that have been submitted and diagnosed at the National HIV Laboratories. In addition, the National HIV Laboratories have developed and manage quality assurance programs for HIV diagnostic testing to ensure that the testing algorithms used by provincial health laboratories and the Canadian Blood Services are maintained at the highest level possible.

Development work on the case surveillance system for HIV and AIDS, to improve the capacity of STD surveillance, and building responsive functionality in the event of emerging infectious disease threats, is nearing completion. The Bureau has maintained active participation in concurrent national initiatives around public health surveillance systems and data standards. All improvements have been done with these in mind. In addition, an integral part of the Bureau team includes IT personnel from ITMD to ensure compliance with the strictest Health Canada IT development standards.

Funding shortfalls anticipated for years four and five (the majority of the MC98 funds were spent in the first three years to "scale up") of the program will result in initial scaling-back and, according to internal respondents, a serious undermining of the system at the national level.

4.4.2 Enhanced Surveillance of Acute Hepatitis B and C

The National Microbiology Laboratory has acquired expertise and human resources to establish, maintain, expand and coordinate a provincially-based strain surveillance system to identify newly acquired acute cases of hepatitis B and C. The goals of the laboratory based surveillance is to characterize at the molecular level the new phenotypes and genotypes of HBV and HCV currently circulating in Canada and to provide risk assessment in relation to blood safety. The Laboratory provides molecular diagnostics on vaccine-escape mutants and newly-emerged viral agents that are transmitted parenterally and may pose a threat to the blood supply.

The Hepatitis C virus has an incidence more than ten times that of any other blood-borne infection. It is the single greatest known and actual risk (as opposed to theoretical risk) to the blood supply and the safety of the blood supply. There are 250,000 Canadians living with hepatitis C infection. It is estimated that as many as 20 percent of these individuals may eventually need a liver transplant, placing a huge burden on the chronic health care system. An example of this is the fact that the Canadian Virus Report records 21,289 Hepatitis C virus positive tests for year 2001, and 20,829 Hepatitis C positive tests for the year 2000. Hepatitis B positive tests are about 5,000 per year in Canada (and increasing).

Not being a front-line laboratory, the National Microbiology Laboratory (NML) receives from the provinces samples that are so-called "difficult or indeterminate" diagnostic specimens, which may represent a higher proportion of hepatitis B and C mutants, which may not be identified in routine diagnostic tests. This puts the NML in a good position, as the National Reference Laboratory, to do this type of surveillance efficiently, as they are already sampling a more diverse subset of specimens. The Hepatitis and Blood-borne Pathogens section at NML completes close to 2400 tests per year for blood-borne pathogens and hepatitis.

The Laboratory has also developed a sequencing database of Canadian circulating strains using sequence-based analysis.

Another area where the laboratory is increasing its efforts is in the characterization of individuals who have developed hepatocellular carcinoma or acute phase hepatitis. Genomic analysis on Hep B/C infected patients, allows the identification of markers which would predict risks of more or less severe consequences to virus infection and the monitoring of both chronic and asymptomatic carriers and infections that have not yet been characterized. Molecular markers that respond to various classes of infection would provide a new tool for doing surveillance for "unknown infections".

An enhanced surveillance system[18] was established in October 1998 to identify cases of acute hepatitis B and C infections in four regions in Canada, with a total population of approximately 3.2 million people. ***Sentinel surveillance*** is the selection of health units or population groups for the purpose of monitoring events and associated factors in these units or groups. The focus on smaller groups allows the timely collection of more in-depth information in a consistent fashion in different population groups. Information on demographic and clinical characteristics, laboratory results and potential risk factors was collected using standardized questionnaires.

Exhibit 4.3 below provides a brief overview of the information that can be gathered through such a sentinel system. Although only one element in the overall surveillance system in Canada, this information can be extremely useful to inform public health decision-making.

[18] *Enhanced surveillance of acute hepatitis B and C in four health regions in Canada, 1998 to 1999*, Shimian Zou & als, Canadian Journal of Infectious Diseases, Volume 12, No. 6, November/December 2001

Exhibit 4.3: Sentinel Site Surveillance Model - Hepatitis B and C

Sentinel Site Surveillance Model - Hepatitis B and C

- Hepatitis B and Care important public health concerns in Canada. It was estimated that over 100,000 Canadians are infected with Hep B virus and approximately 240,000 are infected with Hep C virus.
- Surveillance for viral hepatitis and emerging blood borne pathogens in Canada includes routine, sentinel and targeted surveillance as well as research. Routine surveillance comprises the reporting of viral hepatitis A , B and C through the National Notifiable Disease Reporting System and analysis of other routinely collected data.
- Sentinel surveillance is the selection of health units or populations groups and the monitoring of events and associated factors in these units or groups.
- Enhanced sentinel site surveillance for acute Hep B and C was designed to collect data from acute cases to estimate the incidence and transmission patterns of these two most important blood borne infections in the country.
- The National Notifiable Disease Reporting provides essential data on these two diseases. However, due to inconsistence in reporting practices and the lack of information on possible transmission routes, special effort is needed to enhance the collection of data on occurrence and related factors so that appropriate estimation of national incidence and transmission patterns can be established for these two diseases.
- An enhanced surveillance system was established in October 1998 to identify cases of acute Hep B and C infections in four regions in Canada, with a total population of approximately 3.2 million people. Information on demographic and clinical characteristics, laboratory results and potential risk factors was collected using a standardized operating protocol for data collection. Further, risk factors are collected from each case through telephone interviews.
- Data from the enhanced surveillance can be used to provide national estimates of incidence and transmission patterns and possible changes to such patterns over time. Analysis of virus isolates can trace the spread of a virus in a community, which provides essential information for exploring the cause of an epidemic or a cluster of cases. Such patterns may shed the light on the epidemiological issues that are relevant to occurrence and progression of an infection.

- Additional information is often critical for evidence-based decision-making to prevent and control these diseases in the future.
- The first results for the period 1998 to 1999 were published in December 2001.
- A total of 79 cases of acute hepatitis B and 102 cases of acute hepatitis C were identified from October 1998 to December 1999, resulting in an incidence rate of 2.3 and 2.9/100,000 person-years, respectively. Males had higher incidence rates than females. The incidence of acute hepatitis B peaked at age 30 to 39 years for both males and females, whereas acute hepatitis C peaked at 30 to 39 years for males and 15 to 29 years for females. At least 34% of acute hepatitis B and 63% of acute hepatitis C were associated with injection drug use. Persons who were 15 o 29 years of age were more likely to report injection drug use as a risk factor. Heterosexual contact was reported to be a risk factor for 36.6% of acute hepatitis B cases and 3.5% of acute hepatitis C cases.
- The surveillance provides national incidence estimates of clinically recognized acute hepatitis B and C. Both hepatitis B and C are important public health threats to Canadians. Prevention efforts for both diseases should focus on injection drug use, especially for people aged 15 to 29 years. Risky sexual behaviour is also a major concern in prevention of hepatitis B in Canada.

Sources:

National Surveillance for Community Acquired Blood borne Infections - Viral Hepatitis and Emerging Blood borne Pathogens (excluding retroviruses) in Canada, Bureau of Infectious Diseases, Population and Public Health Branch, Health Canada, Draft, April 2001

Hepatitis C, Paul R. Gully & Martin L. Tepper, CMAJ 1997, 156:1427, May 15, 1997

Enhanced surveillance of acute hepatitis B and C in Canada, 1998 to 1999, Shimian Zou & als, Canadian Infectious Disease Journal, November-December 2001

Surveillance for viral hepatitis and emerging blood borne pathogens in Canada, Shimian Zou and Antonio Giulivi, Canada Communicable Disease Report, Volume 2753, September 2001

Hepatitis C in Canada, Shimian Zou, Martin Tepper, Antonio Giulivi, Canada Communicable Disease Report, Volume 2753, September 2001

4.4.3 Transfusion Transmitted Injuries Surveillance System (TTISS)

The Krever enquiry identified the need for a system to act as the virtual "watchdog" for the safety of the Canadian blood supply arose out of the Krever enquiry. In March 1998, a Surveillance and Epidemiological Working Group was established to determine the risk of blood transfusion for infectious and non-infectious adverse events. In the 1990s many other countries started to plan and implement surveillance systems to monitor blood safety (US, UK, France, Denmark).

The system[19] depends on hospital reporting of all adverse events to the provincial government surveillance unit. This information is aggregated for the province and provided to Health Canada through computer reporting. The pilot TTISS was funded from the MC 98 money and four provinces are participating in the program: Prince Edward Island, Nova Scotia, Québec and British Columbia. All sites have a provincial adverse reporting system as a component of their central transfusion registry. A core working group meets four times a year and data will be transferred to Health Canada twice a year. The following tools were developed for the TTISS: provincial database; national database to compile and store provincial data, Canadian Transfusion Adverse Event Reporting Form ; and, a user manual. BC, Québec and PEI agreed to provide data from April 1, 2001.

According to both internal and external stakeholders, future challenges will include the transition from a pilot project to a national system; finding dedicated financial and human resources at the federal, provincial and territorial level; and, developing mechanisms to encourage reporting of adverse events from the hospital level. Hospital reporting is not legislated by the federal government as hospitals operate under provincial and territorial authorities.

Knowledge about adverse effects of transfusion can help regulators in the definition of appropriate risk management strategies and the development of new or modified policies. It also helps public health authorities to assess and manage risk, set benchmarks, develop practice guidelines and educational material, and targeted research.

4.4.4 Surveillance and R&D of Prion Diseases

Responsibility for the epidemiology and surveillance of cCJD and vCJD lies with the Bureau of Infectious Diseases, while research on prion diseases is carried out by the Winnipeg Human and Animal Prion Reference Laboratory. According to internal respondents, maintaining the independent strength of these two parts of the operation is important. Both epidemiological research and laboratory research are important facets of a surveillance program.

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[19] *Pilot Transfusion Transmitted Injuries Surveillance System (TTISS),* Progress Report, A. Giulivi, December 18, 2001

On the ***scientific R&D*** side, a laboratory was created *de novo* in Winnipeg in late 1998; it is now approximately half equipped and staffed. To date, the laboratory has been able to provide ongoing advanced human molecular genetic diagnostics to support the Canadian CJD Surveillance System and has established scientific research programs to investigate prion diseases mechanisms and prion stain variation. The laboratory has also discovered novel human mutations associated with prion diseases. In addition, laboratory staff have established national and international collaborations and are able to provide scientific and technical advice to support risk assessment and risk management for prion diseases.

However, due to resource constraints, the following major segments of the R&D program remain essentially undeveloped according to Health Canada staff:

- development and implementation of new diagnostic and screening tests for preclinical prion diseases, especially to screen the Canadian blood supply;
- support for intensified surveillance as necessitated by implementation of screening tests;
- research and validation studies on process safety (e.g., clearance of prion infectivity during plasma fractionation, prion removal and inactivation in hospital infection control practice);
- capacity to perform bioassays to detect, quantify and characterize prion infectivity; and,
- epidemiological research on human and animal prion diseases.

This work will involve increased collaborations with other stakeholders in the system, academic researchers, the Canadian Food Inspection Agency, and Canadian Blood Services.

According to Health Canada staff, without sufficient funding, the program may have to be terminated. In addition, staff felt there was an increasing urgency to develop blood screening tests as a result of:

- an ongoing epidemic of variant Creutzfeldt-Jakob Disease in the UK and France
- the potential global occurrence of bovine spongiform encephalopathy (BSE);
- the possible spread of BSE to sheep;
- the unknown risks of novel prion disease of deer and elk (Chronic Wasting Disease) to domestic livestock and humans; and,
- increasing evidence suggesting the transmissibility of vCJD through peripheral tissues and blood.

On the ***epidemiology side***, a number of activities have been undertaken to expand the current CJD surveillance system. A national surveillance system for CJD in the adult and pediatric population is maintained (the Canadian CJD Surveillance System or CJD-SS), which includes surveillance for vCJD. Health Canada has developed the ability to respond

to potential outbreaks or urgent situations (e.g. draft protocols for investigation of suspected vCJD cases) and has established links with Provincial/Territorial Health Authorities, Health Care institutions and Health Care professionals, and collaborations with the University of Toronto. Health Canada also collaborates with international surveillance programs (UK, Euro-CJD, WHO) , which includes sharing data on CJD in high risk populations. CJD surveillance in haemophiliacs is done under both the Canadian CJD Surveillance System and the Transfusion Transmitted Injuries Surveillance System (TTISS).

Health Canada also maintains a neuropathology reference centre at the Tanz Neuroscience, Neuropathology and Prion Diagnostic Research Centre (TNNPDRC), as a contract facility. This neuropathology reference centre provides diagnostic and consultation services for the Canadian CJD Surveillance System (CJD-SS) and has the capability to implement new diagnostic tests following international and national validation, to pioneer new diagnostic or screening tests, and to provide essential scientific expertise in support of future/ongoing regulatory considerations. This work is done in collaboration with the National Laboratory for Host Genetics and Prion Diseases in Winnipeg.

Health Canada has been involved, as well, in other activities, such as risk assessment and risk management for prion diseases (e.g., development of CJD Infection Control Guidelines for Classical CJD).Officials indicated that additional funding would allow Health Canada to maintain and enhance the activities in epidemiology and surveillance for prion diseases, such as enhancing genetic research and counselling services for familial/inherited CJD, and conducting targeted research on CJD/TSE.

4.4.5 Public Health Investigation of Emerging Blood Borne Pathogens

Health Canada is developing a surveillance network for new or re-emerging blood-borne pathogens. The network consists of health care providers, special patient groups at risk for blood-borne infections, and a sample of the general population. The network provided needed risk assessment for the newly identified blood-borne agent, SEN virus, and will be able to provide effective and timely assessment of health risks any potential blood-borne agents may pose to Canadians in the future.

Health Canada has developed laboratory methods for the detection of emerging blood borne pathogens (BBPs) and provides laboratory services to all provincial and territorial public health laboratories in this field. Between 1999-2001, several potential blood-borne pathogens emerged, e.g. TTV, TLMV and SEN-V. Partially due to the increased funding, Health Canada was in a position to rapidly develop diagnostic assays, complete preliminary testing and, as a result, establish that these agents, even though transmitted parenterally, do not pose a threat to the blood supply and the health of Canadians.

Laboratory activities include targeted research programs in a number of areas – HIV/AIDS and other retroviruses, HIV strains, diagnostic algorithms, retroviral surveillance, molecular epidemiology of blood-borne viruses. Linkages to provincial laboratories and health authorities are now tailored to provincial realities and the national laboratories overall have established strong, often informal, working relationships with the provincial reference labs.

Emerging retroviruses (including ***Simian Foamy Virus*** - SFV) are a key concern. Scientific predictions show that new retroviruses will appear in the human population - all retroviruses that infect humans have crossed species from animals (e.g. HIV).These generally have a long period of latency that allows them to spread in the population before they are recognized.

For example, one pilot research project for SFV was set up, using a Canada Institute of Health Research fellow and funds diverted from other programs, to establish a surveillance protocol among Health Canada workers who are exposed to and work with animals. This kind of project, although important because of the potential policy impact (e.g. blood donor deferral), remains largely unfunded at Health Canada, and depends entirely on external research grants. The evaluation team was told by Health Canada that funds needed to carry out critical research on new and emerging retroviruses are not sufficient at present. Health Canada specialists were of the opinion that the attention paid by the media during the summer 2001 diverted attention from some of the key scientific issues; and resulted in the need to devote a lot of resources to testing for it among Health Canada employees. The US Federal Drug Administration, based on Health Canada data, got involved in the Simian Foamy Virus issue in the Fall and is expected to make a decision with respect to blood donor deferral once advised by an Expert Advisory Committee.

Internal respondents mentioned that the FDA in the US is taking a much more proactive approach to the issue, and is much more advanced in the use of expert committees to set priorities for research in different fields. Health Canada lacks this type of expert committee structure to help define research priorities with the result that research priorities tend to be largely individually driven, with the potential for political expediency as a basis for setting priorities as opposed to scientifically based information.

Exhibit 4.4 below summarizes some of the key developments with respect to the field of Simian Foamy Virus.

Exhibit 4.4- Transfusion Risk from Simian Foamy Virus

Transfusion Risk from Simian Foamy virus (SFV)

- Studying the transmission of simian retroviruses to humans can help define the importance of these infections to public health and inform decisions taken with respect to blood donor deferral.
- Foamy viruses (FV) were first described in 1954 when it was found to contaminate primary monkey kidney cells. The prevalence of FV infection in naturally infected animals is generally high and varies depending on the species and environmental conditions. Seroprevalence is generally high in animals held in captivity. Research demonstrated human infection from FV and raised the question of disease association.
- Studies have also focussed on determining whether specific human populations are at risk of infection with FV. Several studies showed that a significant number of people in East and Central Africa are seropositive by more than one assay. Recent studies with handlers of nonhuman primates such as veterinarians and zookeepers have also indicated a small but significant number are seropositive. There was neither evidence of disease nor of sexual transmission of SFV in one of the studies.
- A look back study was done by the US CDC and the Atlanta Red Cross. The study identified a blood donor who was confirmed to have been infected with SFV since 1981.Between 1992 and 1997, this person, unaware of his infection had donated blood 6 times. Recipients of 7 components transfused between 3 and 35 days after donation were identified. Two recipients had died of unrelated causes. One recipient was not available for testing. Four recipients tested negative for SFV 1.5 to 7 years after transfusion.
- In conclusion, at present there is not enough evidence to implicate FV as a cause of disease in humans, and transmission by blood transfusion has not been shown.
- In May 2001, Health Canada researchers conducted an anonymous, unlinked SFV surveillance study of individuals who work with non-human primates. Indicative of SFV zoonosis, of the 46 participants tested, one serum sample reacted strongly while another serum sample reacted weakly to SFV proteins (Western Blot Analysis).Based on these findings, there was discussion by Health Canada whether the employees handling nonhuman primates should defer from donating blood, tissues or organs until more is known about the pathogenesis of SFV.
- In September 2001, the US Federal Drug Administration (FDA) in consultation with the Centre for Disease Control (CDC) and Health Canada sought advice.
- The US CDC and FDA presented the outline of future studies in both monkeys and humans to address the question of possible SFV transmission by blood transfusion. Based on the outcomes of these studies, FDA intends to re-examine the question of appropriate blood precautions.
- Health Canada should participate in these future studies, yet at present there exists no mechanisms to ensure the funds necessary to support the research are available.

Sources:
Identification of a human population infected with simian foamy viruses, Walid Heneine & als, Nature Medecine, Volume 4, number 4, April 1998
Simian foamy virus infection among zoo keepers, Paul A. Sandstrom & als, The Lancet, 12 February 2000, Vol. 335, no. 9203, pages 551-552
Persistent Zoonotic Infection of a Human with Simian Foamy Virus in the Absence of an Intact *orf-2* Accessory Gene, Margaret A. Callahan & als, Journal of Virology, Nov. 1999, p. 9619-9624
Topic 1: Potential Concerns for Simian Foamy Virus (SFV transmission by Blood and Blood Products, Blood Products Advisory Committee Meeting, September 20-21, 2001, Gaithersburg, MD (FDA)

Currently the Centre for Infectious Disease Prevention and Control and the National Microbiology Laboratory are working towards an integrated enhanced surveillance including strain surveillance for Hepatitis B and C.

The National Microbiology Laboratory also has the capacity to provide diagnostic services for new or novel viruses. **Exhibit 4.5** provides one example of the research carried out by the laboratory with respect to the TT virus which was suspected of being a new hepatitis virus.

Exhibit 4.5 - Research on the TT Virus

Research on the TT Virus

- In 1997, a novel virus, TTV, was discovered by molecular detection techniques[1].
- As the virus was originally detected in an individual having elevated transaminase levels during post-transfusion hepatitis of unknown origin, it was suspected that TTV may represent a new hepatitis virus that is transmitted parenterally.
- The NML rapidly tested various literature-based molecular detection methods followed by institution of a national molecular diagnostic service for detection of TTV DNA in serum, in 1998.
- Additional studies were then conducted to investigate the prevalence of TTV in various specimens (serum, saliva, parotid gland, skin, and hair follicles) from healthy Canadian subjects[2] (n=130).
- Using highly sensitive methods, TTV DNA was detected in the various specimens and was found to have high sequence divergence, including among specimens of the same healthy subject.
- These studies demonstrated that TTV was widely prevalent among the general Canadian population, and that TTV is likely to be transmitted through non-parenteral as well as parenteral routes.
- This finding was in agreement with studies throughout the world which found a high prevalence of TTV in the general population[3].Transmission of TTV was also recognized to occur parenterally and non-parenterally (fecal-oral transmission; sexual transmission; mother-to-neonate).
- This accumulated evidence led the NML to conclude that TTV is not a causative agent of chronic liver disease and thus the TTV molecular diagnostic service was suspended after approximately 4 years of operation.
- TTV may be considered an "orphan" virus, a virus in search of a disease. As yet, no specific clinical manifestations have been explicitly associated with TTV, however; some data support the involvement of TTV in occasional liver injury[4], similar to other viruses know to periodically cause cryptogenic hepatitis (eg. enteroviruses, adenoviruses, cytomegalovirus, Epstein Barr virus, etc.).In addition, there is evidence to suggest that TTV-associated pathogenicity may only become evident upon co-infection with other viruses such as HIV[5,6] or HCV [7].TTV may also produce pathological changes in certain infected tissues, such as lymphoid cells[8,9] or kidneys[10], as opposed to the liver, where histological changes have not been observed.
- As these issues remain contentious, the nature of the threat of TTV to the safety of the Canadian blood system is unknown.
- Health Canada should remain knowledgeable of and monitor any new information regarding TTV infection in order to make the best informed decision on the importance of TTV to blood safety.
- If new information is obtained which indicates resuming diagnostic services for TTV, HC NML is in a position to rapidly update molecular and serological systems for detecting and quantifying all existing TTV strains in Canada. Such testing for TTV or any similar virus which emerges could be brought into effect at short notice.

References:

1. B B R C 1997.241:92-97
2. Hepatol. Res. 2000.16:155-162.
3. Clin. Micro. Rev. 2001.14:98-113.
4. J. Clin. Gastroenterol. 2002.34:86-88.
5. J. Infect. Dis. 2000. 181:1796-99.
6. Dig. Dis. Sci. 2001.46:2401-2407.
7. Hepatol. Res. 2001.21:85-96.
8. Ann. NY Acad. Sci. 2001.945:84-92.
9. J. Med. Virol. 2001.64:190-194.
10. J. Gen. Virol. 2002. 83:141-150.

Health Canada is also developing a ***Rapid Response Surveillance System*** for new and emerging blood borne pathogens. It targets two broad categories: one a group representative of the general population accessed through clinics after informed consent; and, members of special groups, e.g., transplant victims, hemophiliacs, etc. This system is being piloted in Ontario with 1000-2000 participating physicians and groups such as the Association of Hemophiliac Physicians and the Vancouver Transplant Centre. The objective is to develop a database with a healthy population and with special at-risk groups to identify future threats (as identified in special groups).One objective is to organize a cohort who can provide blood samples quickly and who would, with permission, allow Health Canada to test for new viruses. At present, ethical guidelines do not allow the

testing of existing blood samples for new viruses without obtaining consent from the patient. The ethical and legal issues surrounding the testing of existing blood samples can impact on the ability of Health Canada to respond quickly to new emergencies.

Not all stakeholders interviewed were aware of the surveillance programs; but some raised a number of concerns with respect to the data collection costs associated with the broader surveillance systems put in place by Health Canada. The surveillance process to ensure the safety of blood and blood products and ensure "vein to vein" tracking depends largely on hospitals across the country, which are responsible for blood transfusions and use of blood products. There also must be collaboration and buy-in from all provinces and territories in all of these projects. A significant portion of the blood system is under provincial jurisdiction. Both internal and external respondents were aware of the significant issues involved in obtaining this cooperation and compliance. Many felt additional consultations will be needed with those responsible for surveillance in the provinces and territories if a fully integrated surveillance system is to become a reality. The federal government has the national mandate and needs to play a leadership role in this field .However, external respondents felt that it will also have to provide resources (cost-sharing) to sustain some of these activities across Canada. A more detailed action plan that would identify the role of all the players might be useful.

Mitigating factors that affect the implementation of the national surveillance system according to external stakeholders include:

- the need to reach consensus on data/system requirements to avoid system duplication/unnecessary costs for both hospitals and provincial and territorial Ministries of Health;
- the need to review data requirements from a *Freedom of Information and Protection of Privacy Act* perspective, and ensure that requirements, especially those required for Ministry roll-up, meet the confidentiality requirements of different provincial and territorial legislation; and
- the recognition by the federal government of the salary and system costs associated with implementation of a national system, which need to be reimbursed or at least cost-shared with some of the provinces and territories.

Some external stakeholders also expressed concerns that not enough had been done to improve surveillance and that too much focus had been put on pilot projects across the country. Others were very supportive of the pilot projects. Surveillance in Canada was, according to some respondents, was weaker than in the UK or France. They, however, felt that Health Canada had made efforts to improve its risk assessment/management capabilities overall.

4.5 Resource Requirements for Future Sustainability

Health Canada (Laboratory Centre for Disease Control), in a study carried out in June 2000, ***Blood Surveillance and Clinical Product Outcomes***, ***Program Plan 2000-01 to 2002-03***,identified a number of gaps that will negatively impact on its ability to deliver the blood surveillance program.These gaps generally fall into two major categories:

- capacities or capabilities that do not currently exist but which could be developed or acquired with additional resources; and
- capacities or capabilities that already exist but which could be degraded or lost unless sufficient resources are provided to sustain the current level of activity.

The most significant gaps, according to Health Canada staff, include:

- ***Enhanced transfusion surveillance:*** MC funding was sufficient to establish a Transfusion Transmitted Incidents Surveillance System (TTISS) in four pilot provinces. In 1999-2000, centres were initiated in British Columbia, Quebec and Prince Edward Island. Nova Scotia was added in 2000-01.Incremental funding is needed if the TTISS is to become a national system extending to all provinces and territories. In 2000-01, a pilot project was established in one hospital to enable the development of an effective Transfusion Error Reporting System (TERS).Preliminary results were discussed in a recent research article: *Reporting of near-miss events for transfusion medicine: improving transfusion safety,* Jeannie L. Callum & al., Transfusion, Volume 41, October 2001.The ultimate goal is a system comprising eight high volume hospitals.
- ***Hospital-based Surveillance Centres:*** Under the 1996 MC, funding was allocated for routine surveillance, enhanced population-based surveillance, risk analysis and policy development for Hepatitis C, Hepatitis B and emerging blood-borne pathogens (BBP).Under the 1998 MC, funding was provided for laboratory-based surveillance for Hepatitis C, Hepatitis B and emerging BBP including reference services, laboratory support to surveillance activities and investigation of emerging BPPs. According to Health Canada staff, the BBP surveillance network would be significantly enhanced with the inclusion of hospital-based surveillance, which provides direct access to patient pools. Accordingly, hospital-based surveillance was developed in three centres (Winnipeg, Toronto, and Ottawa) in 2000-2001.The funding required to operate the three centres is $495K per year in contributions. About 25% of that requirement can be offset from the existing allocation (MC96).However, new funding will be required for the balance of $365K per year.
- *Transplantation and Xenotransplantation Surveillance:* Surveillance may become a priority in future years for a number of reasons such as the potential conduct of clinical trials in Canada; the risks of a new zoonotic epidemic; and, more recent scientific developments in the US.

- ***HIV Epidemiological Surveillance:*** An integrated epi and laboratory-based surveillance system comprising five specific initiatives for HIV has been developed. While the overall system is in place, some program elements are currently under refinement and implementation. Staff noted that the absence of new funds in years 4 and 5 will result in the initial scaling-back and then the potential dismantling of the program.
- ***Prion Diseases/Epidemiology and Surveillance:*** A number of activities have been implemented to enhance the capacity to conduct surveillance and laboratory investigation of prion diseases. However, funding requirements are below that needed to sustain the activities over time. Staff noted that, without additional funding, important work on the development of a diagnostic blood test for CJD will have to be suspended.
- ***Prion Diseases Diagnostic and Reference Laboratory:*** Established in 1998, this program includes laboratory activities to support surveillance for prion diseases - CJD and its variants in humans and in animals - that are potentially transmissible by blood, tissues, organs or xenotransplantation, as well as targeted research to develop and validate the tools necessary to cope with these diseases. Lack of funding for later years may lead to the dismantling of the program. The only location currently available in Canada for carrying out this work is Health Canada's Level 3+4 containment laboratory facility, housed in the Canadian Science Centre for Human and Animal Health in Winnipeg.

Exhibit 4.6 below summarizes the funding shortfall by bureau as prepared by the Centre for Disease Prevention and Control for the Surveillance Program.

Exhibit 4.6 - Summary of Funding Shortfalls - Surveillance Activities

Bureau	2000-01		2001-02		2002-2003	
	FTE	$K	FTE	$K	FTE	$K
Bureau of Infectious Diseases • Enhanced transfusion surveillance **Hospital-based Surveillance Centres** • Xenotransplantation surveillance • Prion diseases epidemiology and surveillance	0	0 -$365K 0 0	-2 0 -2 0	-$796K -$365K -$710K -$478K	-2 0 -5 0	-$1,979K -$1,125K -$1,125K 0
Total	0	-$365K	-4	-$2,349K	-7	-$3,469K
Bureau of HIV / AIDS, STDs & TB • HIV Epidemiological Surveillance	0	-$165K	-9	-$947K	-9	-$1,771K
National Microbiology Laboratory • Prion diseases diagnostic and reference laboratory	7	-$21K	-10	-$2,015K	-10	-$1535K
Blood Surveillance and Clinical Product Outcomes Program						
Total Short-fall	-16	-$509K	-23	-$5,311K	-26	-$6,775
Offset (from other sources)	0	$1,177K	0	$1,612K	0	$1,612K
New short-fall	-16	$668K	-23	-$3,799	-26	-$5,153K

Source: ***Blood Surveillance and Clinical Product Outcomes***, Program Plan 2000-01 to 2002-03, Laboratory Centre for Disease Control, June 7, 2000

The National Microbiology Laboratory has also identified an area of research that they would like to explore, that is the development of programs for monitoring cellular immune response of acute and chronic hepatitis B and C patients. The determining factor for HBV or HCV acute or chronic response by the host likely may be the cell-mediated immune response. This research could provide markers that could be used to predict viral infection from a new or unknown emerging virus in high-risk groups, such as hepatitis patients. Additional resources would be needed to develop this research program.

4.6 Other Issues

A number of other questions were brought out in the interviews with internal Health Canada staff. These included questions about baseline or performance information, national and international linkages and access to external expertise, and cost effectiveness of program and alternative mechanisms.

Overall staff felt that progress had been made with the additional dedicated resources and that the action plans that were developed addressed the basic concerns of the Krever enquiry. Although progress had been slow initially, the national laboratories felt they had now established good linkages to provincial laboratories and health authorities.

Both epidemiological research and laboratory R&D are important for scientific surveillance activities and the independent strength of these two areas must be maintained according to staff. However, at present there is no established peer review system to provide the kind of leadership needed to establish both research and scientific priorities for the Blood Safety Program.

Baseline or Performance Information

In the first few years of operation, performance information tended to be rather output oriented and focussed on providing information on specific activities to date orin place. Information tended to be descriptive and there were many operational planning documents but few performance or activity reports.
Staff members indicated that there was a risk management process in place which allowed new priorities to be addressed. However, on the surveillance side, there was a great deal of concern with respect to the lack of sufficient resources to address the “unknowns”, the “potential” problems with respect to blood safety. They felt this was the biggest single gap in the system at present.

As for the BSP’s Regulatory Program, our analysis indicated that there was a lack of available baseline performance information and readily available indicators to measure performance against commitments undertaken in the 1998 Action Plan and Health Canada’s objectives for blood safety.

National and International Linkages

All the groups within the surveillance programs were linked internationally to organizations involved in their field of expertise and participated in a number of key committees. Appropriate linkages were also maintained with other players in the public health network. This networking and collaborative efforts were important to maintain internal scientific capabilities at the leading edge and to attract new scientists. It also allowed staff access both national and international expertise when required.

Cost effectiveness and alternatives

According the Health Canada staff, the program has never been extravagantly funded and that funding was not on par with other countries, particularly the US even when adjusting for the difference in scale between the two countries. Existing resources according the Health Canada staff fall short of documented needs. Two additional concerns were expressed by Health Canada personnel: the first dealt with the lack of dedicated senior management for the Blood Safety Program within Health Canada that would provide overall direction to the program; the second was with the lack of an Expert Committee that would provide advice on research priorities and ensure that existing resources focus on the highest R&D priorities.

Both internal and external respondents agreed that the federal government needs to continue to have the core responsibility for the Blood Safety Program and that it should continue to rest within Health Canada. No other alternative exists in Canada. However, its role could be enhanced by building up core capabilities and building lasting collaborations with other stakeholders in the system.

4.7 Conclusions

The following elements of a national surveillance system are now in place:

- investments were made to support both epidemiological research and laboratory research and development, which are important to sustain the surveillance activities and the safety of the blood supply and the health of Canadians;
- the major areas covered by the surveillance activities include retroviruses (including HIV/AIDS, Simian foamy virus, etc.), prions, hepatitis, emerging blood-borne pathogens and transfusion transmitted injuries (TTIs); and
- surveillance is carried out in a number of different ways: health events monitoring and alert; routine surveillance; enhanced surveillance in six sentinel sites; surveillance for new or re-emerging blood-borne pathogens, including mutants of known pathogens; targeted surveillance carried out jointly with the Bureau of HIV/AIDS, Correctional Services, First Nations, and Inuit Health Boards; and special studies.

4.7.1 Contribution of BSP Surveillance Activities

While a national surveillance system is not yet in place, Health Canada has made progress in addressing the Krever recommendations. Therefore, based on the surveillance elements/systems now in place and the ongoing activities of the Surveillance Program, we concluded that the BSP surveillance activities have contributed to:

- **An Enhanced Capacity to Create a Blood Surveillance System Based on a Voluntary Post-Market Surveillance System and a Donor Database**

The Transfusion-Transmitted Injuries Surveillance System (TTIS) is being piloted in four provinces: Prince Edward Island, Nova Scotia, Québec and British Columbia. This means that all four provinces have a provincial adverse event (AE) reporting system as a component of their central transfusion registry. Collected data is to be transferred to the Health Canada national AE database twice a year. As hospitals are not regulated by the federal government, AE reporting is primarily voluntary.

According to both internal and external stakeholders interviewed, future challenges will include the transition from a pilot project to a national system; finding dedicated financial and human resources at the federal, provincial and territorial level; and, developing mechanisms to encourage reporting of adverse events from the hospital level.

- **An Enhanced Capacity to Conduct Statistical Analysis and Risk Assessment and Management**

Health Canada has been involved in risk assessment and risk management for prion diseases e.g., development of CJD Infection Control Guidelines for Classical CJD; and donor deferral policies (see Exhibit 3.3) in 1999, 2000 and 2001 to protect the safety of the Canadian Blood Supply.

- **An Enhanced Capacity to Study the Most Vulnerable Populations and to Conduct Outbreak Investigations**

Health Canada is developing a ***Rapid Response Surveillance System*** for new and emerging blood borne pathogens. It targets two broad categories: one a group representative of the general population accessed through clinics after informed consent; and, members of special at-risk groups, e.g., transplant victims, hemophiliacs, etc. This system is being piloted in Ontario with 1000-2000 participating physicians and groups such as the Association of Hemophiliac Physicians and the Vancouver Transplant Centre.

However, as ethical guidelines do not allow the testing of existing blood samples for new viruses without obtaining consent from the patient, the ability of Health Canada to respond quickly to new emergencies is compromised.

Outbreak investigations have been carried out on blood-borne parasitic diseases such as Babesiosis (a tick-borne malaria-like illness) and Chagas. In addition, a preliminary risk assessment has been carried out for infection through transfusion of these diseases. As more and more Canadians travel to and work in areas of the world where such diseases are prevalent, there is a danger of these illnesses getting into the Canadian blood supply upon their return to Canada. Again there is an issue of resources lacking to continue the work in this area.

- **An Enhanced Capacity to Provide Blood-borne Pathogen Laboratory-based Epidemiological Surveillance**

The *Integrated Surveillance Project* has established a network to address current and emerging issues. MOUs are now in place between Health Canada and British Columbia, Alberta, Saskatchewan, Manitoba, Quebec, Ontario and the Atlantic provinces, establishing new and comprehensive data linkages between national and provincial epidemiology systems that provide demographic and risk variables. Further, *an integrated laboratory-linked surveillance system* specific for HIV strain and drug resistance has been developed which is benefiting HIV diagnostics and screening strategies; informing vaccine development; and assessing HIV transmission patterns, HIV pathogenesis and progression of HIV-related diseases. As a result of this enhanced surveillance system, data submitted from the provinces is in real time (rather than up to 3 years late) and has improved in quality and completeness, leading to improved analyses both locally and nationally.

Federally-hired Field Surveillance Officers (FSOs) are now on location in British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and the Atlantic provinces. Co-supervised by provincial public health authorities, the FSOs assist with the enhanced surveillance program and are in demand for outbreak investigations, presentations and international assignment.

An *enhanced sentinel surveillance system*, consisting of Vancouver-Richmond, Edmonton, Calgary, Winnipeg, Ottawa-Carleton, and New Brunswick has been established for acute Hepatitis B and C. By focussing on smaller populations, sentinel surveillance allows for the collection of more in-depth, timely and consistent data, which in turn, allows for the estimation of national incidence rates of Hep B and C. The first results of this system (covering the period 1998-1999) were published in December 2001.

- **An Enhanced Capacity to Conduct Public health Investigation of Emerging Blood-borne Pathogens**

As noted above, a rapid response surveillance system (RRSS) is being developed.

Between 1999 and 2001, several potential blood-borne agents emerged - TTV, TLMV and SEN-V. In response, the Surveillance Program developed diagnostic assay, completed preliminary testing and, as a result, established that these agents, while transmitted parentally, do not pose a threat to the blood supply and the health of Canadians.

- **An Enhanced Capacity to Conduct Surveillance and Laboratory Investigation of Prion Diseases**

A national surveillance system for CJD in adult and pediatric populations (CJD-Surveillance System), including vCJD has been developed. Draft protocols for investigation of suspected vCJD cases have been developed and links have been established with provincial/territorial health authorities, health care institutions and health care professionals. Health Canada collaborates internationally (UK, Euro-CJD, WHO) on CJD surveillance, which includes data exchange on CJD in high risk populations. For example, CJD surveillance in Hemophiliacs is carried out under the TTISS.

However, while practising physicians are required to report each case of CJD to their provincial/territorial health authority (effective January 1, 2000, CJD became a disease under national surveillance); reporting CJD is not mandatory in all provinces/territories.

Research on prion diseases is carried out by the Winnipeg Human and Animal Prion Reference Laboratory, created *de novo* in 1998. The laboratory is providing ongoing advanced human molecular genetic diagnosis to support the CJD-SS and has established scientific research programs to investigate prion disease mechanisms and prion stain variation.

Through contracts, Health Canada maintains a neuropathology reference centre at the Tanz Neuroscience, Neuropathology and Prion Diagnostic Research Centre, which provides diagnostic and consultation services for the CJD-SS.

Through a collaboration with the Centre for Research in Neurodegenerative Diseases (CRND), University of Toronto, an immunoassay of 14-3-3 protein in the cerebrospinal fluid (CSF) was set up to assist in the diagnosis of CJD. Currently, CNRD is the only facility in Canada which can perform this analysis.

- **An Enhanced Capacity to Link with Public Health Networks**

Health Canada is actively participating in the establishment of the Canadian Viral Hepatitis Network (CVHN) to share valuable information on acute HBV and HCV infection. To date, a hospital/clinic-based surveillance system has been established in 4 centres - Winnipeg, Toronto, Calgary and Ottawa.

4.7.2 Outstanding Issues

We concluded that the surveillance program faces a number of gaps:

- **Funding shortfalls.** Unless these are addressed, there is the risk that the partnerships and collaborations built with different groups (public health organizations and practitioners, hospitals, voluntary organizations, academic researchers, etc.) may be negatively affected. These enhanced and targeted surveillance systems are at the core of building the necessary information systems in cooperation with the provinces and territories.

- **R&D.** There also appears to be gaps in the scientific research and development programs that are needed to sustain surveillance activities. For various reasons, and with Treasury Board approval, the financial resources were "front-loaded"; that is, used to establish the necessary laboratory infrastructure during the first three years. This will result in resource shortfalls during the last two years of the program. Also, very few resources are available to meet new and unexpected challenges. This may impede on Health Canada's ability to provide an adequate scientific and epidemiological basis needed to support sound policy and decision-making.
- **Absence of a Scientific Advisory Committee.** Both internal and external respondents recommended that Health Canada establish a scientific advisory committee to establish research priorities and to determine the nature and type of scientific research needed to sustain the R&D programs that contribute to ensuring the safety of the Canadian blood supply. This type of expert advisory body exists in the US, providing advice to the FDA on research priorities.
- **Provincial/Territorial Support.** Provincial Ministries of Public Health, hospitals and health practitioners are a key element in the national blood regulatory and surveillance system. They are not regulated or subject to federal authority at the present and their participation in many of these activities is entirely voluntary. As mentioned previously, one of the critical issues for the provinces and territories remains the cost associated with implementing new standards and regulations; reporting adverse reactions; and, generally participating in surveillance programs. This situation will result in different funding levels across the country and may, in the end, compromise the integrity of the surveillance system. Adequate consideration needs to be given to the financial implications for the provinces and territories in the implementation and administration of these systems. Some external respondents felt that the federal government needed to be more conscious of this financial burden and share in some of the costs.

4.7.3 Future Requirements

Finally, we concluded that, based on the financial information provided to us during the course of the study we cannot identify future resource requirements for the Surveillance Program.

5.0 OVERALL CONCLUSIONS

We concluded, based on the results of the study, that:

- The Health Canada Blood Safety Program has made considerable progress towards achieving the objectives articulated in the 1998 Action Plan developed in response to the Krever Inquiry and provided as a basis for funding improvements to the Blood Safety Program.
- The level of safety of the Canadian blood system has improved. The actions taken by Health Canada, as well as other players within the blood system, have contributed to this improvement. In most areas, Canada is meeting international standards for blood safety through the introduction of new standards, guidelines, deferral policies, diagnostics tests and research activities;
- With respect to whether the system is fully integrated, the existence of two major blood operators (CBS and Héma-Québec) does not impact on the overall integrity of the system as it was unified through the regulatory activities carried out by Health Canada; and
- Given the many other players in the Canadian blood system (including provincial health authorities, hospitals, academic researchers, voluntary organizations, health practitioners, National Blood Safety Council, expert committees, etc.) that must contribute to ensuring the overall safety of the blood supply in Canada, one cannot say that a fully integrated national surveillance system is yet a reality in Canada.

We concluded that on the *regulatory side*, Health Canada has:

- Expanded its regulatory functions and increased its capacity to carry out inspections/investigation activities of the two major blood operators - Héma-Québec and the Canadian Blood Services - who are responsible for the collection and the distribution of blood and blood products in Québec and Canada;
- Initiated the development, in close consultation with a wide range of stakeholders involved in the Canadian blood safety system, of a new regulatory framework for blood, which will use the *National Blood Standards* as a basis;
- Carried out a number of other regulatory activities in order to meet other pressing demands in the field of biologics, including amendments to the regulatory requirements for plasmapheresis; amendments to the Semen Regulations; and the initiation of a new framework for Cells, Tissues and Organs;
- Taken a more pro-active response, erring on the side of safety, to potential threats to the blood supply in the case of both classical Creutzfeldt-Jakob Disease and its variant form;

- Carried out more effective pre-market activity and post-market surveillance including the conduct of health hazards assessments and evaluations; and
- Developed the *Canadian Adverse Drug Reaction Information System* (CADRIS), a database that will capture adverse drug reactions from both manufacturers (where it is mandatory) and the hospitals (where it is voluntary and not regulated at the present).
- We concluded that on the *surveillance side*, a number of activities were undertaken by Health Canada to put in place elements of a national surveillance system:
- Investments were made to support both epidemiological research and scientific research and development in major areas. Both types of research are important to sustain surveillance activities and ensure the safety of the blood supply and the health of Canadians;
- Surveillance activities are being carried out for the following critical areas: retroviruses (including HIV/AIDS, Simian foamy virus, etc.), prions, hepatitis , emerging blood-borne pathogens, and transfusion transmitted injuries;
- Surveillance activities through many different mechanisms including: health events monitoring and alert; routine surveillance; enhanced surveillance in six sentinel sites; surveillance for new or re-emerging blood-borne pathogens, including mutants of known pathogens; targeted surveillance carried out jointly with the Bureau of HIV/AIDS, Correctional Services, First Nations and Inuit Health Boards; and numerous special studies; and
- A pilot project by Health Canada's Centre for Infectious Disease Prevention and Control Surveillance Program - the *Transfusion Transmitted Injury Surveillance System* (TISS), which integrates an active surveillance of infectious diseases and adverse transfusion-related incidences (ATRs), including errors in the administering of transfusions.

Outstanding Program Issues/Gaps

We concluded that there a number of outstanding program issues:

- Health Canada officials are concerned that there will be resource gaps for both the Surveillance and the Regulatory program .Resource constraints may have a negative impact on Health Canada's ability to deliver a national surveillance program, as there is a high degree of risk that the partnerships and collaborations built with different groups (public health organizations and practitioners, voluntary organizations, academic researchers, etc.) may be negatively affected.
- The financial costs borne by the provincial and territorial authorities for their participation in the national blood safety system both through their funding of blood operators and their participation in surveillance activities are significant. Health Canada will have to consider the future costs and negotiate with the provinces/territories who pays what.

- Hospitals (and other private organizations) are important players in the distribution and administration of blood and blood components. An increase in the hospital sector's collection activities, although previously anticipated, has not yet occurred. Hospitals are subject to the current regulations; however, they are presently being applied only to the blood system operators. This remains one of the key gaps in the overall Canadian blood system. Health Canada is currently developing a new regulatory framework for blood safety, which will be based on the *Blood Safety Standards* and will address hospitals' activities in distribution, administration and collection. However, current practices for enforcement and compliance with the standards will need to be reviewed taking into account the limited resources available to Health Canada.
- In addition, many new establishments will also be involved in the tissues, organs, and xenotransplantation systems. These growing fields and new scientific and technological developments will tax the existing regulatory system at Health Canada and impact on the Department's ability to carry out its regulatory role with the existing resources especially using the current approaches and processes for enforcement and compliance.

Management Practices Issues

Finally, we concluded that there were a number of areas that can be strengthened in Health Canada's management practices related to the Blood Safety Program:

- The complexity of the Blood Safety Program represents a challenge as a horizontal program. At the organizational level, responsibilities and accountabilities for the Blood Safety Program are spread across two branches and many organizational units within Health Canada. As a result, there is a need to strengthen management information and horizontal management to ensure adequate monitoring, tracking and reporting of expenditures and results in comparison to the 1998 Action Plan. This is in part because no one organizational unit was charged with the overall responsibility/accountability for the program;
- The Actions stipulated in the 1998 Action Plan were not necessarily adhered to. Many of the activities/actions required were changed over time, primarily because of changing needs, or inappropriate specification of requirements in 1998. As the changes were not always documented, it is difficult to determine the extent to which the intent of the original action plan was actually met. In future programs, tracking should be improved;
- There were limited performance baseline indicators available to measure progress in the safety of the blood system. Future work on the HCBSP Evaluation Framework will have to ensure that indicators are further refined and agreed upon to facilitate future reporting for the program; and,

- Finally, many of the BSP investments are costly and have long-term financial and regulatory implications. To our knowledge there has not been an external review by an expert panel to ensure the cost-effectiveness and appropriateness of activities undertaken.

Future Requirement

This review provides an assessment of accomplishments in the Blood Safety Program and future needs and gaps. There is a need for Health Canada to build on this review and to make a further assessment of remaining gaps and future resource requirements for the BSP.

APPENDIX A

LIST OF DOCUMENTS REVIEWED

LIST OF DOCUMENTS REVIEWED

1. *Evaluation Framework for Health Canada's Blood Safety Program*, Terms of Reference, Appendix 2 - Accountability Framework, Departmental Program Evaluation Division, Applied Research and Analysis Directorate, Information, Analysis and Connectivity Branch, February 2000
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27. *Report on the Meeting of the Expert Panel on Hepatitis C Epidemiology, June 17-18, 1998*, prepared for Health Canada by Dr. Richard Schabas

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32. *3.0 Analysis - Krever Status Report-TPP*, Draft 4-May 19, 2000

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34. *Sub-Action Plan for Policy and Regulatory Development,* Sub-projects A-F, Biologics and Genetic Therapies Directorate, July 6, 2001

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64. Documents from the web site of The National Blood Safety Council

APPENDIX B

LIST OF INTERVIEWEES

List of Preliminary Interviews

1. **Dr. Mike Coulthart**, Chief, National Laboratory for Host Genetics and Prion Diseases, National Microbiology Lab, Population and Public Health Branch
2. **Jean Lambert**, Director General, Health Products and Food Inspectorate, Health Products & Food Branch
3. **Danielle Dionne**, Director, National Coordination Centre, Inspectorate Directorate, Bureau of Compliance and Enforcement, Health Products and Food Branch
4. **Etienne Ouimet**, Blood, Tissues, Organs and Xeno (BTOX) Compliance Coordinator, Office of Compliance, Planning & Coordination
5. **Marianne Tang & Chantal Trépanier**, Bureau of Policy and coordination, Therapeutics Products Directorate, Health Products and Food Branch
6. **Dr. Antonio Giulivi**(957-1789) Associate Director, Blood-Borne Pathogens Division,centre for infectious Disease Prevention and control
7. **Dr. Wark Boucher** Acting Chief, Transfusion Transmitted Infections
8. **Andrew Armstrong** Office of Management Services, Therapeutics Products Programme, Health Products and Food Branch
9. **Andy Butterfield,** Manager, Office of Management Services, Therapeutics Products Programme, Health Products and Food
10. **Dr. Don Sutherland**, Director, HIV/AIDS, STD and TB, Centre for Infectious Disease, Prevention and Control, Population & Public Health Branch
11. **Dr Judith Glennie**, Manager, Socio-Economic Evaluation Division, Bureau of Policy and Coordination, Therapeutics Products Directorate, Health Products and Food Branch
12. **Dr. Paul Sandstrom**, Associate Director, HIV/AIDS, STD and TB, Centre for Infectious Disease, Prevention and Control, Population & Public Health Branch
13. **Barbara Benning**, Advisor, Biologics and Genetic Therapies Directorate, Health Products and Food Branch
14. **Dr Paul Gully,** A/Director General, Centre for Infectious Disease, Prevention and Control, Population and Public Health Branch
15. **Dr. Peter Ganz**, Chief, Blood and Tissues Division, Bureau of Biologics & Tissues Division, Biologic and Genetic Therapies Directorate, Health Products & Food Branch
16. **Rachel Dansereau**, Blood and Tissues Division, Bureau of Biologics and Radiopharmaceuticals
17. **Dr. Robert Leitch**, Associate Manager, Product Assessment - Biological and Associated Products Division, Bureau of Licensed Product Assessment, Therapeutics Product Directorate, Health Products and Food Branch

18. **Dr. Anton Andonov** Research Scientist, National Library for Viral Diagnostics, National Microbiology Laboratory, Population and Public Health Branch
19. **Maria Carballo** and **Debbie Lépine** (954-4585), Bureau of Medical Devices, Health Products and Food Branch
20. **Julia Hill**, Associate Director General, Biologics and Genetic Therapies Directorate, Health Products and Food Branch
21. **Kwasi Nyarko**, Manager, Product Assessment - Pharmaceutical Division, Therapeutics Products Programme, Health Products and Food Branch
22. **Dr. Robert Peterson**, Director General, Therapeutics Products Directorate, Health Products and Food Branch

List of Interviewees - Phase 2

HEALTH CANADA PERSONNEL

Regulatory

Biologics and Genetic Therapies Directorate

1. Julia Hill, Associate Director General

Centre for Policy and Regulatory Affairs

2. Cathy Parker, Acting Manager, Policy and Promotion Division
3. Nathalie Perron, Project Manager, BTOX
4. Julie Gervais, Policy Analyst
5. Chantal Trepanier, Regulatory Policy Officer
6. Marianne Tang. Evaluation Officer
7. Chantal Roy, Evaluation Officer
8. Rachel Dansereau, Manager, Blood Establishment Regulation Division

Centre for Biologics Evaluation

9. Dr. Peter Ganz, Manager, Blood, Tissues and Organs Division

Centre for Biologics Research

10. Dr. William Wilson (now retired), Acting Director
11. Dr. Larry Whitehorse, Acting Director (as of January 1, 2002)

Therapeutic Products Directorate

Office of Management Services

12. Andy Butterfield, Manager, Office of Management Services

13. Andrew Armstrong, Officer, Operational Planning

Bureau of Licensed Product Assessment, Product Assessment - Biological and Associated Products Division

14. Dr. Kwasi Nyarko, Head, Monitoring and Evaluating Unit

15. Dr. Robert Leitch, Evaluator, Monitoring and Evaluating Unit

Medical Devices Bureau

16. Beth Pieterson, Acting Director

17. Maria Carballo, Acting Head, Invitro Diagnostic Devices Division

Inspectorate (now the Health Products and Food Branch Inspectorate)

18. Jean Lambert, Director General

19. Danielle Dionne, Associate Director General, National Coordination Centre

20. Etienne Ouimet, Blood, Tissues, Organs and Xenografts (BTOX) Compliance Coordinator

Surveillance

Centre for Infectious Diseases Prevention and Control (CIDPC)

21. Dr. Paul Gully, Acting Director General

Bureau of HIV/AIDS, STD and TB

22. Dr. Don Sutherland, Director

23. Dr. Paul Sandstrom, Associate Director

24. Dr. Chris Archibald, Chief, Division of HIV/AIDS, Epidemiology and Surveillance

25. Dr. Tom Wong, Chief, Division of Sexual Health and Disease

Bureau of Infectious Diseases

26. Dr. Antonio Giulivi, Associate Director, Chief, Blood-borne Pathogens Division

27. Dr. Wark Boucher, Acting Chief, Transfusion Transmitted Infections
28. Susie ElSaadany, Chief, Statistics and Risk Assessment Unit, Blood-borne Pathogens Division
29. Dr. Ezzat Farzad, Acting Chief, Transfusion Transmitted Injuries Section, Blood-borne Pathogens Division

30. Dr. Marc-André Beaulieu, Chief, Prion Section, Blood-borne Pathogens Division

31. Robert Gervais, Medical Specialist, Prion Section, Blood-borne Pathogens Division

32. Dr. Shimian Zou, Chief, CABBI Section, Blood-borne Pathogens Division

33. Dr. Jose Campione, Science/Laboratory Advisor, Blood-borne Pathogens Division

National Microbiology Laboratory

34. Dr. Tim Booth, Scientific Director, National Laboratory for Viral Diagnostics (Winnipeg)

35. Dr. Anton Andonov, Research Scientist, National Laboratory for Viral Diagnostics (Winnipeg)

36. Dr. Michael Coulthart, Chief, National Laboratory for Host Genetics and Prion Diseases

External Stakeholders

37. Betty Jeffers, Policy, Federal-Provincial Relations Branch, Alberta Health and Wellness

38. Carol Major, Head of HIV Laboratory, Laboratory Services Branch, Ontario Ministry of Health

39. Dr. Graham Sher, CEO, Canadian Blood Services

40. Dr. David Pi, Director, Provincial Blood Coordinating Unit, St. Paul's Hospital, Vancouver

41. Dr. Shaun Peck, Deputy Provincial Health Officer, Office of the Provincial Health Officer, Ministry of Health Planning, British Columbia

42. Dr. Francine Décary, Directrice générale, Héma-Québec

43. Suzanne Rémy-Prince, Héma-Québec
44. Dr. Bruno Turmel, Responsable du programme de surveillance du SIDA au Québec, Ministère de la santé et des services sociaux du Québec

45. Dr. Colin D'Cunha, Ontario Chief Medical Officer of Health and Director of the Public Health Branch, Ontario Public Health Branch, Ontario Ministry of Health and Long-term Care

46. James Kreppner, Chair, Blood Safety Committee, Canadian Hemophilia Society

APPENDIX C

STUDY INSTRUMENTS

Review of HCBSP Interview Guide 1: HC Program Managers - Regulatory

Name(s): _____ **Position:** _____

_____ **Position:** _____

_____ **Position:** _____

Division: _____

Time/Date of Interview/Meeting: _____

Goss Gilroy Inc. has been contracted by Health Canada to conduct a Review of the Health Canada Blood Safety Program (HCBSP). As part of this review, interviews and/or working group sessions are being conducted with Program staff familiar with the regulatory activities of the Blood Safety Program. These interviews/discussions follow a document review and will be complemented by parallel interviews/discussions with Program staff familiar with the surveillance activities of the Blood Safety Program and interviews with outside stakeholders (CBS, Héma-Québec, Canadian Hemophiliac Society, etc.) of the Blood Safety Program. We are seeking your views on the rationale for the program, its design, program implementation and delivery, impacts and effects, and cost-effectiveness and alternatives.

Introduction

1. Please briefly describe your role(s) in the Blood Safety Program.

2. Before we begin the discussion below, please look at the output column of the Table 2 in Chapter 2 (Regulatory) of the document review report and confirm the information provided, as well as provide us with any additional outputs that we may have missed during our document review. In addition, please fill in the gaps in Table 3 on resources to the extent possible.

A. Program Rationale

3. From your perspective, what kind of progress has been made towards a fully integrated Blood Surveillance System? ***Please elaborate.***

4. What is the federal government's role in a fully integrated Blood Surveillance System? Is this role appropriate?

B. Program Design, Implementation and Delivery

5. Did the Health Canada Blood Safety Program establish the necessary action plans to meet the Krever report recommendations; i.e., are the activities and operational plans established in the Accountability Framework both adequate and appropriate for meeting the Krever recommendations?
   a) If not, are there additional activities and operational plans required? ***Please elaborate.***

6. Have performance baselines been established for the operational plans and activities established in the Accountability Framework? Are outcomes used as a planning tool?

7. To what extent have the Accountability Framework's activities and operational plans been implemented and met?
   a) Are the human and financial resources outlined in the Accountability Framework sufficient for the implementation of these activities and operational plans? If not, what are the additional resources, both human and financial, required to perform and sustain them?

8. Are there any mitigating factors affecting program implementation and delivery (e.g., availability of qualified candidates, resources for training)? ***Please describe.***

9. To what extent have clear, appropriate regulations, policies and guidelines been developed? ***Please elaborate.***
   a) Are the regulations, policies and guidelines in place workable and/or enforceable? Why? Why not?
   b) Are there areas of the HCBSP that remain unregulated? If so, are policies in place or in the process of development for addressing them?

10 Are there criteria for establishing priorities, in the event that operational plans and activities cannot be fully implemented? If so, what are they? Are they used on a regular basis?
   a) Are contingency plans developed and used on a regular basis to assist in meeting the Krever recommendations?

11. What progress have the regulatory activities of the HCBSP made towards:
   a) Enhancing the breadth of blood regulatory expertise to address emerging new blood technologies and blood substitutes?
   b) Enhancing the blood inspection/compliance function, which is expected to grow exponentially with the implementation of a separate blood system in Québec and the emergence of hospital-based and other commercial blood banks?
   c) More effective post-market surveillance, including encouragement of voluntary reporting by health practitioners?

d) The transition to a new blood system?

12. Have international comparisons been established? If so, are these adequately monitored and recorded?

13. Should the HCBSP have an emergency fund built into it in the event of a risk emergency? Why? Why not?

14. Is the HCBSP able to access external research capacity and expertise to fill the gaps in internal capacity?

C. Program Impacts and Effects

15. In your opinion, what progress has the HCBSP made towards enhancing (***Please elaborate.***):
    a) Capacity to conduct compliance and enforcement inspections?
    b) Capacity to conduct pre-market and post-market reviews?
    c) Capacity to perform more effective post-market surveillance?
    d) Capacity to perform regulatory research related to blood safety?
    e) Capacity to conduct regulatory policy development?
    f) Capacity to respond immediately to threats to the blood supply?
    g) Capacity to provide an effective communications interface between regulator and stakeholders?

16. From your perspective, has the HCBSP resulted in improvements to blood safety? If so, what is the nature of these improvements?

D. Cost-Effectiveness and Alternatives

17. To what extent has the HCBSP been cost-effective in meeting its objectives of protecting the Canadian public against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and, to be generally on par with blood regulatory and surveillance programs in other industrialized nations such as the UK, France and the U.S.?

18. Are the funding allocations for the HCBSP sufficient to maintain a safe blood system; i.e., do they reflect operational reality?

19. In your opinion, are there alternative mechanisms for delivering the HCBSP?

E. Other

20. Is there anything else you would like to add to the above discussion?

Review of the HCBSP Interview Guide 2: HC Program Managers - Surveillance

Name(s): _____ **Position:** _____

_____ **Position:** _____

_____ **Position:** _____

Division: _____

Time/Date of Interview/Meeting: _____

Goss Gilroy Inc. has been contracted by Health Canada to conduct a Review of the Health Canada Blood Safety Program (HCBSP). As part of this review, interviews and/or working group sessions are being conducted with Program staff familiar with the surveillance activities of the Blood Safety Program. These interviews/discussions follow a document review and will be complemented by parallel interviews/discussions with Program staff familiar with the regulatory activities of the Blood Safety Program and interviews with outside stakeholders (CBS, Héma-Québec, Canadian Hemophiliac Society, etc.) of the Blood Safety Program. We are seeking your views on the rationale for the program, its design, program implementation and delivery, impacts and effects, and cost-effectiveness and alternatives.

Introduction

1. Please briefly describe your role(s) in the Blood Safety Program.

2. Before we begin the discussion below, please look at the output column of Table 4 in Chapter 3 (Surveillance) of the document review report and confirm the information provided, as well as provide us with any additional outputs that we may have missed during our document review. In addition, please fill in the gaps in Table 5 on resources to the extent possible.

A. Program Rationale

3. From your perspective, what kind of progress has been made towards a fully integrated Blood Surveillance System? ***Please elaborate.***

4. What is the federal government's role in a fully integrated Blood Surveillance System? Is this role appropriate?

B. Program Design, Implementation and Delivery

5. Did the Health Canada Blood Safety Program establish the necessary action plans to meet the Krever report recommendations; i.e., are the activities and operational plans established in the Accountability Framework both adequate and appropriate for meeting the Krever recommendations?
   a) If not, are there additional activities and operational plans required? ***Please elaborate.***

6. Have performance baselines been established for the operational plans and activities established in the Accountability Framework? Are outcomes used as a planning tool?

7. To what extent have the Accountability Framework's activities and operational plans been implemented and met?
   a) Are the human and financial resources outlined in the Accountability Framework sufficient for the implementation of these activities and operational plans? If not, what are the additional resources, both human and financial, required to perform and sustain them?

8. Are there any mitigating factors affecting program implementation and delivery (e.g., availability of qualified candidates, resources for training)? ***Please describe.***

9. Are there criteria for establishing priorities, in the event that operational plans and activities cannot be fully implemented? If so, what are they? Are they used on a regular basis?
   a) Are contingency plans developed and used on a regular basis to assist in meeting the Krever recommendations?

10. What progress have the surveillance activities of the HCBSP made towards:
    a) Developing linkages with public health information systems in order to strengthen public health responses to blood-borne pathogen threats (BBP) threats?
    b) Developing linkages with appropriate partner organizations so that the statistical integration of the Centre for Infectious Disease Prevention and Control (formerly the Laboratory Centre for Disease Control) databases with other external databases can be implemented; i.e., linkages with Stats Canada, provincial laboratories, hospitals, etc.?
    c) Developing analytic and response capacities within CIDPC by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action?
    d) Establishing coordinated research thrusts into new potential blood-borne threats, including prion diseases such as the human form of "mad-cow disease" known as variant Creutzfeldt-Jakob Disease or vCJD ?

11. Should the HCBSP have an emergency fund built into it in the event of a risk emergency? Why? Why not?

12. Is the HCBSP able to access external research capacity and expertise to fill the gaps in internal capacity?

C. Program Impacts and Effects

13. In your opinion, what progress has the HCBSP made towards enhancing (***Please elaborate.***):
    a) Capacity to create a blood surveillance system based on mandated post-market surveillance and CBS Database Management System?
    b) Capacity to conduct statistical analysis and risk assessment and management?
    c) Capacity to study most vulnerable populations and to conduct outbreak investigations?
    d) Capacity to provide BBP (Blood-borne Pathogen) laboratory-based epidemiological surveillance?
    e) Capacity to conduct public health investigation of emerging BBPs?
    f) Capacity to conduct surveillance and laboratory Investigation of prion diseases?
    g) Capacity to link with public health information networks?

14. From your perspective, has the HCBSP resulted in improvements to blood safety? If so, what is the nature of these improvements?

D. Cost-Effectiveness and Alternatives

15. To what extent has the HCBSP been cost-effective in meeting its objectives of protecting the Canadian public against current and emerging health threats arising from the therapeutic use of blood, tissues and organs; and, to be generally on par with blood regulatory and surveillance programs in other industrialized nations such as the UK, France and the U.S.?

16. Are the funding allocations for the HCBSP sufficient to maintain a safe blood system; i.e., do they reflect operational reality?

17. In your opinion, are there alternative mechanisms for delivering the HCBSP?

E. Other

18. Is there anything else you would like to add to the above discussion?

Review of HCBSP Interview Guide 3: External Stakeholders

Name(s): _____

Organization: _____

Position: _____

Location: _____

Time/Date of Interview: _____

Goss Gilroy Inc. has been contracted by Health Canada to conduct a Review of the Health Canada Blood Safety Program (HCBSP). As part of this review, interviews are being conducted with external stakeholder groups familiar with the activities of Health Canada's Blood Safety Program. These interviews are being complemented by parallel interviews/discussions with Program staff familiar with the regulatory and surveillance activities of the Blood Safety Program. We are seeking your views on the rationale for the program, its design, program implementation and delivery, impacts and effects, and cost-effectiveness and alternatives.

Introduction

1. Briefly describe the role of your organization in the safety of Canada's blood supply.

A. Program Rationale

2. From your perspective, has Health Canada established the necessary action plans to meet the Krever report?
   a) If not, are there additional activities and operational plans required? ***Please elaborate.***

3. From your perspective, what are the surveillance systems currently in place for Canada's blood supply? ***Please elaborate.***
   a) Are the various systems fully integrated? If so, how? If not, why?
   b) Are there gaps? What additional surveillance activities need to be in place to fully integrate the Blood Surveillance System?

4. From your perspective, what is the federal government's role in a fully integrated Blood Surveillance System? Is this role appropriate?

B. Program Design, Implementation and Delivery

5. Are there any mitigating factors affecting the implementation of a fully integrated blood surveillance system? ***Please describe.***

6. Are the regulations, policies and guidelines in place workable and/or enforceable? Why? Why not?
   a) Are there activities that affect the safety of Canada's blood supply that remain unregulated? ***Please provide details.***

7. As a stakeholder in the safety of Canada's blood supply, was your organization invited to provide input in the development of regulations, policies or guidelines? If so, what was the nature of this input?

8. From your perspective, has there been progress over the last five years towards:
   a) Enhancing the breadth of blood regulatory expertise to address emerging new blood technologies and blood substitutes?
   b) Enhancing the blood inspection/compliance function, which is expected to grow exponentially with the implementation of a separate blood system in Québec and the emergence of hospital-based and other commercial blood banks?
   c) More effective post-market surveillance, including encouragement of voluntary reporting by health practitioners?
   d) The transition to a new blood system?

9. From your perspective, has there been progress over the last five years towards:
   a) Developing linkages with public health information systems in order to strengthen public health responses to blood-borne pathogen threats (BBP) threats?
   b) Developing linkages with appropriate partner organizations so that the statistical integration of the Centre for Infectious Disease Prevention and Control (formerly the Laboratory Centre for Disease Control) databases with other external databases can be implemented; i.e., linkages with Stats Canada, provincial laboratories, hospitals, etc.?
   c) Developing analytic and response capacities within CIDPC by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action?
   d) Establishing coordinated research thrusts into new potential blood-borne threats, including prion diseases such as the human form of "mad-cow disease" known as variant Creutzfeldt-Jakob Disease or vCJD ?

C. Program Impacts and Effects

10. From your perspective, do you feel that over the last five years, the safety of Canada's blood supply has been improved? If so, in what way?
    a) What remains to be done to ensure the safety of Canada's blood supply?

D. Other

11. Is there anything else you would like to add to the above discussion?

APPENDIX D

DETAILED ACTIVITIES - REGULATORY AND SURVEILLANCE

REGULATORY

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
1. Capacity to conduct compliance and enforcement activities Responsibility of: • Inspectorate (formerly the Bureau of Compliance and Enforcement) • Centre for Biologics Evaluation (under the former Bureau of Biologics and Radiopharmaceuticals or BBR) • Medical Devices Bureau	• Conduct annual inspections of existing and proposed blood and plasma collection centres, and establishments processing, distributing and/or importing donor semen • Implementation of a full program of unannounced inspections • Conduct investigational inspections at targeted facilities • Provide regular analysis of inspection findings, as well as public reports and recommendations to industry • Expand training program to include regular refresher training, regulatory requirements of other countries • Conduct investigational inspection/site visits of manufacturers of medical devices in response to problem reports or non-compliance issues (e.g., blood bag quality problem - 1 MDB technical expert)	During the period 1998-2000: **Blood Establishments:** 39 scheduled and 22 unscheduled inspections were completed as well as 1 joint inspection by BBR/BCE of a medical device manufacturer **Blood Product Manufacturers:** on-site evaluations conducted for 5 manufacturers plus one MRA inspection of Cdn manufacturers **Semen Establishments:** carried out a national investigation of the 100 known establishments to assess compliance to the requirements of the Semen Regulations further to deficiencies brought to the attention of Health Canada, and a multiple of regional investigations **Working Groups/Advisory Ctees** on blood, xenografts, tissues, organs and semen	work progress affected by: • lengthy staffing process • lack of availability of individuals who have both blood-banking experience at a blood manufacturing scale and qualified auditing experience • changing priorities to revise the Semen Regulations, including providing advice for the revision of the guidelines on semen
2. Capacity to conduct pre-market and post-market reviews Responsibility of: • Centre for Biologics Evaluation and Centre for Biologics Research (under the former BBR) • Medical Devices Bureau • BLPA (post-market reviews)	• Provide timely access to new technologies and continued safety of the blood supply system by managing workload within reduced time frames • Review standard operating procedures from foreign collection centres or manufacturing facilities • Contribute internationally to good regulatory practice development and put in place robust systems and networks	• **NA testing of blood**. This technology lowers the window period for detection of HEP C and sets the stage for allowing multiplex molecular testing of blood[20] • Undertook a coordinated study of the drug evaluation process, resulting in recommendations and production process maps for various activities	• $s from MC-1 to do pre-market review but none from MC-2 • recruitment problems - salaries not commensurate with the private sector and staffing process too long

[20] 3.0 Analysis, Blood Regulatory Activities, May 2000

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
2. (Cont'd)		**Medical Devices Bureau:** • Medical Devices Regulations renewed (Canada Gazette II, May 27, 1998) and implemented • scientific review of info sent by mfg for a number of products for licensing, including first Investigational Testing application for blood screening assays using NAT technology for detection of HCV and HIV as well as first applications for HIV test kit for point-of-care use • post-market health hazard assessments and evaluations; e.g, toxicity of plasticizers used in blood bags • development of policies/guidelines to support these activities • currently developing regulations for Lot Release Program once product is licensed • a Mutual Recognition Agreement for non-IVDDs (in-vitro diagnostic devices) signed by Canada with Europe • build partnerships with other regulatory agencies and participate in international regulatory initiatives (such as GHTF) • Fed/Prov WG on Point of Care HIV test kits **Centre for Biologics Evaluation (BBR):** • ongoing evaluation of CBS and Héma-Québec, evaluation of info related to computer systems and evaluation of drug submissions for products derived from blood or plasma • review of license applications for implementation of safety enhancements	

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
3. Capacity to perform more effective post-market surveillance Responsibility of: • Centre for Biologics Evaluation and Centre for Biologics Research (under the former BBR) • Bureau of Licensed Product Assessment (BLPA) • MDB • Inspectorate	• Systematic analysis of blood/ fractionated products with history of acceptable quality • Monitor manufacturers' test results to find problems or to modify product specifications (BBR) • Analyze blood/blood components with additional capacity • Enhance Adverse Drug Reaction (ADR) reporting • Implement systems for collections and analysis of AE data • Link with international regulators in order to harmonize and/or compare actions • Provide regular reviews on adverse reactions, and timely feedback to health care professionals/consumers • Enhance computerized lab IMS for product analysis and establish an on-line reporting system for reporting quality issues concerning blood test kits (BBR) • Signal generation; i.e., ADR data analyses to identify safety concerns • Risk communication • Ongoing development of methodologies to enhance post-market safety	• participation of the Bureau of Licensed Product Assessment in working groups addressing safety issues related to BTO products • advice to HIV/AIDS surveillance project; processed all ADRs received related to HIV/AIDS products • performed post-approval safety assessments on blood products including albumin, SD-plasma • formed a Unit with responsibility for Blood and Blood Products (Monitoring and Evaluating Unit) • **Canadian Adverse Drug Reaction Information System (CADRIS)** - voluntary reporting in the health care sector but mandatory for manufacturers (a general database for AE for therapeutic products (incl. Blood products - does not capture transfusion AE) • Canada participates in regular 3-way video conferences with regulators from U.S. and Australia to discuss current safety-related issues of therapeutic products • Developed a BLPA strategy for post-approval monitoring of blood and blood components • Problem report mandatory for manufacturers of medical devices • Draft of Lot Release Program for Medical Devices	• staffing delays due to lack of a strategic recruitment process • delay in decision on partnership for shared Can-US AERS (Adverse Event Reporting System) database • BLPA monitors adverse reactions to blood products only (but not to whole blood) • lack of seamless communication between the divisions involved in ATR reporting • product licensing has never been fully implemented and international harmonization is critical • pre-market surveillance well established but post-market surveillance needs resources • lack of information system to support work/ lab information systems not yet implemented

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
4. Capacity to perform regulatory research related to blood safety Responsibility of: • Centre for Biologics Research (under the former BBR)	• Complete regulatory research program allowing for investigation into problem areas and identification of new standard methods • Implement regulatory research in new test/data requirements • Meet all competencies identified in the Report of the Medical, Scientific and Technical Working Ctee	• **Method Development:** Participated in international collaborative studies with the European Pharmacopoeia OMCL Network on a method for HCV screening by NAT and on methodology for analysis of Factors II, IX and X. Analyzed EPO samples from various manufacturers by a new CZE method • **Protein folding and prion disease:** Conducted studies on helix to sheet transitions as a model to understand prion formation • **Interaction of antithrombin III with fibrinolytic proteins:** Plasminogen and TPA were found to bind via their kringle domains in a competitive fasion • Continued the characterization of the genetic polymorphism identified in a CJD patient sample as part of the international CJD surveillance study • **Expression of blood proteins in Transgenic plants:** designed new constructs to express GM-CSF in rice	• unavailability of highly qualified candidates and unavailability of capital funding for instruments is impeding progress • sustainability of what is now in place
5. Capacity to conduct regulatory policy development Responsibility of: • Centre for Policy and Regulatory Affairs (under the former Bureau of Policy and Consultation or BPC) • Medical Devices Bureau (MDB)	• Review and overhaul Regulatory Framework to meet present and future needs and convey to all stakeholders • Update regulatory communications to facilitate compliance • Develop regulatory policy including extensive and timely stakeholder/consumer consultations • Ensure equivalence of Canadian policies, regulations, standards • International harmonization in place	• **Blood Regulatory Project:** work has begun on establishing a new regulatory framework for blood (will use blood standards as a basis)- currently only CBS and Héma-Québec are being regulated(i.e., no hospital-based blood bank is subject to the current regulations) - all 920 hospitals in Canada will be kept informed throughout • Expert Working Group completed first Draft Standards for Blood Safety, July 2000; Draft Standard for Blood Safety will be finalized by CSA in spring 2004 • enhanced stakeholder involvement in policy decisions related to vCJD and the blood supply	• need to look at who HC will regulate, who will bear the costs and how regulations will be enforced • staffing and human resource issues are a barrier • no systems in place to measure performance

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**

5. (Cont'd)		• Developing a regulatory framework for the safety of blood and blood components - regulatory process expected to be completed by end of 2004
		• **Xenotransplantation:**
		  • Developing a framework to evaluate the policy development process for xenotransplantation - expect to initiate the evaluation by the fall of 2002
		  • Developing a comprehensive policy recommendation for xenotransplantation (by July 2002), specifically whether or not clinical trials involving xenografts shall be allowed to proceed in Canada
		  • Implementation of the New Medical Devices Regulations - Extract Canada Gazette, Part II, May 27, 1998
		• Draft Guidelines (revised May 2001) for HIV Simple/Rapid Test Kits
		• **Cells, Tissues and Organs:**
		  1) Draft Canadian General Standard on the Safety of Cells, Tissues and Organs intended for transplantation and five subset standards for individual tissues and organ types developed by an Expert WG - will be finalized by CSA in fall 2002.
		  2) Developing a regulatory framework for cells, tissues and organs - regulatory process expected to be completed by end of 2004
		• **Semen:**
		In 1996, new regulations were developed "Processing and Distribution of Semen for Assisted Conception Regulation"
		• **Plasmaphoresis:**
		The regulatory requirements applicable to human plasma collected by plasmaphoresis are being amended	

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
6. Capacity to respond immediately to threats to the blood supply Responsibility of: • Centre for Biologics Evaluation (under the former BBR) • Centre for Policy and Regulatory Affairs (formerly BPC) • Inspectorate (formerly BCE)	• Expand the comprehensive Crisis Management Plan to 24hrs/7 days a week on a national basis • Routinely implement and test contingency plans for various problem scenarios • Manage product shortages efficiently • Assess and manage potential risks for Canada by monitoring international regulatory activities	• existing emergency response manual updated and related procedures used 3 times in the 1999-2000 fiscal year - reviews were conducted of 2 of the 3 situations • two training sessions were conducted with all teams, plus Validex exercise and simulations related to Y2K, including blood scenarios 3 policy directives to make the blood supply safer due to concerns related to vCJD • 1999 decision to defer donations from individuals with a 6-month travel history to the UK between 1980 and 1996 • August 2000 decision to defer donations from individuals who had spent time in France (exclusive of French territories outside the European continent), amounting to a period of 6 months or more between 1980 and 1996 inclusive. • August 2001 decision to defer donations from individuals who have spent 3 months or more in the UK or France since 1980, or they have spent a cumulative total of 5 years or more in Western Europe outside France and the UK since 1980, as well as from individuals who have had a blood transfusion in the UK since 1980 • **Universal leukoreduction** - est. 10,000 Canadians annually will benefit by not suffering sever immune reactions as a consequence of blood transfusions[21]	• In terms of Emergency Preparedness and Response, gaps and new requirements need to be developed

[21] 3.0 Analysis, Blood Regulatory Activities, May 2000

Table 1: Detailed Activities - Regulatory			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
7. Capacity to provide an effective communications interface between regulator and stakeholders Responsibility of: • DG's Office	• Provide education/orientation program to consumers *et al* to allow for enhanced input • Conduct regular liaison activities with stakeholders; e.g., regular meetings with consumer groups and specific disease-oriented groups • Enhance communication with regulated industry	• Held 2 meetings of the Blood Consumers' (CJD) Sounding Board • Developed strategy for increased transparency and public involvement • **Education/Orientation Program:** Developed Fact Sheets on the Therapeutic Products Program • Information kits (Centre for Policy and Regulatory Affairs) • **Xenotransplantation**: Canadians views on whether clinical trials involving xenografts should be allowed to proceed were solicited in 5 cross-Canada public consultation forums, April-Sept 2001 • Questionnaire to all hospitals, tissue banks and clinics in Canada to determine nature and level of activities they conduct as some of these activities may be regulated in the future as a result of the new regulatory frameworks being developed for Blood, Tissues and Organs	

SURVEILLANCE

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
1. Capacity to create a blood surveillance system based on a voluntary post-market surveillance system and a donor database Responsibility of: • Bureau of Infectious Diseases (BID)	**Transfusion-Transmitted Infection (TTI) Surveillance Systems in the CBS** • Develop and implement an Adverse Event Reporting System for recipients of blood/blood products in order to collect adverse events of transfusion • Compile the minimum required data elements at the national level for assessing the magnitude of risks related to transfusion • Establish a specialized surveillance system targeting those at greater risk to minimize individual and system risk (e.g., hemophiliacs, etc.)	• SET Working Group established to develop a plan and design a program for a comprehensive blood surveillance system for Canada (1999 Final Report with 13 recommendations) • Liaison Committee on National TTISS developed to facilitate development of a National TTISS • Core Working Group established to develop and implement a pilot TTIS in 4 provinces - B.C., Quebec, NS, PEI • Canadian Standardized reporting form developed • User's guide with definition of terms for reporting developed • Provincial database, developed by BBPD to facilitate reporting of AEs, implemented and currently being validated • National database developed for AE data compilation at the national level • Agreement reached with pilot provinces on the minimum dataset to be transferred to BBPD for national data analysis and risk assessment (by Feb 2002) • The Association of Hemophilia Clinic Directors of Canada (AHCDC) has received funding and is developing a surveillance system for hemophiliacs for known and emerging BBPs by establishing a secure bank of samples (plasma, DNA and RNA) • The Medical Error Reporting System for Transfusion Medicine (MERS_TM) was piloted in one hospital to capture transfusion errors and related adverse outcome and the near misses, to identifying the problems and causes of error and provide feedback to and training of relevant staff to reduce the rate of errors (Goal - to establish system in 8 hospitals.	• Not yet a national TTIS system (requires incremental funding) and lack of funding to expand MERS_TM in another 7 hospitals • Maintenance of BBP surveillance for Hemophiliacs • issue of stem cell therapy related to blood is a future need • over $400M of health care money is spent annually on bone marrow transplant patients but there is no surveillance system in place to monitor AE or clinical outcome • There is a need to develop a network of transfusion medicine in order to develop a sentinel surveillance system for AEs of transfusion

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
1. (Cont'd)	**Xenotransplantation Surveillance** • Establish standards for organ and tissue transplantation • Studies to determine how to minimize exposure to infection through tissue/organ transplantations • Use an active surveillance program in 20 of the largest transfusion/transplantation ctrs where xenotransplants occur • Establish collaborative relationships with the Canadian Society for Transplantation Medicine to enhance/coordinate current surveillance (national basis)	• Discussion paper on Xenotransplantation was prepared • Public consultation in progress by CPHA to determine public opinion vis-a-vis xenotransplantation In addition, a number of activities to address xenotransplantation surveillance are "in the works": • a framework for international surveillance is being established; and, • lab detection capacity is being developed for known and unknown pig infectious agents.[22]	• While the MC 98 identified the need for xenotransplantation surveillance, the TB requirements cited pertain to human to human transplantation (allotransplantation) not the transplantation of cells, tissues or organs from pigs to humans (xenotransplantation). In any event, no funding has been allocated to either area. • Xenotransplantation Registry and Sample Archiving
2. Capacity to conduct statistical analysis and risk assessment and management Responsibility of: • Bureau of Infectious Diseases (BID)	**Risk Assessment** • Investigate pathogens for potential risk to the blood system • Conduct risk assessments as required or requested • Update existing risk assessments on a real-time basis as dictated by changing national or international scientific indicators	• Risk assessment (RA) for blood safety and Prion diseases was carried out in 1999, 2000, and 2001, which resulted in donor deferral policies by Health Canada • Ongoing updates of literature on current information, trends and techniques • TSE Science and Policy Team advice and collaboration • Collaboration with WHO and other international orgns and health authorities	• require 2 additional epidemiologists

[22] Xenotransplantation Surveillance in Canada, Dr. M. Laderoute

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
2. (Cont'd)	• Hire a laboratory-trained risk assessment manager who can evaluate technology-based risks **Options Analysis** • Acquire expertise and human resources to participate fully in the development , assessment and evaluation of risk management policy options	• Generation of the BBP Routine Surveillance Report with support for subsequent issues • Scenario analysis of the Burden of Hep C virus including, completion of HCV modeling application software and report to policy makers and stakeholders • report on risk reduction from allogenic blood transfusion and presentation of initial (Phase 1) results	
3. Capacity to study most vulnerable populations and to conduct outbreak investigations Responsibility of: • Bureau of Infectious Diseases	• Conduct special surveys/field studies to investigate potential pathogens/unusual infectious patterns not addressed by current screening systems • Enhance the national sentinel health unit surveillance system for other BBPs by increasing the # of participating health units by 1-2 and by increasing support for more intensive lab-based investigation of cases • Prepare proposal for independent or CBS funding to conduct research among populations of highly-exposed people • Evaluation of risks of blood-borne parasitic diseases	• Outbreak investigations (Chagas, Babesiosis) • Apheresis study to determine transmission of HIV, HCV, HBV, CMV, HTLVI, HTLVD and parvovirus in highly exposed apheresis transfusion recipients • Development of a national hemophilia mutation testing program to be used in clinical management of hemophilia patients • Supported implementation of a pilot bone marrow transplantation registry to explore the feasibility of developing a national registry • Supported Canadian Bone Marrow Transplantation Group (CBMTG) to develop a business plan and funding proposal for submission to funding agencies for a long-term sustainable funding for a Cdn Bone Marrow Transplantation Registry and Clinical Trials Network • Developed a rapid response surveillance system for emerging BBPs which supported specific policies for donor screening • RA of vaccine and blood safety has been done and resulted in new regulatory policies for supply of plasma derivatives	• Continuing support of the BMTG network and national risk assessment for this high risk group

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
3. (Cont'd)		• Preliminary RA for parasites infection (malaria, babesia, Chagas) through transfusion was done. As a result, HC supported the development of a Cdn clinical/laboratory surveillance system for parasitic infections in 3 sites (Montreal, Toronto, Hamilton) • Hosted a meeting of the Blue Ribbon Committee on Blood-borne Parasitic Diseases in March 2001 (draft report and recommendations currently being reviewed by members) • Plans for a Cdn Parasitic Disease Network or CPDN (Toronto and Montreal sites) - cannot proceed until contracts signed • Surveillance for S-escape mutants of Hep C (findings presented at 2001 Conjoint Meeting of CACMID, CHICA & CIDS in Victoria Nov 4-8 (see abstract)	• lack of resources will not allow work on blood-borne parasitic diseases to continue and HC will lose capacity to conduct surveillance for these diseases
4. Capacity to provide BBP Laboratory-based epidemiological surveillance **A. Retroviruses & STD** Responsibility of: • Bureau of HIV/AIDS, STD & TB	• Develop and manage an intensive provincially-based blood borne retrovirus and STD surveillance system • Provide full technical assistance to provinces for system development and operation, implementation and support of the surveillance requirement • Provide financial start-up resources for the surveillance system and establish new and complex data linkages between national and provincial epidemiology systems that provide basic demographic and risk variables	**Integrated Surveillance Project:** Network established to address current and emerging issues: **a.** MOUs with provinces developed in place across Canada outlining details regarding responsibilities, funding, deliverables (i.e., serum samples, data, other information). (Agreement pending in Quebec, which includes no FSO achieves the same ends but is responsibe to unique Quebec requirements.) **b.** Integrated laboratory-linked surveillance system specific for HIV strain and drug resistance developed: • first-positive HIV serum submitted to the BHST lab; • linked non-nominal surveillance data obtained; • strain and drug-resistance results returned to provinces and reports developed; and • emerging retroviruses monitored. Several preliminary reports and presentations made at conferences. There is an annual EPI Update and a formal report of data is expected early 2002.	• the funding shortfalls anticipated for years 4&5 of the program (majority of the MC98 funds spent in the first three years to "scale up") will result in the initial scaling back and ultimate collapse of the system at the national level - will lose the early warning system • inability to recruit the middle level researchers due to them being unavailable • lack of linkages among the different units in the Bureau still needing improvement

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
4. (Cont'd)	• Implement a series of contracts with provinces for the development of the required infrastructure at provincial/ territorial levels and the electronic system for data transfer to the national level • Implement multiple prototypes for various retroviruses • Implement HIV strain and drug resistance monitoring	Looking at problem of Simian "foamy virus" - engaged a post doc from CIHR/CBS - found it to be transmissable to humans and looking at potential for transmission via blood transfusions and hence risk to blood supply Ongoing laboratory collaborations: • with CDCs on risk assessment of zoonotic retroviruses in blood • lab support for surveillance programs at the FDA, Mayo Clinic, Baylor University and the CDCs Atlanta for infectious risks posed by xenotransplants • provide input to the FDA's Blood Products Advisory Ctee and HC's Expert Advisory Ctee on Blood Regulations **c.** Federally-hired field surveillance officers (FSOs) now on location in B.C., Alberta, Saskatchewan, Manitoba, Ontario, the Atlantic provinces, co-supervised by the provincial public health authorities, to assist with enhanced surveillance program. FSOs in demand for outbreak investigations, presentations and international assignment. **d.** HQ support (epi, database, software, administrative) in place to support FSOs: • central database and data-transfer systems established for HIV, AIDS and STI; • software meeting specific to provincial requirements developed and placed where needed; and • ongoing upgrading and training for all program staff.	• surveillance system need for a reliable, timely, electronically-based delivery of data nearing completion • gap in surveillance data from Quebec (related to legal issues for transmission of data) or specimens addressed, but still needs work Xenotransplants: The Blood Zoonotics Unit studies the scientific side of zoonotic transplantations. There are currently no $s available for this unit - this means there will be no data available in the event that xenotransplants start in Canada Lab requires additional human resources for data management and to some extent for analysis and report writing. Requires approximately $300K annually to carry on activities.

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
4. (Cont'd)		**e.** Enhanced surveillance benefits seen: • data submitted from provinces improved in quality and completeness; • data now real time, rather than up to 3-year delay; improved local and national analyses as a result; • enhanced data linking location, risk behaviour, strain, drug resistance, co-infections and other data now starting to add to understanding, permits provinces and territories in co-operation with the federal government to mount an evidence-based response in a timely and complementary way • targeted investigations are ongoing on vulnerable populations (e.g., street youth), risk behaviour, related research; and • the U.S. and Europe looking at the Canadian blood safety and FSO surveillance strategy as the model to follow.	• need improved ability to detect situations of co-infection with other diseases and repeat infections • the need for additional field staff as new threats emerge or as new surveillance needs arise
B. Hepatitis Responsibility of: • National Microbiology Laboratory (focus on lab data) - initially had a separate system with 4-5 sites, which overlapped BBPD - now merging 2 systems to form 7-8 sites • BBPD (focus on epidemiological data)	• acquire expertise and human resources (13 PYs) in accordance with MC'98 • establish, maintain, expand and coordinate a provincial-based strain surveillance system for identification of newly acquired acute cases of HBV and HCV • ensure that currently used antibody tests are able to detect the circulating strains and that the tests are used as a tool for epidemiological investigation as a "fingerprint" of the source of the infection being transmitted.	• Human resource capacity of the lab has increased significantly by hiring 3 research scientists and one SI-1 information transfer officer • Additional lab space has been allocated to the Blood-borne Pathogens and Hepatitis Lab (BBP&H) and refitted (at the expense of $250K) to accommodate new staff members • An **enhanced sentinel surveillance system** consisting of Vancouver-Richmond, Edmonton, Calgary, Winnipeg, Ottawa-Carleton, and NB has been established for acute Hep B and C • A meeting of the Expert Working Group for Strain and Laboratory Surveillance of HBV and HCV comprised of 50 participants from the Advisory Committee on Epidemiology, the PPHL, Héma-Québec, LCDC, and the US Centres for Disease Control and Prevention (CDC) was organized and convened by BBP&H at NML in Winnipeg. A summary report and recommendations on the surveillance of HBV and HCV was published in CCDR, vol. 25-20, 1999	Implementation of Blood '98 was somewhat delayed by the move of the lab to Winnipeg in 1998; 2 PYs were hired in 2001 and final staffing (1 RES) will be accomplished in 2002 New funding required for the balance of $365K per year to operate the 4 hospital-based surveillance centres Develop programs for monitoring cellular immune response of acute and chronic HB and HC patients.

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
4. (Cont'd) **B. Hepatitis**		• Testing new kits for their performance; e.g., evaluating the InnoLipa HBV drug resistance kit against in-house methods of detection; investigating the reliability of the InnoLipa HCV II for genotyping • Initially 4 Provincial Public Health Labs (PPHL) joined the lab surveillance program for HBV and HVC (Nfld, B.C., N.S. and Sask) in 1999-2000. In 2000-01, Alta and Manitoba started their participation in the lab surveillance program • A specialized database software developed by a private firm and further updated by Operations & Application Support Section - ITMD/PPHB. The software allows electronic transmission of data between PPHL and BBP&H, NML • To consolidate resources and streamline the enhanced surveillance for HBV and HCV with CABBI at CIDPC, a number of steps were taken to integrate the 2 surveillance systems into one comprehensive national surveillance program, including modification of the software database and running a pilot merger of the two systems in Alberta in 2001	PPHL in Newfoundland could not continue its participation in the surveillance program as local health legislation limited access to collection of certain epidemiological data
C. DNA Sequencing Responsibility of: • National Microbiology Laboratory	• Monitor, identify and characterize at the molecular level, mutant strains of HBV, which may pose a threat to the blood supply and may be able to overcome existing active immune prophylaxis programs • Alert CIDPC, Provincial Public Health Labs (PPHL) and CBS to significant HBV mutant strains and shifts of HCV genotypes	• An automated sequencer "LiCor" has been purchased to create a sequence database of HBV and HCV strains currently circulating in the Canadian population • HBV genotyping and mutant detection systems have been developed to identify and characterize at the molecule level mutant strains of HBV • Sequence database of HBV genotypes has been established	• if $s go down, will not be able to attract world-class expertise
4. (Cont'd) **C. DNA Sequencing**	• Provide lab support to CIDPC and PPHL for outbreak investigation and definitive molecular epidemiological analysis ("fingerprinting") of the source of infection		

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
5. Capacity to conduct public health investigation of emerging BBPs Responsibility of: • BBPD	**Emerging Pathogens:** • Develop laboratory methods for the detection of all emerging BBPs • Provide laboratory services to all P/T health laboratories for emerging BBPs • Develop tests for the detection of potential BBPs such as the Borna disease virus, HHV8 (Human Herpes Virus 8), Parvo Virus B19 and CMV (cytomegalovirus - older pathogen but new issues; i.e., harmful on immunosuppressed individuals)	• Tech-transfer of know-how and reagents plus training of a BBP&H staff in CDC, Atlanta for HHV-8 and parvovirus diagnostics was accomplished in 2000. Currently BBP&H has the expertise and the capacity to provide services for potential BBPs • Between 1999-2001, several potential blood-borne agents emerged; e.g., TTV, TLMV and SEN-V, and BBP&H was in a position to rapidly develop diagnostic assays, complete preliminary testing and, as a result, establish that these agents, even though transmitted parenterally, do not pose a threat the blood supply and the health of Canadians • BBP&H is participating in the development by CABBI, CIDPC of a **Rapid Response Surveillance System (RRSS)** for new and emerging BBPs: 2 broad categories of information: i) representative of general population through informed consent at clinics and ii) members of special groups; i.e., transplant recipients, hemophiliacs, etc. This system is being piloted in Ontario with 1000-2000 participating physicians and groups such as the Association of Hemophiliac Physicians and the Vancouver Transplant Centre - developing a database with a healthy population to identify future threats (as identified by the special groups) • working to organize cohorts of people to obtain blood samples quickly and ask permission to test for new viruses (cannot legally do this with existing samples of blood)	
6. Capacity to conduct surveillance and laboratory investigation of prion diseases A. **Epidemiology and Surveillance** Responsibility of: • Bureau of Infectious Diseases	• Expand current CJD surveillance system, with increased activities targeting cases in advance of death and cases from uncommon populations such as young Canadians or Alzheimer's patients • Collaborate with international teams initiating certain key investigations in Canada	Development and maintenance of a national surveillance system for CJD in the adult and pediatric populations (CJD-SS), including variant CJD (vCJD): • 107 definite cases of classical CJD or cCJD from 258 referrals, as of Oct 1, 2001. Incidence of 0.9 cases per million population per year in 1999 and 2000, consistent with incidence world-wide (0.5 to 1 case per million population per year) • 5 cases of familial/inherited CJD, 3 cases of iatrogenic CJD (dura mater graft). No cases of vCJD reported • proportion of autopsies >70%	CJD-SS staff not fully staffed: senior epidemiologist (ES-05) required for comprehensive data analysis and scientific publications, but not yet recruited Enhanced consultation services to physicians who consult HC on cCJD/vCJD cases Enhanced genetic research and counselling services for familial/ inherited CJD

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
6 (cont'd)	• Conduct multiple studies on CJD; evaluate newly-discovered blood tests; and act as a proving ground for some tests like those for BSE • Selectively participate in ground-breaking studies for diagnostic and screening tests on an equal basis with the international scientific community	• development of the ability to respond to potential outbreak or urgent situation (e.g., draft protocols for investigation of suspected vCJD cases) • links with Provincial/Territorial Health Authorities, Health Care Institutions and Health Care Professionals. Collaboration with the University of Toronto (CNRD). International collaboration on CJD surveillance (UK, Euro-CJD, WHO), which includes data exchange on CJD in high risk populations • CJD surveillance in Hemophiliacs is also done under Transfusion Transmitted Injuries Surveillance System (TTISS) • Surveillance reports, periodic newsletters, scientific presentations • Surveillance for Progressive Intellectual and Neurological Deterioration (PIND) in the Canadian Pediatric Population was conducted and completed in 1999-2000, and provided supportive evidence for the complete ascertainment of CJD cases by the CJD-SS in childhood and adolescence. Pediatric surveillance for CJD is now integrated into the national CJD surveillance system. • CJD has become a disease under national surveillance, effective January 1, 2000; i.e., practising physicians are required to report each case of CJD to their P/T Health Authorities Setting up an advisory committee on CJD to look at future direction of CJD research and surveillance in Canada (to start March 2002) Contribution to the development of a blood test for CJD: Hamster WBC Evaluation Project - Contract for Flow Cytometric Services ($10,000 in 2001) Active participation in TSEs Science Team and TSEs Science Sub-group: Blood and Vaccines	Completion and testing (e.g., exercise) of protocols for investigation of suspected vCJD cases Targeted research on CJD cases and enhanced collaboration with international teams for initiating certain key investigations in Canada (e.g., vulnerable/at risk populations for cCJD/vCJD) Reporting CJD is not mandatory in all Provinces/Territories Ongoing contribution to risk assessment and risk management for prion diseases (e.g., risk of transmission of vCJD through surgical/invasive instruments)

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
6. (Cont'd)	**Tanz Neuroscience, Neuropathology and Prion Diagnostic Research Centre (TNNPDRC)** • Maintain neuropathology diagnostic reference centre once fully developed • Implement new diagnostic tests following internal/national validation and develop the national capacity to pioneer new diagnostic or screening tests	Contribution to risk assessment and risk management for prion diseases (e.g., vCJD and the blood supply) Contribution to Infection Control Guidelines for classical CJD Response to inquiries from the public, health care community, government officials and the media Health Canada, through the CJD-SS, has ongoing contracts for CJD surveillance and diagnosis (total of approx. $470K/year) • Neuropathology, immunohistochemistry, and genetic diagnostic and consultation services, including brain tissue bank activities (Prions Laboratory, University of Toronto). In close collaboration with the National Laboratory for Host Genetics and Prion Diseases (e.g., providing blood for DNA analysis) (see 6.B). Quality control for standardization of lab procedures was done • In 1999, an immunoassay of 14-3-3 protein in the cerebrospinal fluid (CSF) was set up at the Centre for Research in Neurodegenerative Diseases (CRND), University of Toronto to assist in the diagnosis of CJD. The CRND is currently the only facility in Canada which can perform analysis of 14-3-3 protein in CSF	Ongoing contribution to the development/update of cCJD/vCJD Infection Control Guidelines Targeted research on TSE: Prevalence of prion protein in tonsil and appendix tissues of the Canadian population Development and validation of new diagnostic/detection methods for CJD, in collaboration with the National Laboratory for Host Genetics and Prion Diseases (see 6.B)
	• Conduct investigations on Alzheimer's disease and related disorders • Provide essential scientific core expertise in support of future/on-going regulatory considerations	Ongoing clinical and histological investigations on CJD and differentiation from other causes of dementia (e.g., Alzheimer's disease, Lewy Body Disease, etc.) Ongoing development of expertise with the objective of enhancing the clinical application of basic science related to prions Ongoing work on the development of the national capacity to pioneer new diagnostic or screening tests	

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
6. (Cont'd) **B. Winnipeg Human and Animal Prion Reference Laboratory** Responsibility of: • National Microbiology Laboratory (National Laboratory for Host Genetics and Prion Diseases)	• Provide full reference service for genetic diagnostics • Expand genetic testing to include provincial/ territorial requests for family testing • Develop and implement methods for population diagnostics (i.e., screening tests), as developed at TNNPDRC (Tanz Neuroscience, Neuropathy and Prion Diagnostic Research Centre) and internationally • Develop an animal research capacity to investigate the prion diseases of animals in Canada (Scrapie, BSE and chronic wasting disease of deer) to better appreciate the risk of animal-to-animal disease transmission and ultimately the risk to humans • Develop and implement animal diagnostic or screening tests for prion diseases to enhance food, biologic and cosmetics safety • Increase investigations related to transmission of prion diseases through iatrogenic routes such as neurosurgical instruments using animal models	• lab created *de novo* in Winnipeg in late 1998, • now approximately half-way equipped, staffed (10 FTEs) • This took an unexpectedly long time, delaying implementation • ongoing provision of advanced human molecular genetic diagnostics to support Canadian CJD Surveillance System (80 diagnostic reports delivered to date) • scientific research programs established on prion disease mechanisms and prion stain variation • discovery of novel human mutations associated with prion disease • program priorities and long-term plan established • national and international research collaborations established • expert scientific and technical advice to support risk assessment and risk management for prion disease	• major segments of program remain essentially undeveloped: (i) development and implementation of new diagnostic and screening tests for preclinical prion diseases, especially to screen the Canadian blood supply; (ii) support for intensified surveillance as necessitated by implementation of screening tests; (iii) research and validation studies on process safety (e.g., clearance of prion infectivity during plasma fractionation; prion removal and inactivation in hospital infection control practice) (iv) capacity to perform bioassays to detect, quantify and characterize prion infectivity; and (v) epidemiological research on human and animal prion diseases. • these activities require improved co-ordination and collaboration with other agencies (e.g., Canadian Food Inspection Agency; academic researchers; Canadian Blood Services; Health Canada regulation and policy workers) • NML's National Laboratory for Prion Diseases is currently the **only** Health Canada laboratory equipped to work with infective prion agents, and one of only a small number in North America; this is likely to remain so in the foreseeable future.

Table 2: Detailed Activities - Surveillance			
Increased Capacity to Deliver Programs to Meet Long Term Objectives	**Actions to Respond to the Capacity Requirements**	**Outputs to Date**	**Gaps/ New Requirements**
6. (Cont'd)			• newly recognized urgency of requirement for blood-screening test as a result of: (i) ongoing epidemic of variant Creutzfeldt-Jakob disease in UK and France; (ii) potentially global occurrence of bovine spongiform encephalopathy (BSE); (iii) possible spread of BSE to sheep; (iv) unknown risks of novel prion disease of deer and elk (CWD) to domestic livestock and humans; (v) increasing evidence suggesting transmissibility of vCJD through peripheral tissues and blood. • without sufficient funding, the surveillance program may have to be terminated
7. Capacity to link with public health networks Responsibility of: • National Microbiology Laboratory	• Develop information network to provide useful laboratory information about BBPs in a timely fashion to provincial public health laboratories, epidemiologist, CBS and regulators	• BBP&H is actively participating in the establishment of the Canadian Viral Hepatitis Network (CVHN) to share valuable information on acute HBV and HCV infection - a hospital/clinic-based surveillance system has been established in 4 centres (Winnipeg, Toronto, Calgary and Ottawa) • Start-up resources to establish linkages between the PPHL participating in the enhanced surveillance for HBV and HCV were provided by BBP&H at NML to facilitate electronic information transfer	

APPENDIX E

ACCOUNTABILITY FRAMEWORK

ACCOUNTABILITY FRAMEWORK

Strengthening Health Canada's Blood Regulatory and Surveillance Programs

With the additional A-base funds of $125 million, Health Canada will strengthen its blood regulatory and surveillance programs in order to achieve the following two critical objectives:

- To be on a par, in general, with blood regulatory and surveillance programs in other leading industrialized nations, such as the UK, Australia and Germany; and

- To protect Canadians against current and emerging health threats arising from the therapeutic use of blood, tissues and organs.

In support of the above two critical objectives, the following pages outline, for the blood regulatory and surveillance programs, their general goals, the increased capacities in program delivery, the planned actions/results and resources required to deliver these programs. Brief justifications of the resources are included for each increased capacity.

Linkages of increased capacities or requirements are identified to the appropriate general goals for the blood regulatory and surveillance programs on pages 2 and 12.

The resource distribution to increase capacities will vary between issues and from year to year based on existing and emerging priorities.

Blood Regulatory Program

For the blood regulatory program, the following general goals have been established:

- Enhance the breadth of blood regulatory expertise to address emerging new blood technologies and blood substitutes *(Reqmts 4 and 6)*;
- Enhance the blood inspection/compliance function, which is expected to grow exponentially with the implementation of a separate blood system in Quebec and the emergence of hospital-based and other commercial blood banks *(Reqmts 1 and 7)*;
- Perform more effective post-market surveillance, including encouragement of voluntary reporting by health practitioners *(Reqmts 2 and 3)* ; and
- Support transition to new blood system *(Reqmt 5)*.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #1: **Capacity to Conduct Compliance and Enforcement Inspections** <u>Rationale:</u> Hospitals currently manufacturing blood and blood components, new sites in the proposed separate Quebec blood supply system, tissue and organ facilities and semen collection centres must be inspected to ensure compliance with appropriate regulations, thereby assuring safety. <u>Resource Requirements ($M):</u> FY 1998-99: 7 FTEs, $ 1.192 FY 1999-00: 20 FTEs, $ 2.586 FY 2000-01: 22 FTEs, $ 3.329 FY 2001-02: 22 FTEs, $ 2.960 FY 2002-03: 22 FTEs, $ 2.842	• **Annual Inspections** - Inspect existing and proposed collection centres, major hospital centres, tissue and organ transplant facilities, and semen collection/storage establishments. • **Surprise Inspections** - Implement full program of unannounced or "surprise" inspections. • **Investigational Inspections** - Conduct investigations targeted to specific types facilities. • **ISO Inspections** - Inspect/audit against ISO-9000 standards. • **Inspection Analysis** - Provide regular analysis of inspection findings; - Provide public reports and recommendations to industry. • **Training Program** - Expanded to include regular refresher training, regulatory requirements of other countries, and ISO-9000 requirements.	It is forecasted that there will be over 150 blood collection/processing centres in Canada that will need inspection. On inspection, one inspector for every five centres is required (an inspection takes approximately three weeks from preparation, inspection, and report and follow-up thereafter). These inspections will be conducted in such areas as infertility clinics using donor assisted conception, hospital blood banks, tissue and organ transplantation centres, new blood establishments, and new kit manufacturers. Some examples of typical workload increases due to changes include: - hospital blood banks have become manufacturers, with approx. 60 to 120 sites which have not previously been regulated under the *Food and Drugs Act*. - Donor assisted conception and tissue organ transplantation will add approximately 100 more sites to be inspected; - Private operators of blood banks are expected to grow from 2 to 10; - Even though the 17 Canadian Red Cross blood centres will disappear, these will be replaced by some 60 to 100 community-based centres across Canada, run privately which will require inspection; - As Canada imports most of its plasma from foreign countries, inspections of well established blood collection centres and manufacturing facilities will have to be made; and - Continual training of inspection teams to learn how to audit to new standards, practices, International Standards Organization (ISO 9000) and other jurisdictional regulatory practices.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #2: **Capacity to Conduct Pre-market and Post-market Reviews** Resource Requirements ($M): FY 1998-99: 7 FTEs, $ 1.003 FY 1999-00: 14 FTEs, $ 2.222 FY 2000-01: 17 FTEs, $ 3.063 FY 2001-02: 17 FTEs, $ 2.922 FY 2002-03: 17 FTEs, $ 2.794	• **Performance** - Provide timely access to new technologies and continued safety of the blood supply system by managing workload within reduced time frames. • **Foreign Review** - Review standard operating procedures from foreign collection centres or manufacturing facilities. • **International Information** - Contribute internationally to good regulatory practice development; put in place robust systems and networks.	This involves the licence issuing function of the regulatory program. The staff will be involved with the pre-and post-review of sites to ensure that the facilities and operation of blood product manufacturers, semen collection and storage and tissue and organ transplantation centres including hospitals meet Good Manufacturing Practices requirements. This includes assessment of site operating procedures, product information and test kits used to screen donors for infectious diseases. For example, an estimated growth of approx 60 new hospitals manufacturing blood and blood components must be reviewed and licensed. The new Product Licensing Framework under development would require periodic re-evaluation of the safety, quality and effectiveness of products currently available in Canada. More private blood centres (expected growth from 2 to 10) are likely to open. Transition to more than 100 new blood centres and a separate blood supply system for Quebec will create substantial increases in workload. Pre-market assessment of “in vitro” diagnostic test kits used to screen blood for infectious agents will increase dramatically as many manufacturers are now combining several test kits into one thereby increasing the time for its assessment; in such cases, turnaround time for assessments will have to be reduced as assessment reports are of great importance to manufacturers.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #3: **Capacity to Perform more Effective Post-market Surveillance** <u>Rationale:</u> More active post-market surveillance programs will allow the regulator to develop information on risks, to take action to minimize these risks, and to provide this information to concerned Canadians. This includes laboratory based analysis of blood and blood products, as well as monitoring adverse events resulting from the use of those products <u>Resource Requirements ($M):</u> FY 1998-99: 7 FTEs, $ .971 FY 1999-00: 7 FTEs, $ 1.512 FY 2000-01: 9 FTEs, $ 2.093 FY 2001-02: 9 FTEs, $ 1.970 FY 2002-03: 9 FTEs, $ 1.842	• **Laboratory Analysis** - Analyze fractionated products with history of acceptable quality on a systematic basis to ensure continued quality and safety; - Monitor manufacturers' test results to find problems or to suggest modifications to product specifications; - Analyze blood or blood components with additional capacity to analyze blood and blood components in place. • **Adverse Drug Reactions (ADR)** - Encourage proactive ADR reporting; - Encourage proactive quick action by medical personnel in place on reports of adverse events; - Implement systems and networks for collection and analysis.	New staff will endeavour to encourage voluntary reporting of adverse reactions to drugs, blood and blood products and related products used by health care professionals, consumers, hospitals, etc. Staff will be responsible for monitoring and assessing ADR reports, conducting investigations to identify potential adverse outcomes, recommending solutions, and seeking information from other sources as well as communicating findings to the professional community. Laboratory information management systems (IMS) will be implemented to help monitor occurrences, provide linkages to other sources of information and provide access to federal, provincial and public health users and become a useful tool in risk management. Laboratory analysis will be conducted to ensure products meet specifications and are of acceptable quality.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #3: (contd.)	• **International Linkages** - Link internationally to other similar systems, with ability to compare Canadian situation to that in other countries. • **External Interface** - Provide regular public reports on adverse reactions; - Provide advice to health care professionals and consumers. • **IMS** - Enhance computerized laboratory IMS for product analysis; - Establish an on-line reporting system for reporting quality issues concerning blood test kits.	
REQUIREMENT #4: **Capacity to Perform Regulatory Research Related to Blood Safety** <u>Rationale:</u> The research program supports the independence of the regulator and its ability to reach decisions separately from those of the manufacturer, as was recommended by Justice Krever. <u>Resource Requirements ($M):</u> FY 1998-99: 2.3 FTEs, $ .819 FY 1999-00: 7 FTEs, $ 1.374 FY 2000-01: 9 FTEs, $ 1.586 FY 2001-02: 9 FTEs, $ 1.638 FY 2002-03: 9 FTEs, $ 1.554	• **Research Capacity** - Complete regulatory research program allowing for investigation into problem areas and identification of new standard methods; - Implement regulatory research in new test requirements or new data requirements to ensure safety to the blood supply. • **Required Competencies** - Meet all competencies identified in the Report of the Medical, Scientific and Technical Working Committee, which was commissioned by the F/P/T Initiative on Blood System Governance.	Research activities must be in support of safety, quality and efficacy assessments of new types of products, assessments of new types of therapeutic approaches to medical treatment and benefit/risk analysis. TPP must build credibility through research and information gathering and analysis to be able to contribute at par to a fair exchange of knowledge with other international groups. New resources will be used to conduct regulatory research in new emerging areas such as gene therapy; biotechnology-engineered blood substitutes; and participating in international collaborative initiatives to develop harmonized standards. Currently, these regulatory research requirements are not addressed in research conducted outside of government, in Canada or in other countries.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT: #5: **Capacity to Conduct Regulatory Policy Development**. <u>Rationale:</u> Public demand for "zero" risk associated with the blood supply has created the need for a regulatory approach that must be responsive and flexible, and includes extensive consultation. Justice Krever has recommended total revision of the regulatory framework for blood and related products, with removal of outdated regulations on a periodic basis. <u>Resource Requirements ($M):</u> FY 1998-99: 7 FTEs, $1.077 FY 1999-00: 9 FTEs, $1.344 FY 2000-01:10 FTEs, $1.604 FY 2001-02:10 FTEs, $1.662 FY 2002-03:10 FTEs, $1.569	• **Regulatory Framework** - Review and overhaul to meet present and future needs and explain to all stakeholders. • **Regulatory Communications** - Update regularly notices, bulletins, guidelines, etc., to facilitate regulatory compliance. • **Stakeholder Involvement** - Develop regulatory policy including extensive and timely consultations with all stakeholders and consumers. • **National/International Liaison** - Ensure equivalence of Canadian policies, regulations, standards; - International harmonization in place and actively pursued by participating on national/international committees, projects, policy meetings.	Through the use of a standards-based regulatory framework, resources will be used to ensure that National Safety Standards for blood and related products become part of the Regulations. The framework is composed of five phases leading to the establishment of these Standards. - organizing fora or conferences on emerging issues to seek feedback from experts and stakeholders; - developing templates, guidelines, or safety standards for blood or transplantation as working examples; - guiding and building consensus through collaborative discussions and information exchange with practitioners, manufacturers, provincial health departments, other countries etc., in order to move from a template to draft standards; - obtaining accreditation of these safety standards as National Standards, and finally, - making these National Standards part of the Regulations.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #6: **Capacity to Respond Immediately to Threats to the Blood Supply** Rationale: Public demand for "zero" risk associated with the blood supply has created the need for a regulatory approach that must be responsive and flexible, and includes extensive consultation. Resource Requirements ($M): FY 1998-99: - FTE, $ .108 FY 1999-00: 2 FTEs, $ .425 FY 2000-01: 3 FTEs, $ .745 FY 2001-02: 3 FTEs, $ .554 FY 2002-03: 3 FTEs, $ .522	• **Crisis Management Planning** - Expand the comprehensive crisis management plan to 24 hours a day/7 days a week on a national basis. • **Contingency Planning** - Implement and test routinely contingency plans for various problem scenarios; - Efficiently manage product shortages while ensuring that additional risks are kept to an absolute minimum. • **International Monitoring** - Assess and manage potential risks for Canada by monitoring international regulatory activities.	The Department has developed a national crisis/emergency plan to deal with real and potential emergency or crisis situations. This plan utilizes the plans and procedures developed by Emergency Preparedness Canada. Resources will be tasked in developing various emergency/crisis scenarios in order to facilitate the decision making process, reduce risks and identify players. It is anticipated that scenarios will be developed for 5 high probability priority emergency situations. For example, during last winter's Ice Storm disaster if several major pre-written disaster scenarios had existed, they would have assisted and guided people involved in dealing with, for example, the availability, movement and safety assurance of blood and blood products and control of diseases. Contingency plans need to be developed with potential users, agreed upon, communicated and regularly updated for emergency situations such as product shortages, test failures, disease transmission situations. There is an eventual link with those scenarios established by Emergency Preparedness Canada.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #7: **Capacity to Provide an Effective Communications Interface between Regulator and Stakeholders** Rationale: The regulatory program must respond to the demands of consumer-based organizations and other stakeholder groups to provide more information, and to become more proactive. Actions must be explained in order for stakeholders to begin to trust the regulator and to accept its decisions. Resource Requirements ($M): FY 1998-99: 1 FTE, $ .432 FY 1999-00: 3 FTEs, $ 1.009 FY 2000-01: 4 FTEs, $ 1.117 FY 2001-02: 4 FTEs, $ 1.187 FY 2002-03: 4 FTEs, $ 1.091	• **Education/Orientation Program** - Provide to consumers and others to allow for enhanced input. • **Stakeholder Liaison** - Dedicate resources and use appropriate communication vehicles; - Enhance two-way communication with all stakeholders; - Provide information on an ongoing basis; - Conduct regular meetings with consumer and specific disease-oriented groups; - Enhance communication with regulated industry.	The Krever Commission clearly expressed that the public, consumer groups and other stakeholders are demanding more consultation and a voice on issues relating to the safety of the blood system and related blood/blood products. In response, these new resources: - will undertake extensive consultations (estimated at 10 to 15 per year) with consumers and other groups concerning such subjects as emerging threats to the blood supply (e.g., CJD); - will receive, provide and exchange information during policy development and participate in an advisory capacity. Training in such areas as communication skills, facilitation, media relations etc. will be given.

Blood Surveillance Program

For blood surveillance activities, the following goals have been established: (individual goals are supported by the appropriate requirements as noted)

- Develop linkages with public health information systems in order to strengthen public health responses to blood-borne pathogen (BBP) threats; *(Reqmts 1 and 7)*
- Develop linkages with appropriate partner organizations so that the statistical integration of Laboratory Centre for Disease Control (LCDC) databases with other external databases can be implemented (linkages with Stats Canada, provincial laboratories, hospitals etc) *(Reqmts 1 and 4)*;
- Develop analytic and response capacities within LCDC by acquiring the professional staffing resources for statistical analysis, policy development and appropriate follow-up action *(Reqmts 2 and, 6)*; and
- Establish coordinated research thrusts into new potential blood-borne threats, including prion diseases such as the human form of "mad-cow disease" known as Variant Creutzfeldt-Jakob Disease (VCJD) *(Reqmts 3, 4, 5 and 6)*.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #1: **Capacity to Create a Blood Surveillance System Based on Mandated Post-market Surveillance and CBS Database Management System** <u>Rationale:</u> The final report of the Krever Commission has emphasized the need for enhanced national and international surveillance. The infrastructure created in the regulatory proposal will be designed, adapted and supported by surveillance experts in LCDC. Transfusion-transmitted infection risk derives from the risk present in the community and hence surveillance activities must be based in the community. Since provincial surveillance data form the basis for all national estimates, a shift in the current surveillance paradigm will require a considerable investment to reorient provincial/territorial surveillance systems. Through a F/P/T partnership, both federal and provincial resources will be required to bring about an enhanced capacity for HIV surveillance and for encouraging the investigation of BBPs. Epidemiologic investigations must include the development of routine surveillance systems, the analysis of that data and the publication of results of that analysis in a timely fashion and within a HPB risk management framework, in close	• **Transfusion - Transmitted Infection (TTI) Surveillance Systems in the CBS** - Expand the TTI surveillance system to include an additional 10 high volume centres - Establish a specialized surveillance system targeting those at greatest risk so as to minimize individual and system risk (e.g., hemophiliacs, etc.). • **Public Health Infrastructure** - Establish and coordinate surveillance for BBPs in provinces to ensure blood transfusion safety and investigate community-based risk for BBPs; - Alert transfusion centres to important shifts in BBPs patterns within the community, allowing transfusion centres to change donor screening criteria.	About 1 million people donate blood each year; about 600,000 people receive transfusions each year. Over the next five years, a provincial/regional surveillance information network and supporting system will be established to collect information from sites on how much blood is transfused and on how many illnesses resulted from blood transfusion. While there are over 900 hospitals in Canada that use blood/blood products, only about 20 of them will require staff to do the data collection. About 20 sites will be specifically designated as centres for excellence and will require their own full time staff to collect daily information in the hospital about blood transfusions, about the health of the recipients (recorded in computers). Analyses will be conducted at central coordinating sites in each province/region and statistics will be collated at a provincial/regional level and used to determine the true safety of the blood system. This information will be fed into a national centre. The national centre will collect all the provincial/regional data and provide information on the safety of blood in Canada. The national centre's additional federal staff will be expert in epidemiology, informatics and in policy development. They will analyse the data on a quarterly to semi-annual basis. Staff in the transfusion sites and in the national site will work together on investigations, some of which will require the collection of information from other data sources such as death records

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #1: (Contd) collaboration with the surveillance framework established and operated by the regulator and by the CBS. Surveillance and risk assessment activities for blood should be extended to include all activities within the xenotransplantation and organ/tissue domain (blood is a tissue). <u>Resource Requirements ($M):</u> FY 1998-99: 2 FTEs, $ 1.119 FY 1999-00: 4 FTEs, $ 2.344 FY 2000-01: 5 FTEs, $ 2.714 FY 2001-02: 5 FTEs, $ 2.594 FY 2002-03: 5 FTEs, $ 2.749	• **Xenotransplantation Surveillance** - Establish standards for organ and tissue transplantation and act as a consultant on risk; - Design studies to determine how to minimize exposure to infection through tissue or organ transplantations; - Use an active surveillance program in 20 of the largest transfusion/ transplantation centres where xenotransplants occur; - Establish collaborative relationships with the Canadian Institute for Health Information and the Canadian Society for Transplantation Medicine to enhance and coordinate current surveillance (national basis).	or hospital admission records.The surveillance system will detect outbreaks of new diseases by reviewing for new disease patterns on an ongoing basis. The surveillance system will be used to investigate high risk problems such as newly discovered diseases or those which are newly discovered to be transmissible by blood. The new federal staff will design special studies about new disease problems. Approximately 5-6 new studies will be undertaken each year. These studies will require weeks to months of effort. Xenotransplantation surveillance systems will answer the question "will humans become infected with serious diseases if they receive transplantations from animals ". This surveillance system requires a staff member to liaise with the regulatory authority to conduct studies which involve the identification of all recipients and the collection of all relevant information in approved formats (this requires several days of work per recipient); to attend meetings with the principle investigators to monitor the health outcomes and possibly conduct field interviews with recipients; and to gather the newest information about the health risk of xenotransplantation and to make this information available to responsible authorities as well as to the public.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #2: **Capacity to Conduct Statistical Analysis and Risk Assessment and Management** <u>Rationale:</u> Within a risk management framework, detailed analysis (risk assessment) must be conducted on all procedural changes, on unusual adverse reactions or suggested emerging pathogens. To facilitate appropriate responses by the CBS and/or BBR, these analyses must be completed in a comprehensive and timely fashion. Any additional emergency field investigations in conjunction with the risk analyses will form the scientific basis for all risk management within the new blood system. <u>Resource Requirements ($M):</u> FY 1998-99: - FTE, $ .261 FY 1999-00: 2 FTEs, $ .755 FY 2000-01: 3 FTEs, $ .765 FY 2001-02: 3 FTEs, $ .758 FY 2002-03: 3 FTEs, $ .682	• **Risk Assessment** - Investigate pathogens for potential risk to the blood system; - Conduct risk assessments as required or requested; - Update existing risk assessments on a real-time basis as dictated by changing national or international scientific indicators; - Hire a laboratory- trained risk assessment manager who can evaluate technology-based risks. • **Options Analysis** - Acquire expertise and human resources to participate fully in the development, assessment and evaluation of risk management policy options.	Risk assessments will answer the question "is this product causing illness or death among humans who use or receive it?" To conduct a risk assessment, staff must review all relevant literature, varying from several hundred articles to a very small number. This literature review must be written in accepted format, requiring several months. If there is little in the formal literature, staff must conduct comprehensive interviews with recognized experts in the field. This information must be amended with more recent information available only through site visits and conference attendance. These results must be reviewed by external authorities and amended, often requiring several weeks of additional work. They must then be made available to policy makers for their review. It is anticipated that between 4 and 6 risk assessments will be conducted per annum and that each risk assessment will take from 2 to 6 months. Policy development for harm avoidance is usually done by a team, involving staff from other parts of the organization, participation in inter-agency groups, etc. These policies must be supported at senior level meetings and hence several weeks of work can follow for a senior staff member. To be fully updated on the potentially harmful products made from blood, staff must be aware of all the most important international developments and must become knowledgeable by attending meetings and conferences, as well as by attending multi-lateral meetings with their partners such as the regulatory authority, the Canadian Blood Services, etc.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #3: **Capacity to Study most Vulnerable Populations and to Conduct Outbreak Investigations** Rationale: Some populations (hemophiliacs, thalassemics, persons living with cancer or HIV infection) are very vulnerable to transfusion-transmitted infections and they warrant special studies. Following these populations over time is resource intensive and expensive. Additionally, rapid deployment of staff and epidemiologic intelligence are the cornerstones of outbreak investigation. In the event of the identification of unexpected outcomes, LCDC must be able to deploy trained personnel with expertise in identification and control of blood-borne disease outbreaks. Resource Requirements ($M): FY 1998-99: -- FTE, $ .238 FY 1999-00: 1 FTE, $ .762 FY 2000-01: 1 FTE, $ .785 FY 2001-02: 1 FTE, $ .703 FY 2002-03: 1 FTE, $ .703	- Conduct special surveys and field studies to investigate potential pathogens or unusual infectious patterns not addressed by the current screening system; - Enhance the national sentinel health unit surveillance system for other blood-borne pathogens by increasing the number of participating health units by 1-2 and by increasing the support for more intensive laboratory-based investigation of cases; - Prepare proposal for independent or CBS funding to conduct research among populations of highly-exposed people (these studies will ensure their safety and provide information about new pathogens before they might appear in the general transfused populations).	Some populations, such as haemophiliacs, will be identified and studied to determine the frequency of certain diseases which may be caused by blood and to determine if blood exposure caused their illnesses. To do this, an epidemiologist will coordinate the writing of a protocol for each at-risk population, which may take several months. They will have to collect information on each case which requires the review of medical records, the collection of laboratory information and the creation of data sets for analysis. The analysis may require the input of several epidemiologists and clinicians, including public health departments and blood centres. The cause of outbreaks will be identified and rectified through field work and interviews (investigations) with all involved persons. This may take several weeks to several months depending on the number of people involved and the geographic area. If it is essential that an outbreak be investigated more quickly, more than one person will have to go to the field. For example, during FY 98/99, LCDC investigated putative outbreaks or unusual cases four times.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #4: **Capacity to Provide BBP Laboratory-based Epidemiological Surveillance** Rationale: There is currently in Canada no capacity to undertake intensified, laboratory-based surveillance for HBV, HCV, HGV, HTLV 1/11, Herpes simplex virus, human papilloma virus, among other STD. These infectious diseases are all diagnosed by laboratory testing, and the detection of mutations and strains requires the linkage to laboratories and the intensive search for associated epidemiological data. Laboratory DNA sequencing of HBV is needed to monitor mutants. Provincial surveillance systems are incapable of providing this information due to serious reductions in public health surveillance capacities. While the surveillance of HIV strains in Canada has been funded by previous MCs on AIDS, additional emerging HIV surveillance issues, such as the monitoring of drug-resistance levels through laboratory-based molecular studies must be addressed. The only possibility of detecting these infections and protecting the blood supply in Canada is to have a high index of suspicion of where to look for them and a network of surveillance centres connected to a laboratory capacity that can detect or develop the technology to test for them. The current system is designed and funded to detect known clades and strains but must be enhanced greatly to detect emerging threats from STD that could threaten blood safety.		

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #4: (Contd) **A. Retroviruses & STD:** Technical assistance must be provided to the provinces and territories through the assignment of qualified federal personnel to provincial retrovirus and STD laboratory and epidemiological surveillance programs. Support for declining provincial surveillance infrastructure and capacity is essential to develop a	- Develop and manage an intensive provincially-based blood borne retrovirus and STD surveillance system; - Provide full technical assistance to provinces for system development and operation, implementation and support of the surveillance requirement; - Provide financial start-up resources	In collaboration with the provinces/ territories, new staff will develop an enhanced HIV surveillance database and provide them with technical assistance. Qualified federal personnel will be recruited and assigned to both national and provincial HIV/ epidemiological surveillance programs to assist in the development of a unified laboratory/epidemiological HIV database
A. Retroviruses & STD (Contd) unified laboratory-based and epidemiological retrovirus and other STD surveillance system at the provincial level that is both standardized and compatible among all provinces and territories. <u>Resource Requirements ($M):</u> FY 1998-99: 5 FTEs, $ 1.612 FY 1999-00: 5 FTEs, $ 1.798 FY 2000-01: 5 FTEs, $ 2.386 FY 2001-02: 5 FTEs, $ 1.541 FY 2002-03: 5 FTEs, $ .655	- for the surveillance system, and establish new and complex data linkages between national and provincial epidemiology systems that provide basic demographic and risk variables; - Implement a series of contracts with provinces for the development of the required infrastructure at provincial/ territorial levels and the electronic system for data transfer to the national level; - Implement multiple prototypes for various retroviruses; - Implement HIV drug resistance monitoring.	at the provincial/territorial health and laboratory level that is both standardized and compatible among all provinces and territories. Through a series of contracts, financial resources will be provided to develop the required infrastructure at provincial/ territorial levels as well as the electronic system for data transfer to the national level.
B. Hepatitis: Comprehensive national laboratory surveillance for HBV, HCV and HGV is essential. Data on the incidence of HBV, HCV and HGV in high risk individuals and in new blood donors are fragmented and incomplete. Laboratory surveillance will provide	In addition to the methodology currently under development, the laboratory will: - Develop strain surveillance for HBV, HCV and HGV; - Ensure that currently used antibody tests are able to detect the circulating strains and that the tests are used as a tool for epidemiologic investigation,	In 1998-99 and 1999-00, the program to develop and adopt new methods, through a series of projects, to identify new strains of HBV, HCV, and HGV in the general population and in blood donors will be implemented.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #4: (Contd) the essential data for utilization within the HPB risk management framework. <u>Resource Requirements ($M):</u> FY 1998-99: 5 FTEs, $ .794 FY 1999-00: 5 FTEs, $ 1.064 FY 2000-01: 5 FTEs, $ .836 FY 2001-02: 5 FTEs, $ .878 FY 2002-03: 5 FTEs, $ .890 **C. DNA Sequencing:** DNA sequencing of HBV is needed to monitor mutants. Such mutants escape detection by current serological assays. Genetic diversity of HBV in the Canadian population has not been investigated. <u>Resource Requirements ($M)</u> FY 1998-99: 3 FTEs, $ .349 FY 1999-00: 3 FTEs, $ .606 FY 2000-01: 3 FTEs, $ .402 FY 2001-02: 3 FTEs, $ .458 FY 2002-03: 3 FTEs, $ .460	as a "fingerprint" of the source of the infections being transmitted. - Sequencing of HBV is needed for outbreak investigation and also to monitor the introduction of new strains of HBV; - Enhance outbreak investigation capacity.	Technical staff will support the developmental work initiated by the research scientists. By year 2000-01, the staff will be in a position to provide services to clients (provincial health laboratories, major hospital centres, and approximately 40 to 50 Canadian laboratories) for the detection of HBV, HCV, and HGV mutants. Expanded services to clients will be provided for blood-borne pathogen variants in the following year. The staff will initiate the DNA sequencing program for the detection of HBV, HCV, and HGV mutants. Initially, this will involve equipment acquisition and establishing modes of operations. Approximately 200 to 250 samples of HBV, HCV and HGV positive specimens will be sequenced per year coming from provincial health laboratories. They will support the surveillance of HBV, HCV, and HGV mutants through sequencing as well as support outbreak investigations.

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #5: **Capacity to Conduct Public Health Investigation of Emerging BBPs** <u>Resource Requirements ($M):</u> FY 1998-99: 3 FTEs, $ .388 FY 1999-00: 3 FTEs, $ .880 FY 2000-01: 3 FTEs, $ .536 FY 2001-02: 3 FTEs, $ .659 FY 2002-03: 3 FTEs, $ .647	• **Emerging Pathogens:** - Develop laboratory methods for the detection of all emerging BBPs; - Provide laboratory services to all P/T health laboratories for emerging BBPs; - Develop tests for the detection of potential blood-borne pathogens such as Borna disease virus, HHV8, B19 and CMV.	The staff will develop and adopt new methods to detect potential blood borne pathogens. For example, this includes molecular and serological detection methods for detection of Borna disease virus, human herpes virus 8, parvovirus and cytomegalovirus. Technical staff will support the developmental work performed by research scientists. By 1999-00, the staff will be in a position to provide services to clients (provincial public health laboratories and major hospital centres in Canada) for the detection of potential blood-borne pathogens with expanded services. By year 2001-02, they should be able to improve response time to any blood- borne pathogen which may emerge (plan target: less than one week as operations become more familiar).
REQUIREMENT #6: **Capacity to Conduct Surveillance and Laboratory Investigation of Prion Diseases** <u>Rationale:</u> Prions are the most rapidly expanding area of concern regarding infectious diseases. Delayed decision on and passive management of the prion file in the UK led to the development of a totally new disease in humans: variant-CJD. The U.K. can no longer use plasma from its own population. Canadians may be at risk for this disease through blood and blood products. Protection of our food supply, many biologicals and cosmetics is essential to limiting human exposure and limiting further transmission. <u>Resource Requirements ($M):</u> FY 1998-99: 16 FTEs, $ 2.857 FY 1999-00: 19 FTEs, $ 4.887 FY 2000-01: 19 FTEs, $ 4.685 FY 2001-02: 19 FTEs, $ 2.145 FY 2002-03: 19 FTEs, $ 3.176	• **Epidemiology and Surveillance** - Expand current CJD surveillance system, with increased activities targeting cases in advance of death and cases from uncommon populations such as young Canadians or Alzheimer's patients; - Collaborate with international teams initiating certain key investigations in Canada; - Conduct multiple studies on CJD; evaluate newly-discovered blood tests; and act as a proving ground for some tests like those for bovine spongiform encephalopathy (BSE); - Selectively participate in ground- breaking studies for diagnostic and screening tests on an equal basis with the international scientific community.	CJD research is a rapidly advancing area and little of the most important information is available through the published literature. Published literature often lags 1-2 years behind information provided through conferences, which is in turn about 6 months to 1 year behind information available thorough formal and informal contacts. Extra staff are required to keep up with the new information load, and to analyse the information in the conduct of risk assessment. It is anticipated that there will be between 10 and 20 meetings per year where staff will attend, prepare and distribute reports and update the status of LCDC's 5 to 15 new project areas per annum. It will be necessary to prepare approximately one new guideline per annum, and update an existing guideline approximately every 2-3 years. Guideline preparation in areas such as hospital infection control, autopsy for persons with suspected CJD and mortuary guidelines are all anticipated. This might involve consultation with very large numbers of people (300). LCDC's surveillance system will contribute to the identification of the means by

Increased Capacity to Deliver Programs to Meet Long Term Objectives	*Actions to Respond to the Capacity Requirements*	*Resource Justifications*
REQUIREMENT #6: (Contd.)	• **Epidemiology and Surveillance** (Contd.)	which CJD can be transmitted and hence LCDC will be able to recommend how to prevent these transmissions. It can be expected that 30-35 confirmed cases per year will occur; however (from the experience in the UK), there could be twice as many cases to investigate. Staff will conduct investigations which involve contacting doctors, family members, hospitals, collecting blood samples and conducting lab analysis, preparing reports for national stakeholders and the European Union (4 times a year). Last year, there were 6 publications and more than 10 public presentations made. Tissues from people with CJD will be collected for future analysis and correlation of data: est. 2 to 20 organs collected per person, from 100 people annually. This requires protocols and guidelines for proper collection and collaboration of those involved. Semi-annual newsletters will be issued to hospitals, doctors and the public.
A. Tanz Neuroscience, Neuropathology and Prion Diagnostic Research Centre (TNNPDRC):	- Maintain neuropathology diagnostic reference centre once fully-developed; - Implement new diagnostic tests following internal/national validation and develop the national capacity to pioneer new diagnostic or screening tests; - Conduct investigations on Alzheimer's disease and related disorders; - Provide essential scientific core expertise in support of future/on-going regulatory considerations.	TNNPDRC will provide core support to all the surveillance system studies being coordinated by LCDC, hence technicians will collect all the brains used for the study (up to 120 per annum, because even though LCDC only expects 30 confirmed cases of CJD, many other diseases are easily confused with CJD). Neuropathologic studies of the brains of persons with suspected CJD (approximately 80 per year) will be conducted. This requires staff to collect, prepare and analyse the brains (this is being done through the Canadian Brain Tissue Bank). New diagnostic tests being developed worldwide will first be tested at TNNPDRC. Staff will determine how to conduct the tests in Canada; including whether or not the testing must be offered to the medical community and their patients. If the tests are offered to the Canadian medical community to aid in the diagnosis of CJD, the Centre may have to conduct several hundred tests per year, and if epidemiologic studies are conducted, several thousand tests will be conducted.

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REQUIREMENT #6: (Contd) **B. Winnipeg Human and Animal Prion Reference Laboratory:**	- Provide full reference service for genetic diagnostics; - Expand genetic testing to include provincial or territorial requests for family testing (not currently conducted, except as a courtesy); - Develop and implement methods for population diagnostics, as developed at TNNPDRC and internationally; - Develop an animal research capacity to investigate the prion diseases of animals in Canada (scrapie, BSE and chronic wasting disease of deer) so as to better appreciate the risk of animal-to-animal disease transmission and ultimately the risk to humans; - Develop and implement animal diagnostic or screening tests for prion diseases to enhance food, biologic and cosmetics safety; - Increase investigations related to transmission of prion diseases through iatrogenic routes such as neurosurgical instruments using animal models.	A few examples of workload: - Genetic tests will be conducted on all persons with suspected CJD to determine if the disease is inherited. If the family members of persons with familial CJD request this test, it is expected that every case seen within the system (approx. 80 per annum) will be examined and that up to 20% will be familial (16), and testing will be conducted on approximately 80 to 160 family members. Each complete test requires a minimum of four days to conduct. - Genetic studies will determine if there are special genes which identify high risk populations. To determine this, every case entered into the surveillance system (about 30-35 cases per annum) will have special studies performed, requiring about 2 to 4 weeks of extra laboratory study. They must be compared to people who did not develop disease (a control population). The results must be compared with an international series of studies also underway, requiring intensive review of the science in an ongoing manner by the chief of the investigations. - Animal prion disease will be studied in order to learn how to diagnose prion diseases in animals; to know how frequently they occur in Canada, including such animal populations as deer, feline, ovine and bovine populations. For example, studies to determine how extensive scrapie is spread in Canada and whether it has contaminated the animal food chain. - Determine if there are hospital surgical procedures which are transmitting prion diseases in hospital settings by conducting transmission studies using animals; initiate a study for iatrogenic transmission of prion diseases in hospital settings. - Health Canada has already received requests to conduct these studies.

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REQUIREMENT # 7: **Capacity to Link with Public Health Information Networks** Rationale: The information network will provide full support to provincial and territorial laboratories to create an effective link and cooperative and fair exchange of information between laboratories. This closes the loop of an intergrate network. Resource Requirements ($M): FY 1998-99: 2 FTEs, $ .220 FY 1999-00: 2 FTEs, $ .312 FY 2000-01: 2 FTEs, $ .248 FY 2001-02: 2 FTEs, $ .235 FY 2002-03: 2 FTEs, $ .238	- Develop an effective information network to provide useful laboratory information about BBPs in a timely fashion to provincial public health laboratories, epidemiologist, CBS and regulators.	