Contact: Fern Levine, Therapeutic Products Directorate
Telephone No.: (613) 954-9479

MEETING NOTES
ADVISORY COMMITTEE ON MANAGEMENT

THERAPEUTIC PRODUCTS DIRECTORATE (TPD), BIOLOGICS AND GENETIC THERAPIES DIRECTORATE (BGTD), INSPECTORATE

TPD Boardroom
Holland Cross, Tower B, 1600 Scott Street
Ottawa, Ontario
May 9 - 10, 2001

Members:	Jim Blackburn (Chair) Andrea Baumann John Blatherwick Robert Goyer Ruby Grymonpre Mitchell Levine Stuart MacLeod Kenneth Michalko Brenda Nunns-Shoemaker John Parks Jack Rosentreter Bonnie Salsman John Stewart Pamela Zabel	**Secretariat:** OSPCQ **Presenters:**	Robert Peterson Fern Levine Ross Duncan Julia Hill Jean Lambert Eric Ormsby
Regrets:	Luis Barreto Malcolm Seath Beverley Townsend	**Observers:**	Lynn Bernard Dennis Brodie Vicky Hogan Marion Law David Clapin (Wed. a.m.) Danièle Dionne

1. Opening Remarks *(Jim Blackburn)*

Dr. Blackburn welcomed everyone and initiated a roundtable of introductions.

Dr. Peterson introduced **Lynn Bernard** as the Associate Director General for the Therapeutic Products Directorate and announced the following Management changes:
Marta Caris has accepted an assignment in the Healthy Environments and Consumer Safety Branch (HECS);
Dr. Chris Turner is the Acting Director for the Bureau of Pharmaceutical Assessment (BPA);
Vicky Hogan is the Acting Director for the Bureau of Licensed Product Assessment (BLPA).

2. Review of Agenda and the January 17, 2001 Meeting Notes *(Jim Blackburn)*

The meeting of January 2001 were approved as presented.
The following item was added to the agenda for May 10, 2001 time permitting:
10. Drug investigation and Children. Stuart MacLeod

3. Realignment - Update *(Robert Peterson / Julia Hill / Jean Lambert)*

Dr. Peterson updated members on the progress of re-alignment i.e. the creation of BGTD, TPD and the Inspectorate. A consultant has been hired to analyse the various options for ensuring that each Directorate has appropriate common services. This will involve sharing of some services and replication of others. This is expected to be complete by the end of June.
Realignment in TPD is currently focussing on examining and redesigning the structure of BPA. Staff will be involved in the process. Factors which may influence the final structure include international partnerships, the Common Technical Document with its 3 separate modules on Clinical (Clinical Sciences), Non-Clinical (Pharmaceutical Sciences Evaluation) and Chemistry & Manufacturing (Quality). New types of performance measures are also being developed.

There is also a need to review and determine the appropriate organizational structure of BLPA to better address our responsibility in post-market assessment and to realign with other Bureaux in TPD.

Julia Hill, Associate Director General presented the realignment update for the Biologics and Genetic Therapies Directorate (BGTD). The structure of the new Directorate will be announced July 1, 2001. There are currently 130 staff. It is anticipated that this number will increase to approximately 200 but this will depend on the outcome of a study of staffing needs for Biotechnology and Policy. It is hoped that a new Director General for BGTD will appointed within the next 6 months.

Jean Lambert, Director General provided an update on major activities for the Inspectorate. He stressed that the Inspectorate now provides services for the Branch. This new office currently has 178 staff. A Quality System - ISO Audit and Evaluation has been completed, with minor changes accreditation is expected by end of 2001. The development of processes, procedures and guidance documents are required before the Clinical Trials audit initiative can be implemented. With respect to MRA, the Inspectorate has the lead on negotiations with the EC and Australia as well as the Tripartite negotiations between Canada the USA and Mexico. However, the Department of Foreign Affairs and International Trade (DFAIT) will have the lead on any new MRA.

A short report on the Branch Planning Retreat was provided. The Branch strategic priorities are Risk Management, emphasis on horizontality, communication, human resources, capacity building and a focus on creating a National Program.

4. Project Updates *(Robert Peterson)*

A summary handout was provided on Cost Recovery, Performance Measurement Framework, the Transparency Initiative, the Quarterly Performance for Review, Clinical Trials, NOC/C-priority review, e-submissions and the Common Technical Document.

Clinical Trial Reform

It is expected that the Clinical Trials package will be signed off by the Minister within 3-4 weeks. The major impact of this proposed legislation will be a 30 day default for all IND submissions. This will require either a reallocation of existing resources or new resources. BPA has been staffing aggressively and are well positioned to manage this change in default time.

Medical Devices Bureau:

The new regulations are in place and functioning well.

Product Monograph

The new Product Monograph Guidelines (Sec. 1&2) should be drafted by November 2001. It is the intention then to introduce a pilot process to validate these guidelines. Certain legal and operational aspects determining ownership and dissemination of the Product Monograph are still under review.

Advisory Panel on Product Licensing Review Process *(Robert Goyer)*

The meeting of April 24-25, 2001 was reported. From the committee's perspective, the realignment is seen as a great opportunity to review the needs of TPD and identify how to assist and address some fundamental issues such as review time frames and lack of resources. However, the panel members are concerned and unsure of their role and the future of the panel given this organisational change.

Dr. Peterson explained that the original intention for creating the Panel was as a means to assist us in becoming more transparent and open. The TPD may need to work at making this Committee more effective. This could include a review of expectations, the membership, balancing the perspectives of all parties, and the issues to be addressed. Dr. Peterson emphasised the importance of having groups such as this and how government as a whole will need to increase interactions with Committees of this type to assist in increasing transparency of our processes and decision-making.

5. Maximizing and Extending the Use of Advisory Bodies *(Eric Ormsby - Presenter, Ross Duncan - facilitator)*

The TPD Management wants to explore maximising the use of external advisory bodies and the feasibility of extending their input to more "management/operational" issues in addition to the scientific expertise on which we rely currently .

To move this ahead a number of issues need to be addressed. These include: conflict of interest (perceived or real) criteria to determine when (when not) to involve advisory panels, accountability and timing for the ultimate decision, and cost associated with the management and logistics of panels.

Other comparable regulatory agencies have made and continue to make use of advisory bodies and, in the past, the Eastman and Gagnon Reports have recommended that a multidisciplinary expert review committee be set up.

There are many advantages to moving in this direction and it was agreed that would be beneficial to place emphasis on mechanisms to gain input to more operational issues as currently, with the existing expert advisory committees, scientific and clinical input is

well organised. This type of approach would provide a way to more closely involve the Provinces and other partners in our work and create a venue for better understanding of each role and provide the basis for broader based decision making. It would be useful to examine the EMEA model as there are parallels with our relationship with the provinces.

Following the discussion about perceptions around Conflict of Interest, the following considerations were identified:

- A standard form should be developed. Caution is required while developing this form to ensure that it does not result in loss of expertise.

- Full Disclosure by potential representatives is critical. The advice and input provided would then be judged within this context.

- The scope and composition of the Committee should be determined and the Terms of Reference should include the knowledge and skills required. For Expert Groups, the need to get the right people should be the highest priority.

Recommendations from ACM:

- Further explore the issue of using more external advisory bodies;
- Mandatory involvement of medical/scientific community - criteria need to be determined;
- the need for an advisory body to address new chemical entities was identified
- explore the EMEA model more fully and consider using this as a way to link federal and provincial responsibilities.

Action: Office of Science to review and incorporate ACM advice into an Issue Analysis to be discussed at a future meeting.

6. Discussion on briefing materials provided to the members

Members support the idea of having an orientation binder. In terms of providing material prior to the meeting, a one or two pager should suffice. If document is too long, a link to the website should be provided.

7. Challenges and Opportunities *(Robert Peterson/Dennis Brodie)*

The intent of this agenda item was for the ACM members to learn about and provide their opinion on the challenges and opportunities facing the TPD as a result of realignment, the strategic priorities of the Branch and a number of Government-wide initiatives.

Dr. Peterson initiated the discussion outlining a number of challenges specific to the **Review Process**. These include:

Budget allocations - targeted funds for specific activities may not be used for other purposes so additional funding is still required for initiatives such as Priority Review. BGTD currently has one-third of its submissions as Priority Review, whereas in BPA it's only 5 - 10%. The Priority Review Policy could be reviewed because Canadian criteria are different from other countries.

Cost Recovery - fees are being examined to evaluate fairness for the different submission types.

Default periods - 30-day default is the shortest default time that can be handled for Notifiable Changes and IND.

Generics - Great impact on health care costs re: provincial formularies. How could cost savings be used to provide more resources for approving New Drugs.

Prescription to Non-prescription switches - new guideline developed and implemented to make it more timely. This guideline facilitates a more timely review of the information which results in quicker market access benefiting both producers and consumers.

Priority Setting - There are legal and policy implications for assigning submission priority levels.

Priority Review Policy, Impact on Public Good - this is an opportunity to review the Priority Review Policy to examine how the Canadian criteria differ from those of other countries and if changes were made, how they would have an impact on both human and financial resources. If regulatory changes are needed, it could take 1-2 years to take effect.

Dennis Brodie/Marion Law initiated a discussion on specific government priorities that the TPD also has to manage, such as transparency, government on line, workplace health etc.

Additional Agenda Item: Roles and Future of ACM:

The ACM members requested this item be added to the agenda as a number of issues need to be addressed. These issues included participation and attendance by Directorate senior management, process, improvement related to the meeting management, criteria for issues brought forward and role of the ACM in the future, i.e. advising TPD, the Inspectorate and BGTD or just TPD and the link with the Branch.

The members of ACM indicated that they want to focus on critical issues that impact on the Directorate and limit these issues to only a few in order to follow progress and measure success. This influences the role of the committee and it was discussed that the committee should assume a more strategic focus and could become more of an advocate for the Directorate. Management and members share a commitment to process improvements and a clearly defined, mutually acceptable role for the ACM.

Action: The TPD management team will discuss and suggest process improvements including identification of issues to bring to the committee, clearly identified focus for each issue, expected deliverables and appropriate background information. The new approach will be shared with committee for approval. Both the management and ACM will discuss their vision for the ACM and report back at the next meeting.

8. Cisapride Inquest Recommendations *(Robert Peterson)*

Dr. Peterson recapped his presentation on the QT Prolongation to the Science Advisory Board. The intent of the presentation to the Science Advisory Board (SAB) was to emphasise that the situation resulting in the death of Vanessa Young is not just an issue about Cisapride, but one that extends to include other drugs and, therefore, would possibly result in other similar situations in certain members of the population who have a genetic predisposition to sudden cardiac death.

This information illustrates the very complex nature of this case and the wide-reaching issues. With respect to the recommendations of the jury, an internal TPD steering group has been set up to manage TPD's response to the recommendations. A project plan and action plan have been developed and approved. TPD will move ahead to address the recommendations that are its responsibility and, in fact are in a good position as work is already underway which will address issues such as patient information, more timely risk communication, adverse event reporting.

The Project Plan and Action Plan will be forwarded to ACM.

Action: OSPCQ to forward information to ACM members.

9. Discussion on Article: Tales from the Other Drug Wars *(Robert Peterson)*

This item was discussed very briefly. It was agreed that the article did not receive the attention that was previously anticipated and therefore as yet there have been no negative repercussions. In addition, some members commented that pursuing this issue further may not be appropriate for the ACM.

10. Drug Investigation and Children *(S. MacLeod)*

Dr. MacLeod reported that clinical studies in children are improving and that the US is heavily involved with this initiative. Canada is lagging behind in this area and the larger issue about whether Canada should continue to be a bystander rather than participant needs to be addressed. In order for this to move ahead, drug companies need to be provided with incentives to become involved.

The pharmaceutical sector recognises this is an important issue as there is limited dosage information for children; and therefore, most prescribing information is technically off-label use.

Dr. MacLeod proposed that this issue should be brought forward to the next ACM for more in-depth discussion to determine if the TPD and the ACM could play a more proactive role.

Action: *Dr. MacLeod to provide more information.*

11. Other Issues Arising for possible discussion at future meetings:

Antimicrobial Drug Resistance: What is the TPD/BGTD responsibility for requesting information on this?

Ethics of Placebo Control use in Clinical Trials. Patients should not be placed at risk. The Helsinki Accord was recently reaffirmed and is endorsed in an ICH document (ICH-E10 or E11). The recommendation is that comparative studies should be performed instead of using placebo. Dr. Peterson has been discussing this issue with Alan Bernstein, President, CIHR, with the intention of organizing a joint Health Canada - CIHR workshop in the early fall to discuss this issue. Background documents will be available.

Action: Dr. Peterson to provide documents when available.

12. Next meeting: August 22-23, 2001 (10:00 am start on August 22nd)
TPD Boardroom, Room 2048, Holland Cross, Tower B
1600 Scott Street

Original signed by

Jim Blackburn
Chairperson