MEETING NOTES
THERAPEUTIC PRODUCTS DIRECTORATE (TPD)
ADVISORY COMMITTEE ON MANAGEMENT (ACM)
May 8-9, 2002

TPD Boardroom
Holland Cross, Tower B, 1600 Scott Street
Ottawa, Ontario

ACM Members

Attending

Jim Blackburn, Chair
Luis Barreto (Day 1)
Andrea Baumann (Day 1)
Bernadette M. Connaughton
Ruby Grymonpre
Stuart MacLeod
John Parks
David Skinner
Beverley Townsend (Day 1)
Pamela Zabel

Regrets:

John Blatherwick
Mitchell Levine
Brenda Nunns Shoemaker
Jack Rosentreter
Michael G. Tierney
Jacques Turgeon
David Windross

Health Canada

Presenters

Robert Peterson, Co-Chair, Director General (DG) TPD
Hélène Bélanger, Bureau of Operational Services (BOS)
Andy Butterfield, BOS
Pauline Gaudry, BOS
Sultan Ghani, Bureau of Pharmaceutical Sciences
Brian Gillespie, Senior Medical Advisor Bureau (SMAB)
Abdullah Hassan, Bureau of Gastro-Enterology, Infection and Viral Diseases
Micheline Ho, SMAB
Pat Huston, SMAB
Naheed Israeli, Policy Bureau (PB)
Robert Leitch, Marketed Health Products Directorate (MHPD)
Karen Proud, Office of Regulatory and International Affairs
Paul Roufail, Bureau of Metabolism, Oncology and Reproductive Sciences
Roland Rotter, Medical Devices Bureau
Philip Waddington, DG Natural Health Products Directorate
Mike Ward, PB
Brigitte Zirger, Bureau of Cardiology, Allergy and Neurological Sciences

Observers

Lynn Bernard, Associate DG TPD
Roger Farley, DG Office of Consumer and Public Involvement
Trish Larwill, BOS
Louis Boulay, Veterinary Drugs Directorate
David Lee, Office of Patented Medicines and Liaison
Supriya Sharma, MHPD
Barbel Traynor, BOS

Secretariat

Susan Tessier, PB
Denise Quesnel, PB
Chantal Tremblay, PB

DAY 1 - May 8, 2002

1. Opening Remarks

Dr. Blackburn welcomed all. A roundtable of introductions followed.

Bernadette M. Connaughton, President and General Manager of Bristol-Myers Squibb Canada was welcomed as a new member. Three additional new members, who had sent their regrets and will attend the next meeting, were announced. They are:

Dr. Michael G. Tierney, Pharmacy Department, Ottawa Hospital,
Dr. Jacques Turgeon, Dean, Faculty of Pharmacy, University of Montréal and
Mr. David T. Windross, VP, Government and Professional Affairs, Novopharm

Dr. Peterson encouraged ACM members to provide their feedback and advice into the organizational changes that were taking place at TPD, in part as a result of Health Canada realignment. He announced that Ian Green, the Deputy Minister of Health, would be guest speaker at dinner that evening.

2. Review of the December 5 & 6, 2001 Meeting Notes and Agenda

The previous meeting notes were accepted as distributed.

David Skinner wished to add an agenda item: update on the future of ProxTox. This pilot is a project of the Centre for Disease Surveillance in the Population and Public Health Branch and, as such, not within the mandate of TPD. D. Skinner was directed to the appropriate individuals. The agenda was accepted as distributed.

3. Management Issues

3.1 TPD Reorganization

Dr. Peterson reported that TPD has undergone significant restructuring. This was done after careful consideration of several models and staff and focus groups' statement of operational needs. These changes have also been reviewed at the Branch and Departmental levels and were announced formally on April 2, 2002. The Bureau of Pharmaceutical Assessment has been divided into five functional units which respond to workload distribution, performance measures, quality systems, backlog and screening program requirements. These processes used to be discrete but are now integrated into the review itself. The new Senior Medical Advisor Bureau has brought together a number of stand alone responsibilities, including the Clinical Trials and Special Access Programme, product information, non-prescription drug evaluation, risk management, quality assurance and level 1 appeals. Patents is a growing issue within Canada and the US; a new Office of Patented Medicines and Liaison reports directly to the DG. The ACM suggested that work with the Patented Medicines Review Board would be useful and reduce duplication of efforts.

a) Senior Medical Advisor Bureau (SMAB)

Dr. Brian Gillespie gave an overview of this new unit. He described the Clinical Trials and Special Access Programme (SAP) and their experience under the modernized regulatory framework which was introduced in Sept. 2001. The SAP is a single window which administers blood products and biologics as well as drugs and has responsibility for emergency response regarding supply of these products. Also profiled were the Nonprescription Drug Evaluation Unit, Product Information Division and the Risk Management/Postmarket Liaison Division. It was clarified that clinical trial inspections are done by the Health Products and Foods Branch (HPFB) Inspectorate, supported by TPD who does the review. TPD handles, on average, 4 switches/year and it can take significant time to resolve the clinical issues in these cases. Most applications are for ingredient, rather than class, switches. The difficulties in advising and communicating with health care professionals and consumers was acknowledged; the TPD is committed to working with MHPD to minimize these.

b) Bureau of Metabolism, Oncology and Reproductive Sciences (BMORS)

Dr. Paul Roufail described the Metabolic and Musculoskeletal Drugs, Anti-neoplastic Drugs and Reproduction and Urology Divisions within this group. The benefits expected from the new organization is equitable workload, close relationships between divisions, flexibility in distributing workload among divisions and improved review performance. As well, it is anticipated that there will be more interaction between the managers and reviewers and industry resulting from the smaller divisions. The challenges will be efficiency of reviews and performance targets, balances between internal resources and external experts, priority review and Notice of Compliance with Conditions (NOC-C) issues. The ACM felt that using pre-review panels paid for by industry to look at issues and give a report to TPD would be a reasonable way to get external scientific expertise. The information from the panel could contribute to information for the review, but this would not replace external evaluations.

c) Bureau of Gastro-Enterology, Infection and Viral Diseases (BGIVD)

Abdullah Hassen reported on behalf of Dr. Jacques Bouchard. The BGIVD has 3 divisions: Gastroenterology, Anti-infective Drugs and AIDS and Viral Diseases. The challenges include implementation and staffing of the new structure, introduction of the Common Technical Document and the use of advisory panels in review.

d) Bureau of Cardiology, Allergy and Neurological Sciences (BCANS)

BCANS monitors submissions on an ongoing basis with the intent to divide the workload fairly. The Bureau houses the Central Nervous System Division, Cardio-Renal Division, Allergy and Respiratory Drugs Division and Submission Management Unit. Management challenges are: resourcing, reviewing the use of external reviewers, submission review performance, backlogs, workflow and linkages. Administrative challenges of change are somewhat complex in a 5 bureau structure since certain amount of consistency is desirable. Brigitte Zirger has the responsibility of coordinating common issues among the 5 bureau managers.

e) Bureau of Pharmaceutical Sciences (BPS)

Sultan Ghani confirmed that the evaluation of the quality (chemistry and manufacturing) and biopharmaceutics portions of drug submissions is an integral part of the regulatory process. Key challenges of BPS are international activities and collaborations (ICH, U.S.P., EMEA), streamlining submission process, guidance documents, team building for generic drugs to meet performance standards and staffing.

f) Bureau of Operational Services (BOS)

Hélène Bélanger described BOS as a centralization of administrative services and having 5 divisions: Planning and Management Strategies, Finance and Administration, Information Management, Submission and Information Policy and Proprietary and Scientific Information Assessment. The key challenges are defining and clarifying the roles and responsibilities, work descriptions, staffing, accommodation, and implementing improved ways of serving clients. The goal is to create a centre of expertise and excellence in service delivery.

g) Policy Bureau (PB)

Naheed Israeli reported that the objective of the PB was to develop a model and governance structure for an integrated approach to policy development in the TPD. The key deliverables are prioritization of workload, project management system supported by Microsoft Project and an organization structure which will optimize workflow. Inter Directorate policy is managed through bilateral meetings and a strategic planning table at the Branch level.

h) Medical Devices Bureau

Dr. Peterson announced that Beth Pieterson has moved to Healthy Environments and Consumer Safety Branch. He stated that the TPD is fortunate in having Roland Rotter as acting Director. The structure of the MDB has not changed, and they face challenges of responsiveness and international harmonization.

3.2 Biologics and Genetic Therapies Directorate (BGTD)

After extensive recruitment, a DG for BGTD still has not been named.

3.3 Marketed Health Products Directorate (MHPD)

Robert Leitch reported for the Chris Turner, the Acting DG of MHPD. MHPD has broadened the scope of the former Bureau of Licenced Product Assessment to include natural health products and novel foods, resulting in its acquiring more resources and Directorate status. MHPD is interested in continuing to participate with TPD's ACM. The activities of the MHPD include:

- monitoring and collecting adverse reaction and medication incident data
- reviewing and analyzing marketed health product safety data
- conducting risk/benefit assessments of marketed health products
- communicating product related risks to health care professionals and the public
- overview of regulatory advertising activities
- active surveillance and product effectiveness projects

Regulatory responsibility for marketed health product lines will remain with the currently responsible Directorates. A team approach involving pre- and post-approval regulatory officers will be used to avoid duplication of efforts and enhance consistency of approach.

National adverse reaction (AR) reporting activities are coordinated by the Marketed Health Products Directorate of Health Canada. Voluntary reports are currently collected by five Regional AR Centres (British Columbia, Saskatchewan, Ontario, Québec and Atlantic) in addition to the National Office (Ottawa, Ontario). Regional Centres perform an initial review of the quality and completeness of the reports which are then processed and further analyzed at the National Office.

An example of a surveillance pilot project is the Mother Net Pilot Project . It is creating a system that will share information on the effects of drugs used by pregnant or breast-feeding women on their fetus or child. The information can then be used to advise women and health care professionals on the potential side effects or benefits of starting or continuing to take a given drug during pregnancy or breast feeding. The MHPD was encouraged to include pharmacists in their such surveillance pilot projects. Pharmacies could be used to post advisories that direct people on how to report an AR and alert consumers to references in the Compendium of Pharmaceuticals and Specialties (CPS).

4. Policy/Regulatory

4.1 Enviro nmental Assessment

Karen Proud, HPFB's project manager for Environmental Assessment Regulations (EARs), delivered a presentation aimed at providing the ACM with an understanding of the key issues with respect their potential impact on pharmaceuticals and medical devices. Under the *Food and Drugs Act (F&DA),* Health Canada (HC) is responsible for safety, efficacy and quality of food, pharmaceuticals and health products. Under the Canadian Environmental Protection Act, HC shares responsibility for protection of the environment. In September 2001, HC published a Notice of Intent in Canada Gazette (CG) Part I to inform Canadians that it would be developing EARs for substances in products regulated under the *F&DA,* to minimize pollutants in the environment. An open dialogue is ongoing with stakeholders on this initiative. A national science agenda and education initiatives are being developed and implemented. International requirements are being compared and a regulatory framework for consultation is being established. It is HC's intent to have regulations ready to be published in CG 1 by fall 2003. More information can be found at their website at www.hc-sc.gc.ca/ear-ree.

4.2 National Placebo Initiative

An executive summary of the National Conference on the Appropriate Use of Placebos in Clinical Trials (March 22-23, 2002 in Ottawa) was distributed. P. Huston gave an overview of the progress to date, plans for 2002-03 and the future challenges. The aim is to find common ground and consensus building through probing beliefs of both research ethics and regulatory guidelines. The ACM commended Pat on her process of objectively looking at evidence and assumptions. More information can be found at www.cihr-irsc.gc.ca/services/forums/placebo/index_e.shtml.

4.3 Regulator's Role in Biodefense

Dr. Peterson described the regulator's role in biodefence. Mechanisms in the *Food and Drugs Act* currently available to the regulator to approve drugs are clinical trials, Notice of Compliance for new drugs and the Special Access Programme. These may not be suitable or adequate to provide access to drugs that would treat, reduce or prevent the toxicity of chemical, biological, radiological and nuclear substances. Options are being considered that would enable Health Canada to respond more quickly and effectively to emergency events. TPD heard comments from the ACM on the positive nature of this initiative and indicated an interest in receiving updates as progress is made. These include consideration of the regulator's role, challenges of meeting public health security needs in the event of a bioterrorist event and the challenges of considering drug submissions that do not fit our current Act and regulations.

4.4 Information Management Renewal

A. Butterfield provided the ACM with an overview of the status of TPD's knowledge management projects and the strategy for renewal. An action plan will be developed for phasing in of e-review, guided by an inter-directorate Steering Committee. Needs and gap analysis relative to the prototype E-SAP and e-CTA applications have been completed, and the decision taken to discontinue further development. Depending on the conclusions regarding phasing of e-review, an alternative application for e-CTA may be developed using standard tools. Priority will also be given to developing an electronic application to support SAP. A date for accepting submissions electronically in Common Technical Document format (eCTD) is not yet defined, but will likely be in July 2003. The TPD website is undergoing a facelift and updating.

The ACM members commented that they have experienced difficulty in successfully using Health Canada's search engines. It was proposed that it is not helpful to put documents in the "what's new" category if only the name has changed; this should be done when there is content change.

4.5 TPD Strategic Plan

Mike Ward and Naheed Israeli provided a report on the February 2002 extended management retreat on strategic planning. Themes, priority areas and linkages were identified and trends and issues were named within the context of the key drivers.

The ACM participated in an interactive brainstorming session with the presenters to further define issues:

- Demographics - shift in types of therapeutic products used; use in smaller populations; targeted use; shorter clinical trials; larger volume of products submitted; anti-aging bias leads to new products (Botox for seniors); 100+ years of healthy living; sophistication in understanding of chronic illnesses which can lead to an increase in sophistication of self use kits for diagnosis; more patient involvement in what goes into one's body; complexity of many microtherapies interacting with each other; smart medical devices that blend science with IT; blending of biologics and drugs
- Environment - impact of environment on natural immunity - disinfectants, closed environments lead to increase in allergy and asthma; need to manage the chemicals we put into environment by targeting; sensitivity of measurement identifies more environmental contaminants; impact vs probability as criteria for developing strategy; risk management strategy important; public expectations and perceptions: feeling vs being healthy
- Economics: what you can control, who takes on accountability; globalization issue driven from productivity, innovation, attracting growth; anti harmonization movement;
- Science and Technology: conditional approval of drugs - NOC/C could become the norm; smart technology for internet empowers consumer; disruptive technologies replacing old ways of doing things in the health care provision environment; product life cycles puts pressure on regulator and industry
- National and International Governance: challenge between failing to share sovereignty and the importance of doing so
- Perceptions, Beliefs, Values and Attitudes: changing demand for risk analysis and communication; major shift in public perception that all drugs are the same; interaction of health care processionals with their patients; behaviors should be considered in this category also - behaviors vs what people think you want to hear

All agreed that the TPD needs to do short, medium and long term strategic planning and must build in the flexibility to adopt plans easily.

DAY2 - May 9, 2002

4.6 Recap of Day 1 and Administration Issues

J. Blackburn will write a letter to the Deputy Minister of Health thanking him for attending the ACM dinner the previous evening and his candor.

4.7 Cost Recovery Policy

Andy Butterfield informed the ACM on the status of the Cost Recovery Initiative 2 (CRI-2) and sought feedback on key questions:

- if there is agreement in principle to increased fees to meet performance targets, what conditions should apply?
- what regulatory activities should be covered?
- what would be the definition of agreed service levels and associated costs?
- what would be the consequences for not meeting service levels?
- do stakeholders have concerns with the Drug Establishment Licencing fee structure sufficient to warrant developing a simplified approach?
- how do we make this a dynamic model that meets needs over time?
- what are the expectations regarding performance?

The target implementation date for revised drug fee regulations is October 2003, with medical device fee changes following in April 2004.

The existing Treasury Board "Cost Recovery and Charging Policy" the draft TB "External Charging Policy" were compared.

It was noted that the draft policy supports defining an agreed level of service during consultation on fees. The cost of delivering this level of service would then be the basis for the proposed fees. The TPD assume that there would be certain conditions for stakeholder support for this, including: accountability for performance; costs based on efficient processes; transparency of costing; and, clear allocation of revenue to activities for which it was charged.

The HPFB intend to ensure that any fee increase is not linked to further decreases in appropriation funding.

The current fees are based on costing done between 1994 and 1998 and have not changed, while cost of operations and salaries have gone up. Revision to bring fees into line with costs is clearly required. Health Canada will be changing its time tracking of reviews to ensure an increase in fees has a clear identifiable link to improved review time. New considerations include an increase in post market activities, which are now handled elsewhere in the Branch, and cost effectiveness.

ACM comments varied, from complete agreement with the assumptions TPD have made regarding stakeholder conditions for supporting larger fees, to agreement with them in principle, but recognition that financial consequences for not meeting review targets could be problematic. It was suggested that TPD canvas members via e-mail to obtain further comments.

4.8 Drug Investigation and Children

Dr. MacLeod reported on the April 26-27 meeting in Ottawa sponsored by the Canadian Pediatric Society and CIHR. HC and academia were also in attendance. Communication with the Minister of Health last fall indicated that drug investigation and children was not a priority. There is concern regarding the inaction of HC on the question of a regulatory framework for drug investigation in Canadian children. The Best Pharmaceuticals for Children Act in the US has modernized approaches in this area. In Canada, off label use of pharmaceuticals in children makes proactive studies imperative. Dr. McLeod follow up with writing the appropriate authorities and identifying a research niche in Canada to bring this forward.

4.9 Regulation of Natural Health Products

Micheline Ho of SMAB gave presentation on TPD's responsibilities in the regulation of natural health products (NHP). It was clarified that the decision to do a detailed risk assessment on AR reports either in Canada or from other countries depends on the number of cases and severity of symptoms as determined in MHPD. They will be also be actively looking at NHP interactions with other drugs. A disease software scanning capability (Global Public Health Information Network) exists within HC and this could be modified to include drug names. Product licence holders are required to report serious ARs to HC within 15 days.

Philip Waddington presented on the development of regulations for NHPs. They are guided by advice from consultations and external advisory committee. Further details can be found on the website at http://www.hc-sc.gc.ca/hpb/onhp/. Under the *Food and Drugs Act*, these products will be a subset of drugs. All NHPs will fall under the *Natural Health Products Regulations*. Ingredient-based product monographs are being developed. Claims will be allowed with a range of Standards of Evidence (SOE) relative to risk of the product and treatment. The proposed SOE range from traditional references to clinical trial. This is similar to the current situation within TPD, where claims for herbs can be made based on traditional or scientific references. However, the new Regulations should help consumers know the basis of the information upon which claims are made for these products.

Issues discussed included site licencing, ARs, public perception, safety, ethnic use of NHPs, risk of replacing other standard forms of therapy and international harmonization. It was acknowledged that research into the metabolic processes of drug/NHP interaction is needed rather than picking this up through ARs. Label warnings for these potential interactions should accompany both the drug and NHP.

Dr. Blackburn concluded by stating that NHPs are of great interest to the ACM and they would like to invite Mr. Waddington back in the future.

5. Tabled Reports

The following reports were tabled for the information of members. There were no presentations. Members identified that further discussion was desired on 5.2.

5.1 Product Monograph Project

5.2 Risk Communication

Bill Leslie reported that the report from the Communicating Drug Safety Information Workshop will be circulated to ACM members once the participants have approved the draft. He stated that a similar meeting in Montreal on Risk Communication dealt largely with the same issues. These were debated by the ACM and are summarized as follows:

- public perception of HC, need to be transparent
- how to get information out
- objective of the message
- audience
- level of trust in the messenger
- level of knowledge of the messenger
- public education
- impact of and relationship with the press
- definition of risk, public vs professional
- risk perception differences (gender, ethnic)
- risk tolerance of new vs old product
- positioning the message: positive vs negative
- evaluation of effectiveness of risk communication

It was recommended that HC could start a training program for science and medical reporting and continue producing fact sheets. The health professional was recognized as an important link to the patient and their help should be sought in communications.

5.3 Draft TOR Expert Advisory Panel on Anti-Infectives

5.4 Human Resources Initiative (Final Report)

5.5 Transparency

5.6 Quarterly Report

6. Workplace Health

6.1 TPD Workplace Health Issues Plan

Pauline Gaudry, chair of TPD's Morale and Recognition Committee, shared information on TPD's recognition process. She emphasized that the enthusiasm and energy brought about from TPD reorganization was being harnessed through Committee linkages, volunteering and social activities.

The ACM commended all on the good progress.

7.0 Next meetings: August 28 & 29, 2002
December 4 & 5, 2002

Meeting adjourned at 2:00 p.m.

Prepared by: Susan Tessier
Date: May 15/02
Revised: June 4/02