Health Canada Santé Canada

REPORT OF THE FIRST MEETING OF 2001

RAPPORT DE LA PREMIERE RÉUNION de 2001

SCIENCE ADVISORY BOARD

LE CONSEIL CONSULTATIF DES SCIENCES

February 13-14, 2001
les 13 et 14 février 2001

Health Canada
February 2001

Santé Canada
février 2001

---------- **Note:** Contents of the Meeting Report are a reflection of the discussions of the February 13-14, 2001 Science Advisory Board Meeting. The points contained in this document are those of the Science Advisory Board and do not necessarily reflect the views of Health Canada and its employees./ Le contenu du présent rapport est le reflet des discussions de la réunion du Conseil consultatif des sciences tenue les 13-14 fëffvrier 2001. Les points de vue qui y sont exprimés sont ceux du Conseil consultatif des sciences et ne reflètent pas nécessairement les points de vue de Santé Canada et de ses employés.

Day 1 - Tuesday, February 13, 2001

In Attendance: Roberta Bondar, Yves Morin, Doug Elliott, Allan Ronald, Russ Graham, Karen Grant, Rodney Ouellette, Stuart Macleod, Michel Bergeron, Leslie Millin, Gabriel Plaa, Neena Chappell, Carol Herbert, Richard Lessard

Ex Officio Members: Ian Green, Marie Fortier, Diane Gorman, Kevin Keough, Robert McMurtry

Secretariat: Kata Kitaljevich, Valerie Marshall

1. Opening Remarks - *(Chair - Roberta Bondar)*

The Chair welcomed the members to the first meeting of the year. She reflected on the three years she had spent on the Board and noted this was her last meeting. The Chair suggested to other members whose terms were finishing that they might want to provide some input into agenda items in the future or suggestions for improvements.

The Chair outlined some changes in timing on the agenda. She noted there had been a suggestion that the Health Canada Science Advisory Board meet with the Environment Canada Science Advisory Board meeting on April 11-12 to discuss areas of mutual concern.

Dr. Bondar also noted that Health Minister Allan Rock was scheduled for surgery and suggested the Board draft a letter of best wishes and send it to him.

2. Health Canada: A Report *(Ian Green)*

The new Deputy Minister was introduced to the Board by ADM Diane Gorman.

The Deputy thanked Board members for their welcome and noted the Minister sent his regrets in being unable to attend the meeting because of surgery. While the Minister is recuperating, the Honourable Herb Grey will be acting Minister.

The Deputy introduced the Board to Dr. Kevin Keough, who is the first Chief Scientist for Health Canada, a position which was created in response to a SAB recommendation. The Deputy noted that he expects a long and productive relationship between the Chief Scientist and the SAB.

The Deputy spoke on the tremendous advice on health science-based issues the Board had provided and noted the recent media interest in such issues as the suspension of importation of Brazilian beef and beef products and the recommendations of the Royal Society. The interest in these issues continue to highlight the need to enhance public confidence in Health Canada decision-making.

The Deputy outlined recent announcements in the Throne Speech which promised more funding for research, increased interest in children and families, disease prevention and community-based health promotion and continued work on the safety of water supplies and other environmental areas.

In reporting back to the Board on their previous recommendations, the Deputy noted they would hear a progress report on Health Canada's efforts on Research Ethics Boards in the first morning of this meeting.

In the area of Therapeutic Products' Cost Recovery, Health Canada is pushing hard to include questions asked by the Board in the Treasury Board policy review on cost recovery.

The Canadian Institutes for Health Research are a priority for this government. The Deputy pointed out Dr. Robin Hill's appointment to the CIHR Standing Committee on the Oversight of Grants and Awards Competitions as an example of the commitment Health Canada and the CIHR place on fostering a strong relationship.

A presentation on Emerging and Re-Emerging Pathogens which will respond to the Board's questions and concerns, raised at the last meeting, has been scheduled for a later date.

On the issue of Peer Review, the Office of Endocrine Disrupting Substances (OEDS) has been created within the newly formed Safe Environments Program of HECSB. An acting Director has been appointed for the new Office. The OEDS will be run by a senior scientist with a suitable level of expertise in EDS issues. One of the first tasks for the OEDS will be to establish a strategic plan on EDS for the Department.

The Deputy stated the Department will continue to work actively towards systematic peer review of all scientific work undertaken across the Department.

The concerns expressed previously by the Board on water quality have been echoed in the Throne Speech. The federal government will take the lead in developing stronger national guidelines for water quality. Steps have been taken towards developing a national strategy on water to maintain and improve the safety of Canada's water supplies.

The Office of Consumer and Public Involvement has taken SAB's advice with regard to

employing a variety of communication tools in addition to the Internet.

The Deputy said the role of science and the issue of decision-making is of great concern to Canadians and goes straight to public confidence. He pointed to recent news stories surrounding the suspension of importation of Brazilian beef and beef products as examples of the difficult balance between freedom of expression and duty of loyalty to the public service.

Discussion included the following points:

- Speculation on government decision-making is a major issue.
- The Board needs to be very careful about endorsing any decision without being aware of all the facts and evidence.
- The presentation on TSE on the agenda which had been planned for the second day of the SAB meeting has been expanded to include the recent decision regarding Brazil. Officials from CFIA will be invited to the meeting.

The Deputy concluded by reiterating his support for the work done by the Science Advisory Board and the importance of science within Health Canada. The Science Advisory Board plays an important role in the health of Canadians by providing its best advice to the Minister and Department.

3. **<u>Chief Scientist</u> -** *(Kevin Keough)*

Health Canada's first Chief Scientist was introduced to the board by the Chair.

Dr. Kevin Keough thanked the Board for recommending the position of Chief Scientist be created, but acknowledged that once he begins work at Health Canada in April, he will spend much of the first few months getting up to speed on the operations of the Department.

The Chief Scientist spoke of the core issues he believes are important for the Department and for the role of Chief Scientist. He was pleased there was more money for research and development promised in the Throne Speech. It is important that Health Canada deal with this investment in significant ways. The Chief Scientist told the Science Advisory Board that he intends to use expert panels to advise him.

There are long-term challenges in getting systems and structures in place. One of the larger, over-arching issues is the quality of Health Canada science: this means subjecting Departmental science to peer and other rigorous reviews.

The whole area of staffing and facilities is also important. First-rate science does not happen with second-rate gear and this is an issue the Department needs to deal with. Health Canada needs to maximize access to facilities. The universities and the private sector will be in competition with government for scientists. Making public service attractive to young people is critically important. He expressed an interest in developing collegial aspects in the Department, working on science exchanges and getting young people to work in the department.

The question of morale is important, including the morale among science managers. One of the key elements in this area is communication. Good communication and good science means if the processes are good and people accept them, it can diffuse potential problems.

Partnerships with other agencies and provinces will be important. Health Canada will need those partnerships in terms of strategic research investments.

Scientific foresight is another important element: how does /should the Department obtain that advice, externally and internally?

Ethics is another over-arching issue. How does Health Canada balance the regulatory requirement and policy requirement? How, and if, can Health Canada work with the private sector?

The Chief Scientist concluded by saying he looked forward to receiving the Board's advice.

Discussion included the following points:

- The science mandate in Health Canada is broader than the Acts administered by the Department.
- The Chief Scientist sees his job as making sure that Health Canada gets the very best science and science processes as possible. He would also like to interpret "scientist" in the broadest possible sense and include social science and possibly the humanities.
- Sometimes there is no science, or insufficient evidence, to back up an issue. But a decision must be made.

4. **<u>Strengthening the HC-CIHR Relationship</u>-** *(Kim Elmslie)*

HC recently created the Health Research Secretariat (HRS) as the departmental focal point

for connecting with CIHR.

In addition to promoting information sharing and the development of joint objectives between the two organizations, the work of the HRS will ensure that the Department takes full advantage of opportunities provided by CIHR.

Significant linkages that already exist include the Deputy Minister in his role as an ex-officio member of both the CIHR Governing Council and Executive Committee; HC representation on a majority of Institute Advisory Boards and HC participation in the CIHR Working Group of Partnerships. There are discussions underway to include HC researchers as members of CIHR peer review panels.
Initiatives already underway within Health Canada include the Working Group on HC Researchers in the CIHR Environment, the development of a Visiting Scientific Exchange Program, the establishment of HC's Research Ethics Board and the development of a research database to describe HC's investments in research and research capacity.

Discussion included the following points:

- It is important to know what research is going on throughout the country to get a better picture of what Health Canada can plug into, not just what is funded by CIHR.
- Involving graduate students in opportunities at Health Canada and CIHR is very important.
- There is a need for expanded effort in risk analysis and risk management both at Health Canada and in the academic community. Improved research on risk would ensure that more decisions are science-based.
- There must be a mechanism for setting research priorities.
- Encouragement in strategic partnerships will begin to get the message out to scientists about working togther in research teams.
- The Board could advise on ways to engage Health Canada and CIHR to focus on risk analysis and management. Decisions must be based on good science.

Recommendations:

- *The Board applauds the work of the Health Research Secretariat in its communications and links with the CIHR and emphasizes the iterative nature of this process.*

- *The Board reiterates its position that Health Canada and its senior managers must continue to increase their activity in promoting the participation of departmental research scientists in the CIHR.*

- *Care must also be taken that the Department not solely rely on its relationship with the CIHR, that it needs to develop its own network by reaching out to universities and other research organizations.*

5. Establishing Health Canada's Research Ethics Board (REB) *(Kim Elmslie)*

HC has undertaken to establish a REB in order to assess the ethical acceptability of intra-mural research, research that is contracted to non-HC researchers and research applications to CIHR by HC researchers (in cases where such research involved human subjects) and to provide an educational function to HC researchers and managers.

HC's REB will satisfy prevailing norms regarding independence and transparency with respect to reporting structure, composition, nominating and operating procedures. It will function in accordance with the Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans (TCPS).

Discussion included the following comments:

- This is an important issue for Health Canada and needs to be implemented as soon as possible.
- There are research ethics boards in every institution in the country.
- It might be helpful for the people involved to speak with the Tri-Council for guidance on this issue.
- Educational work will be key in getting the process to work.
- In the absence of a research ethics process, mechanisms must be in place to prevent research on human subjects.
- The scope of the REB might have to be narrow.
- It may be necessary to have two REBs to facilitate the different kinds of research being done, in bio-medical and social sciences.
- It is critical that reviewers are knowledgeable in the area of review.

Recommendations:

- *The Board recognizes the progress made towards the development of the Research Ethics Board. The Board underscores the urgency in setting up such a body.*

- *The Board recommends that the Department seek out advice from individuals and institutions who have such Boards and learn from their experience.*

6. **<u>Establishing a Canada-Wide Policy for Accreditation of Research Ethics Boards</u> -** *(Ian Shugart)*

There have been long-standing concerns with the integrity of research ethics and the adequacy of some Research Ethics Boards and the growing workloads they face. The fundamental issue of public trust around the protection of human research subjects is central to the operations of REBs.

The United States government had moved quickly to set in place research subject protections. Canada is facing the challenge of meeting the standard newly set by the U.S. To that end, 2001 is a transition year to stabilize the existing regime, involve central agencies and other key Cabinet-related decision makers and to promote a discussion of research ethics education and other issues.

Clear roles and responsibilities for research ethics governance will be established under a Government of Canada policy framework. The aim is to have a governance regime that is respectful of the public trust, transparent, comprehensive, inclusive, effective and efficient.

Discussion included the following points:

- There are a number of departments involved, including Industry, HRDC, National Defense and the Department of Indian and Northern Affairs, who must discuss how REBs should be set up.
- Not all REBs across the country deal with health research.
- There is still a sense of urgency to deal with this issue, especially given that the Americans have moved so decisively. Canadian sites which receive money from NIH must meet American standards.
- There is a disparity amongst REBs across the country.
- One of the problems with REBs is resources. It is important that they are funded properly.
- To participate in NIH projects, the terms set down must be followed.
- A major problem could be in terms of legalities and litigation. What happens if the board is not accredited?
- There is also the problem of funding research in resource-poor countries and the decision of whose ethics apply.
- There is a concern that this agency could become a bureaucracy that could drain funds.
- This has to be addressed in a Canadian way which goes well beyond just meeting American standards. If action is not taken, there will be no more clinical trials in Canada.
- What is called for is not necessarily legislation, but regulation.

Recommendations:

- *The Board reminds the Department of the urgency in developing a Canada-wide policy for accreditation to address the disparity across the country.*

7. **<u>The Precautionary Approach: A Discussion of a Draft Federal Framework</u> -** *(Ian Shugart)*

In February 2000, as the Interdepartmental ADM Working Group on Risk Management presented its final document to the Clerk of the Privy Council, the Working Group received direction to undertake further work on a clarification of a Canadian position on the Precautionary Principle/Approach. Ian Shugart has been the representative of Health Canada on this working group.

Over the past year, Departments have worked to produce an initial discussion document which is now being used for initial consultations with a view to clarifying a Canadian position. In the last few years, domestic and international debates on the precautionary principle have been most prevalent in sectors where science is implicated, such as the environment, health, biotechnology and resource conservation. The increased profile today also reflects an increased focus on the role of science in public policy, risk assessment and risk management and is clearly in the public awareness about health and environmental risks.

Ian Shugart introduced the draft document to the Science Advisory Board, noting it was a government-wide process. Precautionary approaches in risk management are self-evident for Health Canada, he suggested, but not necessarily for other departments.

General discussion included the following points:

- The connotation of the words "principle" and "approach" are very different. Care must be taken in discussions on this issue as to which word is the most appropriate. The Canadian public will have different opinions on what is meant with the use of these words.
- This will be a public document at some point. At the moment, it is a draft for discussion purposes. Health Canada is more familiar with the kinds of concepts expressed in this document. Other departments are less familiar.
- For the public to fully understand this document, concrete examples must be used.
- This is an important concept for Canada to adopt. It is important for Canada to speak in one strong voice on this issue, especially in international circles.

- There is some concern that health is obscured in this document. The health role should be more visible.
- Judgement is intrinsic to this precautionary principle. What do we know and how alarmed are we? The threshold will vary depending on the issues.

Discussion included the following points on specific areas:

2.4 Legal Issues

- There was a caution regarding legal standards. Where the standard of action is a national standard in Canada, courts will look at other countries to see if the Canadian approach was careful enough in certain cases. This was the case in the Krever inquiry.

3.2 The precautionary approach refers to situations where there is a need to make a decision about a risk of serious or irreversible harm and where there is significant scientific uncertainty.

- This section is central to the whole concept, but is not qualified. Almost everything carries with it an element of risk. There is some doubt as to what is meant by the words "significant scientific uncertainty".

3.3 It is legitimate for decisions to be guided by the chosen level of protection against that risk.

- The oral presentation was more helpful in understanding what this section meant. The issue concerns what risks society is prepared to take. Concrete examples would make this section clearer.

- People's perception of risk is different, particularly on the health side where there is so much personal risk. The perception is different if the risk is to an individual or to a group.

3.4 Sound scientific evidence must be the basis of applying the precautionary approach, particularly with regard to: (i) the decision to act or not to act (i.e., implement precautionary measures); and (ii) the measures taken once a decision

has been made.

- The bullet in this section on "urgent situations" is the overriding concern. The main question to be asked is whether the situation is urgent and is serious. If the measure that might be taken is practical, cost-effective and suitable, then it must be taken. Lessons learned from the Krever Inquiry show the way in this area.

3.9 Precautionary decisions and measures should be proportional to the potential severity of the risk being addressed and to society's chosen level of protection.

- This section should be closer to the front of the document. This section is key. The "proportionality" issue must come ahead of scientific exploration.

3.10 Precautionary measures should be non-discriminatory and should be consistent with measures taken in similar circumstances

- The use of the word "non-discriminatory" must be very carefully defined in the bullets under this section. There is a difference between unlawful discrimination and legal distinctions that have a reasonable scientific foundation.
- In Canadian law and culture, the word "discrimination" has a certain meaning. Although the word in this section could be defined, another wording might be better.

3.12 Precautionary measures should be least trade-restrictive.

- This section raises some concern.
- This is not inherent in the precautionary approach, but comes into play when a decision has been taken.
- This is a hot-button section. As soon as you talk about commerce as a principle, it is guaranteed to cause problems.
- It would be useful to think about the ordering and the priority they are accorded. One could interpret that each of these are equally important.
- Clarity on this issue is important.
- There is a sense of unease with this section. This relates much more to government's perspective than a strictly health one.

8. **<u>Biotechnology: Report to the SAB</u>** (*Dr. Karen Dodds*)

Biotechnology is a significant issue for the department, as it touches on health in several ways. Biotechnology has the potential to enhance human health and public opinion polling shows that Canadians see this as a top priority for the federal government. Canadians are also concerned about possible risks to human health and again look to the federal government for action.

The speed of developments with respect to the human genome, issues related to the use of genetic information, and the continuing high visibility of genetically-modified foods pose challenges to the department and to the health community at large. The issues relate not just to direct health impacts, but also to ethical, social and legal considerations.

As a result of Realignment, a new "Office of Biotechnology and Science" was established in the Health Products and Food Branch, effective October 16, 2000. The Office has a mandate to address biotechnology across the department and to be a contact beyond the department with respect to biotechnology.

The classic definition of biotechnology is "the application of science and engineering to the direct or indirect use of living organisms or parts or products of living organisms, in their natural or modified forms."

Health Canada faces challenges in dealing with biotechnology in terms of legislative tools (transparency, genetic testing, stem cell research); recruiting manpower in science, regulatory areas, policy and communications and improving the science infrastructure, equipment and linkages. Specific topics for the department to address include: gene therapy, the use of human genetic testing and information, xenotransplantation and genetically-modified foods.

Discussion included the following points:

- Priority setting is important and would help identify new products which may warrant investigation.
- Biotechnology is not a science unto itself, but rather an approach.
- Members noted that public concern about genetically-modified food was described by Dr. Dodds as "mild", and sought reassurance that this finding is based on sound methodology.
- This is a new area, but Health Canada is going to have to get into it very quickly. This is a prime example where Health Canada should be reaching out and seeing what already exists.
- The Royal Society Report expressed concern on the transparency of

"substantial equivalence": that they did not have enough information to express an opinion on some issues.

- The Royal Society Report discussed some of this topic and has good definitions and good introductions on this subject. Health Canada should have reacted more positively to this report.
- The Department needs to be preparing for things like pharmacogenomics, the issue of the interaction with the human genome and the environmental impact. Important ethical and societal issues will arise.

Recommendations:

- *The Board would like to have a discussion on the Royal Society Report and its findings at their next meeting which is scheduled for May 7th and 8th at which time they would like the authors of the Report to present. They would also like to hear the Department's analysis of the Report.*

Day 2 - February 14, 2000

In Attendance: Roberta Bondar, Yves Morin, Allan Ronald, Russ Graham, Karen Grant, Rodney Ouellette, Gabriel Plaa, Carol Herbert, Stuart McLeod, Leslie Millin, Michel Bergeron, Neena Chappell, Doug Elliott

Ex Officio: Diane Gorman, Marie Fortier

Secretariat: Kata Kitaljevich, Valerie Marshall

9. **Approval of September 2000 Meeting Report** - *(Chair - Roberta Bondar)*

Board members with specific concerns on the wording of some sections asked that area be corrected, with more information being added to some sections. The Report will be deemed approved when these changes are made.

10. **The National Microbiology Laboratory: New Directions** - *(Dr. Frank Plummer, Dr. Robert McMurtry)*

The National Microbiology Laboratory, newly created in realignment and elevated to directorate status, is housed in the Canadian Science Centre for Human and Animal Health in Winnipeg. This state-of-the-art, world-class facility was located in Winnipeg with the vision that it would create a national and international centre of excellence for research and science in microbiology and infectious diseases, through partnerships with academia, the regional health sector and industry. In September 2000 a new scientific director was hired with the mandate to realize the vision.

The National Microbiology Laboratory functions include reference microbiology, offers support to the epidemiology program, surveillance, applied research, discovery research and development of new products.

Recent examples of work done by the NML include work on the Walkerton epidemic; West Nile Encephalitis surveillance, monitoring antimicrobial resistance, bioterrorist threats, Ebola Hemorrhagic Fever. The challenges facing the NML include increasing the intellectual capital, integrating the NML into the CIHR, bringing the best to the NML, opening the doors of the NML; increasing funding, strengthening partnerships

within Population and Public Health Branch and the provinces and territories, creating opportunity for synergy, cutting edge science and commercialization of discoveries.

The new vision for the NML is to be a world-class infectious disease research and training organization in Winnipeg to show excellence in public health programming, to do research that informs public policy, offer better health for Canadians through cutting edge research, to have outstanding training programs, to be the centre of the knowledge economy and encourage commercialization of discoveries.

The creation of an International Centre for Infectious Diseases as a virtual centre with links throughout academia and the research community is in its beginning stages with links to the University of Manitoba. Potential areas for excellence are HIV and STD, zoonotic diseases, tuberculosis, antimicrobial resistance, prions, genomics and proteomics, bioterrorism and viral diseases.

Discussion included the following points:

- Joint partnerships are important to both the NML and scientists. The NML is a resource that needs to be used.
- There are national needs that must be met, for example, bioterrorism, but public health is an important area.
- There is co-operation one-to-one between scientists at the NML and the CFIA, but a troublesome aspect is the lack of co-operation at the top levels.
- Working with the private sector is an opportunity that must not be missed, but there are questions about conflicts of interest and intellectual property.
- The importance of undergraduate students and post-doctoral students using the NML and participating in research cannot be overstated.

11. **<u>Response of Health Canada and the NML to Recent Public Health Concerns</u>** - *(Dr. Ron St. John, Dr. Frank Plummer, Dr. Robert McMurtry)*

Recently, Health Canada was called upon to respond to several public health threats, including a suspicious package delivered to Citizenship Canada and a woman from the Democratic Republic of Congo suspected of carrying the Ebola virus. In these, and other examples, the National Microbiology Laboratory in Winnipeg played a vital role.

The first threat was a suspicious package delivered to citizenship offices in Ottawa on January 31, 2001. The package and its contents were suspected to be biochemically-contaminated and were transferred to the Level 3 facility in Winnipeg where the process of determining the contents began..
The second episode illustrates the problems with a a more closely connected world, where

a woman travelling to Canada fell ill with suspected viral hemorrhagic fever. The Winnipeg laboratory was involved in trying to identify the cause of her illness, which had not been diagnosed at the time of this meeting.

The Scientific Director of the NML, Dr. Frank Plummer, said scientists at the lab worked steadily on these emergencies. There were no major gaps in the NML response.

Discussion included the following points:

- The Science Advisory Board members laud the NML and its employees for the work done in these cases.
- There must be collaboration between agencies in cases where public health is at risk from known or unknown threats.

Recommendations:

- *The Board is impressed by the tremendous strides made by Dr. Frank Plummer and his colleagues at the Laboratory. It is a facility that the Department can take great pride in and should be used as a model of science within Health Canada.*

- *The Board applauds the vision of Dr. Plummer and the partnerships being forged with the public and private sectors.*

- *The Board also encourages partnerships with universities including the involvement of graduate students, post doctoral students and other trainees, and looks forward to collaboration between the National Microbiology Laboratory, other government laboratories as well as the CFIA laboratories.*

- *The Board recommends that Health Canada initiate a memorandum of understanding with the CFIA to ensure appropriate sharing of skills and facilities in rapid response situations, including serious threats to human life and well-being.*

12. **<u>Transmissible Spongiform Encephalopathies (TSEs)</u> -** *(Dr. Marc LeMaguer, Dr. André Gravel) (Also present: André Dulude, Myles Kirvan, Renee Harden, Dr. Sarah Kahn and Dr. Ron Rogers)*

The initial presentation was to provide SAB members with the background, the current Canadian situation, the European situation and issues for Canada with regard to TSEs, as well as an understanding of roles and responsibilities of Health Canada, the Canadian Food Inspection Agency (CFIA) and Agriculture and Agri-Food Canada with regard to TSEs.

The presentation was amended to include a presentation by Dr. André Gravel, Executive Vice-President of the CFIA, on the suspension of importation beef and beef products from Brazil.

Canada only imports beef from countries that have demonstrated that they are free of BSE. There is no test on live animals or humans which can diagnose BSE; it remains a disease to be detected in infected tissues after death.

The CFIA is the enforcer of standards set by Health Canada. With respect to BSE, the Brazilian government had been requested to fill out a questionnaire about the potential risks of BSE in that country. This request was made in 1998. There were two trigger points which lead to the recent actions: in January 2001, the FAO announced that possibly contaminated feed had been exported to many countries; the CFIA also learned that between 1990-99, Brazil imported up to 4,500 cattle from Germany and France. The incubation period for BSE is from five to seven years. Brazil has not demonstrated any BSE to this point. Members were assured that the decision had been taken solely on scientific grounds and that no external non-scientific considerations were involved.

There are three major components to an effective BSE control program: control and tracking of imported animals, control of animal feed and feed mills and testing on an adequate number of animals to detect possible cases of BSE. Brasil is being asked to demonstrate they had a system in place to track animals and the feed sector. Canada implemented a feed ban in 1997. Experts from the United States, Canada and Mexico in feed and control are currently in Brazil, evaluating the overall systems and feed mills. Brazil is being asked to demonstrate they have collected adequate test numbers.

Discussion included the following points:

- The suspension of the importation of beef and beef products was done under the *Health of Animals Act* and the *Food and Drug Act.*
- As part of the North American Free Trade Agreement, Canada has responsibility for South America and its decisions are binding on its NAFTA partners. The United States and Mexico took action at the same time under NAFTA.
- The CFIA was aware this could be seen as a trade action, but were convinced to act because of the questions on public health and safety.

- Canada does not import from countries that do not have an inspection and regulatory system close to ours.
- The issue was seen as a trade issue by the media.
- It was reported that Canada also imported feed from Europe. The CFIA is currently reviewing every import permit for the past five years. To this point, the CFIA has not found that there was a single importation of risk material.
- Processed meat products from Europe may be imported to Canada; the meat doesn't come from European beef but may be processed there.
- The World Health Organization is still examining the issue of milk as a transmission agent for vCJD.
- Communications with staff at Health Canada on this issue also need to be improved.
- There is scientific basis to BSE and vCJD; this is not a theoretical risk.
- Canada is not imposing standards on other countries that it does not impose on itself.
- The Board was critical of the Health Canada communications with the media and the public.

Recommendations:

The Board passed the following resolution and wrote a letter to the Minister supporting the actions of the government with respect to the suspension of the importation of Brazilian beef and beef products. (See Annex 1):

- *The Science Advisory Board supports the appropriate application of the precautionary approach in responding to threats to the health of Canadians. The Board has been made aware of the scientific evidence that supports the theory of transmissibility of variant Creutzfelt-Jakob Disease (vCJD), the catastrophic nature of vCJD, and the evidence that potentially contaminated European meat may have entered into the Brazilian beef industry. The Board believes that the temporary suspension of imports and removal of Brazilian beef and beef products are justified actions on scientific grounds. These are practical and proportionate measures to protect Canadians from the potential threat of an undetectable, incurable and life-threatening disease, pending an investigation as to whether any contaminated material in fact entered into the Brazilian beef industry. These measures are consistent with the rigorous and successful steps taken by Canada domestically to ensure that our country remains BSE-free.*

- *The Board recommends that the CIHR Institute of Infection and Immunity review the Canadian science capacity for prion research in viral and animal diseases and, if necessary, develop a strategic plan to further develop this research area.*

13. **Science Advisory Board WebSite Demo** *(Kata Kitaljevich, Brenda Pilon)*

Brenda Pilon, of HPFB Systems Development, outlined changes in the Science Advisory Board's website, explaining a template for the new site. The site would conform to the Government of Canada's common look and feel. The site would contain up-to-date information about membership, meeting reports and materials presented to the Board.

Discussion included the following points:

- The problem at the moment is accessing the Science Advisory Board website. It needs to be prominent and easy to find.
- An archival system is important to keep historical information.

14. **Report Back on Board's Self-Evaluation Exercise** (*Monte Doyle*)
(See annex for questions and results)

An overall positive picture emerged from the 11 respondents to the questionnaire, although there are some specific issues that emerged, including updated Terms of Reference and the role of the Chief Scientist with respect to the Science Advisory Board.

Members rated themselves strongly in terms of independence of decision-making, working well as a board, individual contributions and leadership.

Discussion included the following points:

- Feedback from the Department to the Science Advisory Board would have been helpful.
- There has been good feedback from Senior Management, but there remains a question whether or not the Board has been useful to the rank and file.
- The Board was in place before realignment and has never received Terms of Reference that reflect that shift.
- In the original Terms of Reference, the Board was to address the concerns of the public and public perception. There is some feeling that the Board has never addressed this problem.
- For the average Canadian, the concerns are for a safe, nutritious food supply and effective medications for illness.

15. <u>Business Arising from the Meeting</u> *(Dr. Roberta Bondar)*

At the next meeting, Board members would like to continue discussions on the report of the Royal Society of Canada. The co-authors are to be invited to the meeting. The report, as well as the analysis done by Health Canada, should be forwarded to the members before the next meeting.

Before concluding the meeting, the Chair told members it had been a real privilege to be on the Board. She also thanked the members and wished them well.

Members retiring from the Board, including Dr. Roberta Bondar, Doug Elliott, Russ Graham, Dr. Gabriel Plaa and Leslie Millin, were presented with certificates of appreciation.

The meeting adjourned at 3:30 p.m.

ANNEX 1
Science Advisory Board
February 13-14, 2001

February 14, 2001

The Honourable Allan Rock, P.C., M.P.
Minister of Health
Brooke Claxton Building
16th Floor
Tunney's Pasture
Ottawa, Ontario
K1A 0K9

Dear Minister:

The Science Advisory Board, at its February 13-14, 2001 meeting, discussed the suspension of importation of Brazilian beef and beef products. The Board felt that, because of the importance of this issue, its unanimous resolution should be forwarded to you immediately.

"The Science Advisory Board supports the appropriate application of the precautionary approach in responding to threats to the health of Canadians. The Board has been made aware of the scientific evidence that supports the theory of transmissability of variant Creutzfelt-Jakob Disease (vCJD), the catastrophic nature of vCJD, and the evidence that potentially contaminated European meat may have entered into the Brazilian beef industry. The Board believes that the temporary suspension of imports and removal of Brazilian beef and beef products are justified actions on scientific grounds. These are practical and proportionate measures to protect Canadians from the potential threat of an undetectable, incurable and life-threatening disease, pending an investigation as to whether any contaminated material in fact entered into the Brazilian beef industry. These measures are consistent with the rigorous and successful steps taken by Canada domestically to ensure that our country remains BSE-free."

On behalf of the Board, I am pleased to bring this resolution to your attention.

Yours sincerely,

Roberta L. Bondar
OC, O. Ont., MD, Ph, FRCP(C), FRSC

c.c. Ian Green, Deputy Minister

Annex 2

This document represents the views of the author alone, presented purely to stimulate discussion, and should not be taken as a document of either Health Canada or its Science Advisory Board.

1. Background

1. At the November , 2000 meeting of the Science Advisory Board, we discussed follow-up to the Report of the Committee on the Drug Review Process. An issue that had concerned the Committee was the Cost Recovery Initiative policy as it applied to the Therapeutic Products Programme, especially as regards public confidence in the scientific research integrity of TPP. The Committee chair, Doug Elliott, pointed out that the report prepared for TPP by KPMG Consulting LP failed to address the important question of the negative impact of cost recovery on consumer confidence, and indeed the fundamental question of the appropriateness of cost recovery in a regulatory setting. I agree wholeheartedly with this position.

1.2 Another concern of your Committee was post market surveillance, which clearly was a major weak spot in the entire drug review process. And another related concern was that of Orphan Products—that is, therapeutic products for which there is a need, quite possibly urgent, that are not offered to the Health Canada review process because the Canadian market is deemed by the manufacturers to be too small.

1.3 The purpose of these notes is to suggest a way to deal with some of these isues while recognizing that the current environment of management thinking at the senior levels in Ottawa is such that the Treasury Board's policies on cost recovery are unlikely to disappear in the near future. My belief is that it may be possible to adapt those policies to work to the advantage of all concerned.

2. Problem

2.1 Public confidence in the scientific basis for the work of Health Canada, especially in the drug review process, has eroded greatly in recent years. This is recognized in the first of the SAB's Terms of Reference, and should thus be an SAB priority. Your Committee heard much about this lack of confidence. An important element was a widely held perception that the payment by pharmaceutical manufacturers of user fees—termed "cost recovery" by the Treasury Board—might lead to an improper influence on the drug review process. Your Committee found no credible evidence of any such impropriety. Yet the intuitive judgement of the public is that when pharmaceutical manufacturers pay at least some of the cost of the review process, they must expect in return some influence over that process. And indeed they do: that is clearly documented. What they have stated they expect is not unreasonable—they want the Canadian review process to be as timely as it tends to be elsewhere, especially in the United States. But criticisms persist both within and without Health Canada that in fact more than this is expected.

2.2 Health Canada introduced user fees under considerable pressure. The federal government was drastically reducing the department's budget as part of a cross-government austerity drive, and the Treasury Board—ultimately, the paymaster—was simultaneously pushing its cost recovery philosophy. HC probably had little option; but that is a management question beyond the purview of the SAB. Our concern has to be with the quality, integrity and comprehensiveness of HC's science activities, as our mandate so clearly sets out. But the pressures on the department without doubt had at least two negative effects: the loss of public confidence, and the loss of internal morale amongst scientific staff. Other factors of course were in play. HC's scientific activities were clearly in need of review and reform, and employee morale was bound to be affected, even if budgets were not being reduced.

2.3 The consequent impact on public confidence has harmed HC in many ways. More important, it has arguably harmed the Canadian public. HC's capacity to recruit and retain the best scientific minds has certainly been impaired. Loss of internal morale has clearly had an effect on productivity. Far more important, the loss of confidence by the public has reduced HC's capacity for reform, since any change immediately attracts suspicion. Finally, loss of public confidence in HC's science drives ordinary Canadians into the hands of those who wish to profit by the sale of products with no scientific pedigree.

2.4 Yet it seems highly unlikely that Parliament will vote to provide the department with the necessary appropriations to carry on a comprehensive and meaningful scientific program without some contribution from the pharmaceutical industry.

2.5 Quite simply, the public perceives that the payment of fees by the pharmaceutical companies creates for them a client relationship with HC. This, the Board has been told, is not so. But the KPMG report states clearly and bluntly that this is exactly the result of user fees, and indeed is the *intended* result (see, for example, p. 236). The problem then is to reconcile some form of financial transfer by the pharmaceutical companies with the public's expectation of a drug review process that is not primarily driven by economic motives.

2.6 A cogent and troubled description of this problem is to be found in the December 2000 report of the Auditor General at 24.90, p. 24-29. "... As there is a greater dependency on fee recovery, a client-provider relationship could be established, and in some areas that might not be entirely healthy." He was speaking specifically of the drug review process.

3. Myths

3.1 Before going further, it is necessary to dissipate some myths about cost recovery. Those who were present at the November meeting are aware that my general opinion of the KPMG report is not glowing. But when it talks about practical management, it often makes a lot of sense.

3.2 In its section entitled **Cost Recovery Myths**, (pp. 235-236), it points out the following:

- "The existence of the TPP CRI does not, in itself, enable the TPP to meet its performance targets";
- "The CRI fees alone will not directly result in improved business practices";
- To use the concept of comparing public and private benefits "as the means of providing a definitive measure for determining the mix of user fees (*sic*) and tax-based funding would be ill-considered."

3.3 Another myth disposed of in the KPMG report is the notion that cost recovery payments encourage applicants to prepare their applications better. No evidence for this could be found by the investigators.

3.4 Finally, it is sometimes suggested that user fees are a global phenomenon. They aren't. The FDA in the United States is often cited, but it applies user fees only to prescription drugs; it has a well developed Orphan Products Program to offset some of the drawbacks of a purely industry-driven system; and in any case it uses a method of capturing and using the fees that no other country seems to find appropriate, and that in Canada would almost certainly be illegal. Other jurisdictions apply user fees in very different ways, but oddly the outcomes don't seem to vary much. In some cases, and I shall return to this later, the at least some of the revenues from such fees are used in ways that help to reassure the public of the integrity of the system.

4. Post-Market Surveillance

4.1 Most clinical trials for new drugs are typically conducted using young men, usually fit or with only a single ailment, who are sufficiently literate to qualify for post-secondary education. Most drugs, however, are prescribed for elderly, infirm patients of both genders who may or may not be able to read labels, and who often are suffering from multiple ailments for which they may be taking a range of prescribed or unprescribed substances. Many are prescribed for children, or for pregnant women. Given that the actual population may well be quite different from the trial population, adverse reactions are inevitable. The challenge is to manage them within acceptable limits.

4.2 Prescribing physicians are the obvious primary source of ADR information. In Canada, this presents certain difficulties. Most such physicians in this country are paid on a fee-for-service basis, and thus the work involved in ADR reporting is voluntary. Much of what they know about a new drug comes from representatives of the manufacturer. Remarkably few family physicians are computer-literate, so reporting often means a cumbersome hard-copy process adding to what is usually a very heavy workload. As HC's Canadian Adverse Drug Reaction Newsletter notes: "Most adverse drug reactions can only be considered suspicions, for which a proven causal association has not been established. Because ADRs are under reported and because a definite causal relationship cannot be determined, spontaneous ADR reports cannot be used to estimate the incidence of adverse reactions." As the Committee warned more than a year ago, post-market surveillance seems to be the weakest part of the drug review process. Manufacturers, of course, have a legal and moral obligation to report ADRs that come to their attention, but as long as the reporting system relies on spontaneous, voluntary action by prescribing physicians, this weakness will persist.

4.3 The December, 2000 Report of the Auditor General expresses concern about the HC post-surveillance approach--concern that senior HC managers seem to share. Interested readers may wish to consult remarks at 26.37 through 26.40, p. 26.13. The Report notes, *inter alia*, that: "... We have learned that the Department does not review adverse reactions from industry in other countries; it stores them in boxes." It acknowledges that HC cannot compell prescribing physicians to report ADRs, because of provincial jurisdiction over medical practise, but it seems not to have taken into account an approach used by the UK's Medicines Control Agency. This is referred to but not elaborated on at length in a study commissioned by HC itself. MCA is entirely funded by user fees, and it uses some of its revenues not to *compel* prescribing physicians to report, but to *motivate* them.

4.4 This excellent report was prepared for Health Canada some two years ago by HDP Group Inc. of Ottawa, entitled *Functional Review of Post-Approval Drug Assessment Operation Activities*. On pp. 41-43 it provides a very good analysis of the ADR challenge. This report, which was submitted in March, 1999, was made available to the SAB in November, 1999 when the work of the SAB Committee was over, which explains the lack of reference in the text of the Committee Report. It notes a significant point regarding user fees which I had missed in the research undertaken for the Committee: "In the United Kingdom, the system requires the first 20,000 prescribing physicians to report [ADRs] *and it pays them to do so.*" (emphasis added). This is particularly significant in that the UK system is entirely funded by user fees.

4.5 Most ADRs, of course, are relatively minor, and the weakness in the reporting system is of less import. The problem lies with the rare catastrophic events—thalidomide is the classic example—which are at the heart of public anxiety about new pharmaceuticals and the ability of HC science to guard public safety.

5. Global Trends

5.1 Canada is not the only country whose citizens view with some alarm the world's increasing complexity, nor are prescription drugs the only area of concern. But there most certainly is a growing international consensus that human safety and even life may be at risk where corporate prosperity is the pre-eminent goal of those who supply the necessities of life, and a belief that only national governments acting in concert can provide some measure of safeguard. Some of these concerns are undoubtedly groundless; many are probably exaggerated. But when, as recently happened, international drug companies admit to having colluded to fix the price of pharmaceutical products, when they are seen to withhold their products from countries too poor to pay world prices, then the public may be entitled to conclude that protecting and improving human life and doing business in an ethical way is not necessarily a top priority.

5.2 What is emerging among the industrialized countries is a matching consensus that where there is a genuine risk of catastrophic failure—however rare—in government-regulated industry, there is a corresponding need for a capacity to investigate such failures *independently* of the regulatory structure. Further, there is consensus that such a capacity will require formal international structures. The independence of such investigatory bodies is essential because, in the contemporary complex world, conflicts of interest are inevitable. International structures—which in today's world of course may be

'virtual'—are essential, because the kind of catastrophe that may occur, however unintentionally, through the activities of XYZ Inc. in Canada are equally likely to occur because of identical or very similar activities of the same corporation in some other jurisdiction. But since each country has national responsibilities that it cannot shirk, each will require a national independent investigatory capacity through some arm's-length agency that will provide the link with the international structure. A clear and highly successful precedent is Canada's Transport Safety Board and its membership in the International Transportation Safety Association.

5.3 During the extensive briefings provided to the SAB in its first year or so of work, there were several presentations on international activities covering several areas of concern. I can recall no initiative regarding ADRs, although this may well be under way. Certainly it was noted as a concern in the HDP Report (p. E-4) that international co-operation regarding ADRs by HC seemed actually to be diminishing, other than with the FDA's CDER.

5.4 The idea of a national drug safety board for Canada was raised in the contribution by Dr. Michèle Brill-Edwards to the publication *Tales from the Other Drug Wars*, about which I circulated a note just before Christmas. In my note, I wrongly suggested that this idea might be new. In fact, it has been the subject of an article in *The New England Journal of Medicine,* as in fact she acknowledges; and I apologize for the error. The idea has also been raised in articles in *The Journal of the American Medical Association* in the context of the effects of user fees on the drug review process.

6. Conclusions

6.1 Public confidence in Health Canada's independence from the corporate agenda is diminished by the dependence on user fees under the Cost Recovery Initiative. A major element in public distrust of the corporate agenda is the fear of some catastrophe arising from corporate pre-occupation with profit and an inadequate, perhaps compromised, scientific capacity within HC. The weakest part of the drug review process is post-market surveillance. HC is unlikely to escape the CRI policy in the foreseeable future. What opportunities may there be here?

6.2 Let me suggest the following, so that its defects may be exposed:

- Simplify user fees and if possible put a clear distance, visible to the public, between them and HC's scientific work;
- Demonstrate that post-market surveillance is a top priority at arm's-length from the approval process;
- Move without delay to create an independent national capacity to investigate serious ADR events, with a mandate to move to the creation of an international capacity.

6.3 For example, instead of various and apparently not always collected user fees, simply require each application to be accompanied by a deposit held in trust. If the applicant cannot satisfy HC within some specified time, the deposit is forfeit—historical data suggest this would be very rare. If the application is successful, return half of the deposit. Retained and forfeited deposits would go to support post-market surveillance scientific activities—including paying prescribing physicians to report on the outcome of the first however many applications of a new drug—and the capacity to investigate serious ADR events. Some might go to support an Orphan Products Program. CIHR might be an appropriate trustee for the deposits, but no doubt other arrangements can be found.

6.4 This would have the advantages of breaking the public perception, however misguided, of a pharmaceutical company applicant having client status with HC. It would simplify a user fee system that is an unwieldy attempt—and, according to KPMG, ultimately fruitless—to reconcile private and public benefit. It would ensure that corporate money would go only to support scientific activities of the type most valued by the public, rather than being mingled with departmental appropriations and thus susceptible to redirection. It would considerably strengthen the weakest link in the drug review process, not least by motivating physicians to add to the stock of knowledge of new products. It would remove at least one weapon from the arsenal of those who are determined to blackguard Health Canada. And it would provide reassurance to the public that serious funds were being committed not only to health science but in the two areas that, in my judgement, worry the public most.

6.5 Such an initiative would require a well developed communications strategy and the visible involvement of the Chief Scientist, as well as the Minister and senior departmental officials. The SAB should consider carefully the potential rôle of its Chair, and the possible interaction with a general communications strategy for the SAB itself.

Leslie Millin
February 12, 2001