Health Canada Santé Canada

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HEALTH PRODUCTS AND FOOD BRANCH (HPFB)

SUMMARY BASIS OF DECISION (SBD) EXTERNAL CONSULTATION

June 10-11, 2004

CONSULTATION REPORT

On June 10 and 11, 2004, Health Canada hosted a multi-stakeholder consultative workshop on a key transparency initiative entitled Summary Basis of Decision (SBD). The workshop engaged interested parties, including patient and consumer groups, to provide input into the direction of the SBD initiative as well as the proposed content, format and publication of SBD documents. As proposed, SBDs would be targeted to the "informed public" (i.e., use technical language), and would outline the scientific and benefit/risk based decisions that factor into Health Canada's decisions to grant market authorization for a drug or medical device. A phased implementation strategy is proposed. The consultative workshop included presentations, table discussions, breakouts and plenary reporting.

This report provides an overview of the workshop, with a focus on the key messages and advice from participants.

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EXECUTIVE SUMMARY

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Participant Feedback – Key Messages and Advice

Cascading approach to information

The SBD should provide linkages to other documents and sources in order to facilitate the "drilling down" to additional information by individual users to meet their needs. Such information might include the product monograph, pre-clinical and clinical studies, expertise of reviewers, data from other jurisdictions, adverse reaction reports, post marketing information, Health Canada Advisories and other studies and reports.

SBD content – full disclosure yet not duplicating other sources

The SBD should aim to provide a full accounting of the rationale for approval, thereby providing accountability for regulatory decisions, yet remain respectful of proprietary information. The SBD should complement, not duplicate, information available through other sources.

Internet accessibility

The preferred method of distribution is the Internet through a user-friendly website, with the option of mail-outs/faxes as required. Internet publication would also provide the means to include links to other sources.

Reconsider the target audience of "informed public"

The SBD should be focused on meeting consumer needs by providing meaningful and relevant information. The target audience of "informed public" was seen by some participants to be too narrow. These participants suggested that the target audience could be expanded by use of lay language and inclusion of a glossary of terms and definitions, explanations of the regulatory process, and other reader aides.

Stakeholder satisfaction

There was acknowledgement that it will likely not be possible to create a document that satisfies all needs of all stakeholders. Instead, the SBD could be designed as a "tiered document" with varying levels of scientific detail related to the decision. The provision of links to other sources of further information, such as post-market information, data from other jurisdictions, adverse drug reaction reports, etc., would also help satisfy varying stakeholder needs.

Adequate resources essential

The production of the SBD should not impact the timelines of the review process or efforts to reduce the backlog of submissions. Resources, including internal capacity for SBD production, must be sustainable over the long term.

Publish SBDs for denied and withdrawn submissions

SBDs for denied and withdrawn submissions/applications and non-approved uses (for claims submitted) should be published. This would include information about non-approved off-label drug use, approved uses in other jurisdictions, failed clinical studies, etc. Publication of reasons for a negative decision are particularly important in cases where the same drug or device is available in another jurisdiction.

Timing of Publication of SBD

There was support for publishing the SBD at the time of Notice of Compliance (NOC) issuance, rather than at time of marketing, as the SBD is related to the approval of a product and should not be associated with its marketing. There was also support for issuing the SBD at the time of market notification as not all products receiving approval are subsequently marketed for reasons related to competition, confidentiality and unseen delays. It was further suggested that if the SBD is not published at the time of NOC issuance, a one-page summary or fact sheet should be issued. The SBD should follow within an appropriate time frame.

Closing Remarks from Dr. Robert Peterson, Director General, Therapeutic Products Directorate

Dr. Peterson noted that, from Health Canada's perspective, the expectations of the consultation had been fully met. Participants have a better understanding of the SBD, both its potential and limitations, and its overall objective to increase transparency by placing relevant decision-making information in the public domain.

He emphasized that Health Canada is committed to ongoing stakeholder consultation and to achieving a collegial and cooperative approach that respects the commercial interests of sponsors. Health Canada will continue to receive and respond to comments on how the SBD can best meet these goals and the needs of Canadians.

INTRODUCTION

Transparency is fundamental to good regulatory practice and is a clear expectation of the Canadian public. Health Canada is committed to enhancing the transparency of the regulatory review process for drugs and medical devices. As part of this commitment, Health Canada will be publishing Summary Basis of Decision (SBD) documents, in a phased approach.

A Summary Basis of Decision outlines the scientific and benefit/risk based decisions that factor into Health Canada's decision to grant market authorization for a drug or medical device. An SBD includes the basis of decisions related to regulatory, safety, efficacy and quality considerations. Proposed to be written in technical language for those interested in Health Canada decision-making, SBDs are intended to complement other sources of information, including operator's manuals for devices, package inserts and the consumer section of product monographs for drugs. As a result, SBDs will provide Canadian healthcare professionals and consumers with more information to support informed treatment choices.

Health Canada is proposing a phased implementation strategy to support the SBD initiative. Initially, the documents would be publicly disclosed for market authorizations related to New Drug Submissions (NDSs) for New Active Substances (NASs) and a subset of Class IV medical device applications. The second and third phases of implementation would encompass additional drug submissions and medical device application types, including supplemental new drug submissions and an expanded set of Class IV device applications.

On June 10 and 11, 2004, Health Canada hosted a multi-stakeholder consultative workshop for interested parties, including patient and consumer groups, to provide input into the direction of the SBD initiative as well as the proposed content, format and publication timing of SBD documents.

This report provides an overview of the workshop, with a focus on the key messages and advice from participants.

WELCOMING REMARKS

Dr. Karen Dodds
Associate Assistant Deputy Minister,
Health Products and Food Branch

Dr. Dodds welcomed participants to this important workshop. She noted that the consultation has been designed to provide an opportunity for Health Canada to share its intentions around the Summary Basis of Decision initiative. More importantly, the workshop will enable interested parties to provide input and advice to Health Canada and have their opinions heard on how we can best provide information to Canadians.

There are many challenges facing both Health Canada and Canadians around health information and informed decisions. Scientific discovery is occurring at an incredible pace, and globalization, while it increases our ability to share information, also raises the potential for the transmission of diseases.

Stakeholders and consumers are increasingly well informed and are seeking a new, more partnership-like position with regulators and government. Health Canada is responding with a commitment to transparency and enhanced inclusiveness, strengthened relationships with stakeholder and the public, and cultivation of a culture of openness, accountability, respect and collaboration. The Summary Basis of Decision initiative is an example of how the Health Products and Food Branch is ensuring that its policy development is inclusive and its decision-making, transparent.

Understanding, incorporating and responding to the opinions and needs of citizens and stakeholders is a critical success factor for regulating effectively in the public interest and maintaining and strengthening public confidence in the regulatory system for safety, efficacy and quality of health products. Industry, government, and stakeholders all have roles to play in ensuring the regulatory system works for all Canadians. This multi-stakeholder consultation workshop brings together health care providers, patient and consumer organizations, industry and members of the academic, research and regulatory communities to interact and exchange ideas on the process and outcomes of the SBD initiative. This input will be considered as Health Canada moves forward on the initiative, leading to improved health outcomes for all Canadians.

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SUMMARIES OF PRESENTATIONS

Therapeutic Access Strategy Overview

Abby Hoffman, TAS Coordinator, HBFB

The Therapeutic Access Strategy (TAS) aims to improve the timely availability of safe and effective therapeutic products for Canadians. TAS addresses the full range of factors which influence access to therapeutic products by Canadians, in order to improve health through better access to safe, effective, affordable and appropriately used therapeutic products. It incorporates new business practices to improve efficiency, timeliness and quality, processes to facilitate internal culture change, and rethinking on priorities, ways of working, and leveraging change in stakeholder roles. A key element of the strategy is improved provision of information to consumers and health providers.

TAS is designed around two tracks. Track 1 focuses on near term business improvements to ensure timely decisions while maintaining standards of quality and safety, priority on pre-market processes and post market activities. Track 2 focuses on longer term, broader issues, including health system sustainability; international regulatory cooperation; innovation; post-market surveillance; transparency, openness and accountability; and operational capacity and efficiency, including ensuring adequate science and regulatory human resources capacity.

Placing the Demand – A Consumer's Perspective

Colleen Fuller, Pharmawatch

PharmaWatch, a non-profit advocacy group, is involved in post-market surveillance of drugs and reporting of adverse drug reactions. The organization believes that patients and consumers must play a central role in prescription drug safety in Canada and that they can provide information and insight that contributes to the effective and safe use of medicines. Reporting by patients and consumers can provide an early warning signal to regulators, manufacturers, physicians, health professionals and other consumers. The goal of PharmaWatch is to highlight and validate consumer experiences and heighten consumer involvement in adverse drug reaction reporting and to raise public awareness about the role of consumers/patients in reporting adverse drug reactions.

Canadian consumers have access to far too little information about the prescription drugs they use. At the same time, consumers want influence over regulatory policy and approval process.

Increased transparency and greater consumer involvement in HPFB processes is welcomed by PharmaWatch. However, the current draft proposal for SBD falls short of expectations. High standards of transparency are required to ensure high quality, complete information is available to the public. There is a need to provide an expressed commitment to meaningful and effective public involvement, for example through participation on SBD advisory panels and, most importantly, the building of capacity to participate on these panels and other groups.

Transparency is crucial in the approval process and also in post market surveillance. ADR reporting and advertising are two areas where transparency needs to improve, along with public awareness of ADR reporting.

Background and Overview of the SBD Initiative

Tara Bower, SBD Project Lead, TPD

SBD represents a key transparency initiative for HPFB and directly responds to the public's increased demand for information on the benefits and risks of therapeutic products. SBDs will provide a factual and objective presentation of the scientific and regulatory basis for a decision, in language that is written to the intended audience of the "informed public." They will be accurate reflections of the evaluation reports written in a clear and concise manner that will complement, not duplicate, the product monograph (PM).

Templates have been developed for drugs and medical devices and are currently being tested in pilot exercises. Health Canada has consulted with the European Medicines Agency (EMEA) and U.S. Food and Drug Administration (FDA) on the development and implementation of similar documents. Phase I of the initiative is on track to begin in the fall of 2004, which will see the drafting of SBDs for New Drug Submissions (NDSs) related to New Active Substances (NASs) and for a subset of Class IV devices.

Stakeholder feedback is being actively sought on various aspects and principles related to the process and content of SBDs, and will be used in the development of revised templates. This consultation/workshop session aims to provide participants with the opportunity to gain a mutual understanding of the perspectives of a wide range of stakeholders, as well as increased understanding of their role in the process and how feedback will be addressed. Organizers are also seeking to identify issues for future consultations.

Industry Perspectives on Pilot Exercises

Alison Maloney, AstraZeneca Canada

The product used in the pilot exercise was Crestor (rosuvastatin calcium), a medication to reduce cholesterol that is manufactured by AstraZeneca Canada.

Overall, AstraZeneca found the pilot project to be a positive experience and Health Canada very open to collaboration and suggestions for improvement. The SBD will provide a valuable information resource for Canadians. It is more concise and easier to understand than the similar FDA and EMEA documents, while being respectful of the Access to Information (ATI) Act, which protects proprietary information. There are still issues to be considered, including questions concerning timing and resources, relevance to marketing (PAAB and Rx&D Code), ATI requests and generic involvement.

A number of areas for improvement on the SBD process were evident from the pilot exercise. The SBD should be written during the product review and data cut offs should be clearly defined. There is a need for a clear communication plan to all stakeholders. The language used should be either easily understood by all stakeholders, or the consumer section of the product monograph should be appended to the document.

Alison Vanlerberghe, Genzyme Canada

The product used in the pilot exercise was Fabrazyme (agalsidase beta), a biologic produced by Genzyme Corporation for use in the treatment of Fabry disease, a rare genetic disorder. Fabrazyme, which was commercialized as of April 2004, has been provided through the Special Access Program and formal clinical trials since 2001.

Genzyme found the SBD for Fabrazyme to be a credible document that presents information clearly and without compromising proprietary data. The document reflects the review by Health Canada and Health Canada's "ownership" of the process, and provides a clear analysis of the benefit/risk balance of the therapy.

For health care providers, the SBD provides a balanced assessment of the benefits and risk of treatment with Fabrazyme and highlights patient management tools. For members of the public, the SBD may increase awareness of the disease and thereby promote early diagnosis and treatment.

Transparency at the EMEA: Current Status and New Initiatives

Noël Wathion and Martin Harvey-Allchurch, EMEA

The European Medicines Agency (EMEA) is a decentralised body of the European Union. It has its headquarters in London since January 1995. The EMEA works as a network, bringing together the scientific resources of the Member States to ensure the highest level of evaluation and supervision of medicines in Europe.

New legislation was introduced in 2003 to ensure the widest access to EMEA documents, while protecting proprietary information. EMEA documents are classified as either confidential, restricted or public. Requests for documents are made in writing to the EMEA Executive Director, who must provide justification in cases where access is either partially or completely denied.

The development and implementation of initiatives to increase transparency are important to the EMEA and include its website (where all public documents are published), European Public Assessment Reports (EPARs), news releases, position statements, committee guidelines, and annual reports.

The EPAR is issued following a decision to granting market authorization of a specific medicinal product. It provides an overview of the regulatory and procedural aspects of the review, documentation provided by the applicant, and the scientific discussion and basis for the decision. The EPAR is published to the website approximately three months following the decision. As of November 2005, EPARs will also be prepared for negative decisions.

The Summary of Opinions (SMOPs) document was introduced to provide information on the decision in a more timely manner. It is a one-page document that provides a summary of the main benefits/advantages of the product along with any potential risks and side effects. The SMOP is issued directly following a positive or negative committee decision for market authorization. There is currently no public release of information when a product is removed from review by a sponsor (although this may be changing in the future).

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New EMEA transparency policy measures for 2004 include improvements to the website, inclusion of more information on divergent opinions and inspections in the EPARs, enhancements to referral procedures and existing communication tools as well as preparation of question and answer documents to assist industry and regulators, and the development of new communication tools and mechanisms. Challenges facing the organization's efforts to improve transparency and access to documents include translation considerations (documents need to be translated into 19 languages).

Drug Information and Drug Reviews: A Medical Community Perspective

Millicent Toombs, Canadian Medical Association

Canadian physicians gain product information through product monographs, PDA applications and other sources. Problems with these sources include lack of user friendliness, difficulty in finding needed information, and issues about whether information is current.

The CMA supports a drug review system that provides decisions in as timely a manner as possible while ensuring improved health outcomes and safety of the drug supply. It supports cooperative agreements with other jurisdictions for drug reviews while retaining final Canadian authority. Openness and transparency, the opportunity for stakeholder input, updates on review status, information about what is awaiting approval, and post market surveillance are all extremely important to a safe, effective and fair regulatory approach.

To be relevant, the SBD should timely and include the clinical bases for decision along with benefit/risk assessment information. To be useful, the SBD should not be overly lengthy due to the limited time physicians have at their disposal to spend reading.

Health Canada Proposal for Phased SBD Implementation

Tara Bower, SBD Project Lead, TPD

Health Canada is proposing that the SBD implementation take a three-phase approach. In Phase 1, SBDs would be issued for all positive decisions on New Drug Submissions relating to New Active Substances as well as a subset of Class IV medical devices. Phase 1 would include an evaluation period (estimated to be 6 to 12 months), with feedback and lessons learned applied to subsequent phases as appropriate.

In Phase 2, SBDs would be issued for all positive decisions on all submissions for new drugs (NDSs, SNDSs, ANDSs, and SANDSs) as well as an expanded set of Class IV device applications. Phase 2 may see the inclusion of additional information as the interpretation of confidential information is reviewed, pending extensive stakeholder consultation. Phase 2 would also include an appropriate evaluation period.

Phase 3 would look at building closer ties with Good Review Practices and E-submission efforts to facilitate the preparation of the SBDs documents as the review progresses. In addition, an assessment and re-evaluation into publication of currently confidential information, including disclosure of negative outcomes or withdrawals, would be explored (consistent with international shifts and changing regulatory boundaries).

The phased approach is recommended to minimize impact on review resources and provide opportunity for evaluation and stakeholder feedback to be incorporated into subsequent phases and processes. To accommodate operational and resource concerns, the use of scientific writers has been proposed to complete the documents (which would be vetted by internal reviewers for accuracy) in early implementation phases.

Perspectives on Confidential Information

Serge Durand, Proprietary and Scientific Information Assessment Section, TPD

The purpose of the Access to Information (ATI) Act is to extend the present laws of Canada to provide a right of access to information in records under the control of government institutions in accordance with the principle that government information should be available to the public. The Act is intended to complement and not replace existing procedures for access to government information. All records under the control of the Federal Government may be requested under the ATI Act.

An ATI request coming into TPD could include the following records: product monographs, operator's manuals, submission indices, comprehensive summaries, medical device applications and reviewer's comments and correspondence.

Some types of information are considered confidential – however, the definition of "confidential" is continually evolving. The current definition (as defined by the Act) relates to "trade secrets of a third party," which may include financial, commercial, scientific or technical information such as clinical trial applications, submissions under review, details of the synthesis and testing for the drug product and Drug Master Files and their holders. Information that meets this definition and which is held by Health Canada must remain confidential. However, once information is made public (for example, through a manufacturer's press release or announcement), it remains public from that point forward. In addition, information made public in other jurisdictions is public in Canada.

The ATI process can be long and resource consuming. The SBD will supplement existing procedures for access to government information. SBDs are proposed to focus on factors contributing significantly to Health Canada's decision to grant market authorization to a product and may include Health Canada's analysis of quality, pre-market adverse event reports and pre-clinical and clinical data. In addition, SBDs will include submission milestones and other information. Expected outcomes of the SBD are a decrease in the perceived secretive nature of the review process and a reduction in the number of ATI requests.

SUMMARIES OF PARTICIPANT DISCUSSIONS AND FEEDBACK

Discussion I:

Focus on the Guiding Principles and Intended Audience

Context

The SBD is designed to reflect the following guiding principles.

The SBD will:

- Be written for intended audience of the "informed public."
- Be a factual and objective presentation of the scientific and regulatory basis of the decision.
- Be an accurate reflection of the evaluation reports.
- Be clear and concise.
- Complement, not duplicate, the Product Monograph.
- Be available in English and French.
- Be easily retrievable and available in a timely manner.
- Be of standardized format and use standardized wording wherever possible.
- Not be resource intensive for reviewers.
- Disclose as much information as possible, respecting the boundaries of what is currently considered to be proprietary information.

Participants were invited to consider these principles in terms of the following questions:

- What would make the SBD document a success for your organization?
- What general principles would you like to see adhered to?

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Participant Feedback and Advice

Question I:
What would make the SBD document a success for your organization?

Participants noted that their comments pertain to SBDs for drugs, rather than medical devices, as they felt there was insufficient information to provide a meaningful response to the question.

There was general agreement that the SBD should take a cascading or tiered approach to information. There is a wide range of potential users, with wide ranging levels of technical understanding. For SBD to meet these wide ranging needs, it should provide linkages to enable users to "drill down" to additional information and data, including (but not limited to): product monographs, pre-clinical and clinical studies, expertise of reviewers, information from other jurisdictions, adverse reaction reports, post marketing information, other studies and reports. The SBD should be current through the provision of updates to information. However, it was suggested that updates be provided as addendums to the original SBD, rather that issuing a revised SBD.

Concern was raised regarding the term "informed public" and the number of people to which this label would apply. Some participants cautioned that the SBD appears to be addressing the need of the regulator for transparency and industry for accountability. The SBD should be focused on meeting patient needs by providing meaningful and relevant information. Such information should include the proposed elements on safety, toxicity, conditions attached to approval, and exclusion regarding use by certain populations, but should also extend further to include adverse drug reactions.

Participants suggested that the SBD include background information for readers on what is required of a sponsor in a submission, the process and the expertise of reviewers. This would help provide the context for the SBD. The SBD should also include areas that the sponsor did not address in the submission and the rationale for the exclusion's acceptance by Health Canada.

Participants noted that the SBD would be more useful if full pre-clinical and clinical data were provided, including information on why clinical trials were stopped and why a submission was withdrawn or not approved. Some participants indicated that the SBD would *only* be useful if these data are provided. From an industry perspective, there is a need to clearly differentiate between the SBD and the product monograph in terms of content and intent.

Other comments and suggestions included:

- Clarity is needed around terms, for example, transparency, public awareness, informed public.
- The SBD should complement, not duplicate, information available through other sources.
- Include Section 3 (consumer section) of the product monograph.
- SBD to be a "living document" that communicates information on an ongoing basis as it becomes available.
- The SBD should minimize ATI requests.
- It will only be a success if it is well-known and easily accessible.

Question 2: What general principles would you like to see adhered to?

There was general agreement that the principles proposed by Health Canada are appropriate.

Participants emphasized that the SBD should aim to provide a full accounting of the rationale for approval, thereby providing accountability for regulatory decisions. Most importantly, the production of the SBD should not impact the timelines of the review process. In this connection, it is important that adequate resources be provided to enable the production and publication of SBDs without drawing on review resources.

There was concern about the level of language to be used. If language is too technical, the SBD may not be meaningful for consumers. Many participants would prefer lay language, noting that this is possible through the use of skilled science writers and appropriate knowledge transfer. Again, a layered approach to information would address language barriers by providing more technical information for those seeking that level.

Other comments included:

- The SBD should clearly be a Health Canada document (i.e., not an industry document).
- The overarching objective should be to enable health care providers with the information necessary to provide the best information to patients.

Discussion 2:
Focus on the SBD Template

Context

To set the context for the second table discussion, Laura Freeman, Office of Business Transformation, TPD, provided an overview of the SBD template. There are two templates, one for drugs and one for medical devices, and each is divided into three major sections. For drugs, these sections are Product and Submission Information; Scientific and Regulatory Basis for Decision; and Submission Milestones. For medical devices, the sections are: Device and Application Information; Scientific and Regulatory Basis for Decision; and Application Milestones.

In both templates, the main focus of the information to be provided are those pre-clinical and clinical studies that played a significant part in Health Canada's assessment and decision. The SBD also references the regulations that are reflected in the decision.

The templates provide a line-by-line description of what needs to be included for each sub-section, sample wording, and areas where proprietary issues may need to be considered.

Participant Feedback and Advice

Template Sections on Pre-clinical and Clinical Basis for Decision (2.3, 2.4, 2.5)

Participants emphasized that any discussion on the appropriateness of the content of the template depends on the target audience for SBDs. This will impact on the level of information that is appropriate, as well as the type of language used.

There was general agreement that if the intent of the document is to illustrate the basis for the decision to approve a drug to an "informed public," then the content as reflected in the template is appropriate. It would be beneficial to include a "note to reader" stating that the document is intended for such an audience (i.e., clearly state that the document is not in lay language). Although the template provides suitable content for the "informed public," there are questions regarding the level of detail that will be provided. A direct tie-in with the product monograph would be useful.

The SBD, in its current proposed form, may not be able to meet the needs of all audiences. It will, however, provide a useful "stepping stone" to other information or to enable a patient to direct a health care provider toward other information.

If the SBD is intended to meet the needs of a broader base of readers (i.e., those without technical medical knowledge/understanding), participants suggested that the content also include an introduction that explains in lay language technical terms, the approval process, types of studies, clinical trial methodologies, etc., to set a context for the reader. Similarly, a summary, fact sheet or readers' guides aimed at specific audiences could be used to provide a simplified version of the information and major conclusions as well as sources of additional and/or more detailed information (e.g., other studies, other authors, detailed clinical data, specialized populations, indications for rare disorders, post market surveillance information, etc.). Other suggestions for providing clarification and ensuring a user-friendly document included a question and answer section, glossary and/or the use of square brackets within text to provide direction to more information or a definition. Participants cautioned that it is important that the document not become too cumbersome or unwieldy, or it will defeat its purpose.

There are specific information requirements that have been expressed by patient groups and which are important from a safety/pharmacological perspective. However, too much information could make the document less useful for other users. An appropriate balance needs to be found – although participants recognized that this is not an easy task. It was also noted that how the information is disseminated is as important as the content itself.

Participants noted that SBDs for withdrawn or rejected submissions/ applications and non-approved uses (for claims submitted) should also be published. This would include information about non-approved off label drug use, approved uses in other jurisdictions, failed clinical studies, etc. The SBD must provide information about why decisions occurred, including negative decisions and decisions that are different from those of other jurisdictions.

Other comments included:

- The template does not provide a "good fit" for radiopharmaceuticals. There may need to be specific categories for these types of drugs, which are mainly used for diagnostics.

- The subheadings, while providing guidance for the reader, may actually limit or restrict content.
- Include information about the credentials/areas of expertise of the reviewers and the standards and best practices that were followed (or not followed) and why.
- Include information from other jurisdictions as appropriate.
- Include the size and length of critical trials (through links to product monograph).
- Provide interpretations of data (explanations of why a result is good or bad), and indicate how data were weighted.
- Health Canada could help build the "informed public" through workshops or a "roadshow."
- Develop a registry of patients taking an approved drug to track adverse drug reactions, side effect and benefits over time (registry should be accessible to the public). Include information about the registry in the SBD.
- Use strong/consistent language (for example, "shall" not "should").

Template Section on Quality Basis for Decision (2.2)

Participants noted that there were questions raised about the intent of the section on quality and what the information would be used for, particularly in terms of how information on product quality relates to or differs from the information contained in the product monograph.

A number of significant concerns were raised around proprietary issues and the Access to Information Act, particularly around the level of detail that may be included. There may be greater proprietary issues related to non-approved submissions, rather than approved submissions.

Participants felt that the detail in the pilot examples was very general, resulting in limited added value for readers. However, this may be reflective of the type of products (i.e., more complex products will have more detailed information). Information related to the timelines of the review should also be provided in the SBD (start date, etc.).

Participants cautioned that it will likely not be possible to create a document that satisfies all needs of all stakeholders. Instead, the SBD could include links to further information or it could be designed as a "tiered document" with varying levels of detail.

There was support for re-ordering the SBD to provide an Executive Summary as the first item and to move the quality section after the pre-clinical and clinical sections.

Template for Medical Devices

Participants noted that it appears that the template is appropriate for the "informed public" and industry. However, greater understanding of the type of information consumers are looking for on medical devices is needed. Additional research should be undertaken to determine the information needs of consumers, and then the template for medical devices should be updated to reflect those needs. Additional consultations on SBD for medical devices are recommended by participants.

The SBD should clearly indicate what type of use the approval is based on (i.e., whether the approval is based on a device being used once or many times (single use devices vs. multiple use)). If multiple use of a single use device poses risk, this should be clearly stated.

Information related to sterilization methods needs to distinguish between sterilization done by the manufacturer, sterilization done by hospitals, and sterilization by users. There was also concern that sterilization may not eliminate all pathogens (e.g., prions). The SBD should identify that instructions for cleaning, which are the responsibility of the manufacturer, were reviewed by Health Canada and found to be acceptable. Risks related to re-using a device that has been improperly sterilized must be included.

A summary of clinical trials, in table format, would be useful. Data should include sites, patients, study design, and calibration as well as tests for statistical significance, fatal and non-fatal adverse events, total adverse events, and withdrawals due to adverse events. ISO standards or other references should be included. Data should also include failure rates (percentage of times) and type of failure in any pre-clinical and clinical trials.

Participants suggested that an explanation of the risk/benefit assessment (intent, terms of reference, etc.) be provided in lay language, with definitions of any technical terms. Include a summary of how benefit(s) relates to risk and how safety and quality reflect regulatory requirements.

Consumers are sensitive to the fact that they have very little information on medical devices. As SBDs are directed to the "informed public," participants recommended that a package insert/device manual, written in lay terms, be appended to the SBD.

Too much information is not recommended as the public will not read it. Participants recommended strengthening linkages to detailed information to satisfy needs for different audiences/consumers.

Other comments included:

- Official labeling should not duplicate the SBD document.
- For the pilot, use a device that is widely used (for example, pace maker).
- Information on the method of manufacturing is normally proprietary.
- Quality portion of the safety and effectiveness section of the SBD needs to have more detail.

Discussion 3:
Focus on Publication and Accessibility

Participants focused on the concerns and issues related to the timing and accessibility of SBDs.

Participant Feedback and Advice

There was a divergence of opinion on when the SBD should be published. Some participants felt that it should be timed to meet the date of market notification, rather than at time of Notification of Compliance. The Product Monograph should be disclosed at the same time. Reasons for preferring this timing included not all products receiving NOC are subsequently marketed, there may be patent issues that delay marketing, and competitive issues to be considered. Publication at market notification will also best manage patient expectations (until commercialization, there is no access anyway).

On the other hand, some participants felt that the SBD should not be related to the marketing of products, and therefore should be issued at the time of NOC. Another suggestion was to issue a fact sheet at time of NOC, and subsequently publish the full SBD within two weeks.

The aim should be to protect proprietary information while providing timely information and transparency, yet without impeding on review resources that may adversely affect the drug review process (i.e., lead to longer times for review). It was suggested that transparency would be increased by providing the opportunity for public hearings as part of the review process.

Some participants felt that manufacturers should have an opportunity to review and provide comment on the SBD prior to publication. It may also be beneficial to provide a period of time for consumer input to a draft version of the SBD.

The preferred method of distribution was the internet/web, with the option of mailouts/faxes to people without electronic access to the SBD. Internet publication would also provide the means to include links to other sources of information, including the manufacturer, post market information, subsequent changes, published clinical trials, reports and studies, documents from other jurisdictions, etc. Participants emphasized that the website used for the SBDs must be user friendly and not buried within the Health Canada site.

Other suggestions included:

- Use advertising to let people know SBDs are available.
- Take a proactive approach and notify interest groups (e.g., disease organizations, charities, etc.) and physicians when SBDs are issued.
- Include SBD (or website information) with product monograph, product insert or on label.
- Publish an annual directory of SBDs for libraries.
- Develop a subscribers' list for notification of SBDs by e-mail.

Discussion 4:
Focus on Perspectives on the Future

Participants discussed issues related to confidentiality, the scope of the proposed future SBD phases, negative decisions, and SBD content.

Negative Decisions

There was general agreement that information concerning negative decisions is important to health care providers and consumers. The term "negative decision" will need to be clearly defined. For example, was the entire submission denied, or just a portion?

Publication of reasons for a negative decision are particularly important in cases where the same drug or device is available in another jurisdiction – Canadians want to know why they are denied a therapy that is approved elsewhere. SBDs for negative decisions would also provide patients with

additional data for making informed decisions about therapy, for example, whether to take an off label prescription.

Similarly, interrupted or withdrawn submissions should also be disclosed through an SBD, especially those that were removed or stopped due to safety reasons. Participants noted that in some cases, a sponsor's decision to withdraw a submission may be based on business reasons, rather than issues related to safety or efficacy. In these cases, disclose may not be necessary or appropriate.

Proprietary Information

Participants noted that the SBD should aim to release as much information as necessary to meet its objectives and purpose. However, the SBD must respect the principles of the ATI Act. Confidentiality issues may arise around clinical data, so it will be important to establish the level of detail that will be included in the SBD and provide clarity around what is confidential and what is not.

There are also timing issues related to some information, particularly data related to clinical trials and future journal publication (journals may not accept data that has already been published).

Some participants would like to see a turnaround in the responsibility regarding confidential material that removes the need to request information by making all information automatically available, with the holders of information having to prove why it should not be released.

Stakeholder Input

Consultation with sponsors is acceptable, provided it does not impact on the impartiality or neutrality of the review process or cause delays in rendering decisions. Guidelines would be useful to help ensure stakeholder input is focused on factual information and to determine mutual agreement on what is considered proprietary.

Some participants felt that consumer involvement in the SBD process is not likely necessary.

It was suggested that a working group with broad stakeholder representation, including industry and patient groups, be established to provide formal input and feedback on the template design, SBD content, and to assist in the evaluation and lessons learned components of Phase I.

Use of Technical Writers

Participants noted that the use of outside technical writers would be acceptable, provided their work is reviewed by Health Canada staff. The role of technical writer would be to convey complex information in an understandable, user friendly manner.

Timing of Publication of SBD

If the SBD is published at the time of marketing rather than at the time of NOC, participants suggested that a one-page summary or fact sheet be issued (similar to the EMEA's Summary of Opinion), to provide information to interested parties immediately upon approval of a new product. The SBD should then be issued as quickly as possible. There should be as short a time as possible between reviewer reports and publication of the SBD.

SBD Content

Participants emphasized the importance of providing full and complete information in as timely as manner as possible. The SBD should include any and all information that the reviewers have relied upon in making the decision. This information does not have to be included in the SBD document itself, but must be available without barrier (i.e., it should not be necessary to go through the ATI Act to receive access). The use of the internet and links to further information, including links to product monograph, package insert, clinical trial data, external reviewer's reports, other jurisdictions, updates and post-market reports, is highly recommended and must be provide on a timely basis (when SBD is published).

Other comments included:

- Provide more detail in the quality section for devices.
- Include the timelines of the review.
- Include all indications, strengths and dosages that were sought, including those not approved.
- Source of any biological material used in medical devices.
- Quantitative list of non-medicinal ingredients (this is provided in the product monograph for biologics but not pharmaceuticals).
- Canada should be as open as U.S. in releasing information.

Discussion 5:
Focus on Participant Selected Topics

Participants had the opportunity to further explore topics of particular personal interest.

Target Audience

There continues to be concern that the target audience of "informed public" is too narrow. There are other populations who will also have a need for SBD information (examples include patients who may be informed or not informed; caregivers; healthcare providers; advocacy groups; charities and associations; private and public insurers; funders; provincial and territorial providers; manufacturers; and lawyers). It was suggested that further study (test marketing, focus groups) be undertaken to determine the most appropriate target audience, which will influence other decisions, such as level of language and detail to be used.

Participants again emphasized the appropriateness of designing a document that supports "drilling down" by users to the level of information desired.

Resources

Participants expressed a lack of confidence that SBD production would not impact on review resources. Products under review and those in the queue should not be delayed due to SBD publishing. Efforts to reduce the backlog must not be sidetracked. Health Canada will need to provide additional resources (reviewers) to ensure performance standards are met, taking into account the learning curve of reviewers and technical writers. An accurate estimate of the number of SBDs required will need to be made (participants were concerned with the potential number of Category IV medical devices and the associated impact on resources). There was also concern about Health Canada's ability to sustain SBD production over the long term as the other phases come on line. It was suggested that full cost accounting and impact analysis (for example, impact of SBD on length of review, on reviewers' time, etc.) of Phase 1 be undertaken before moving forward with Phase 2 and 3. This review should include a cost/benefit assessment.

Post-marketing surveillance and ADRs

While an SBD is "a snapshot in time," it should link with other documents, such as post market information, adverse drug reaction reports, Periodic Safety Update Reports (PSURs), alerts, recalls, etc., as well as other SBDs for related products and reports from other jurisdictions, to ensure the SBD is up to date and relevant. Post market information helps to address "issues" or "concerns" that may have been noted in a reviewer's report and to monitor reactions with a larger population than at trial stage. This supports the transparency objective of the SBD.

Additional SBD Content

The SBD should contain as much information as possible and provide links to sources of additional information. The SBD should be a first step toward access to many other documents and data. Canadians should have access to as much product information as is available in the U.S. Specific SBD content suggestions included:

- Reviewers' expertise/qualifications.
- All indications and dosages sought, approved and denied.
- Information on decisions regarding labeling content.
- Explanations/definitions of terminology.

Use of SBD in Advertising

Participants noted that Health Canada will need to set a policy regarding the use of information in the SBD in product advertising (i.e., rules of engagement, what can/cannot be stated).

Conditions for Endorsement of Summary Basis of Decision

A position statement was presented at the meeting by a number of groups and individuals to outline the minimum conditions for endorsement of the transparency initiative. The group recommended a number of amendments and additions to the process reflecting concerns raised previously throughout this consultation report. The full text is available on the PharmaWatch website (www.pharmawatch.net).

CLOSING REMARKS

Dr. Robert Peterson, Director General, Therapeutic Products Directorate

Dr. Peterson noted that, from Health Canada's perspective, the expectations of the consultation had been fully met. Participants have a better understanding of the SBD, both its potential and limitations, and its overall objective to increase transparency by placing relevant decision-making information in the public domain.

This is new ground for Canadian regulators, and the process will continue to evolve. Health Canada is committed to ongoing stakeholder consultation and to achieving a collegial and cooperative approach that respects the commercial interests of sponsors.

Health Canada will continue to receive and respond to comments on how the SBD can best meet these goals and the needs of Canadians.

Many exciting and challenging ideas have emerged at this consultation for Health Canada's consideration:

- Recognition that SBDs for medical devices will need to be looked at closely, including diagnostics and both invasive and non-invasive products.

- The idea of linking the SBD to other documents and initiatives, both in Canada and elsewhere, was raised. Health Canada will explore the opportunities, limitations and obligations related to this suggestion. The SBD initiative will help other documents, such as the product monograph, become more accessible as well. The idea of including linkages to post-market information was also raised, which will be considered as well, especially around how we can connect with international information databases.

- Resource issues were raised by many participants, in relation both to sustainability and the impact of the SBD on the timeliness of the regulatory review process and our efforts to reduce the backlog.

- There was considerable discussion on whether SBDs should be prepared for non-approved products and products withdrawn from the drug review process. Health Canada will look at this suggestion, particularly in terms of how data on a non-approved or withdrawn product may be useful for subsequent submissions of the same or similar products.

- There were many comments about the target audience. The SBD is intended to disclose government decisions for the principle audience of informed public, as this is believed by Health Canada to be the largest group looking for this type of information. However, Health Canada will look at how the SBD might be adapted to other audiences.

Health Canada is committed to addressing these and other issues that have been raised at this and other consultations, and to providing ongoing opportunities for stakeholder input and advice. There are also lessons to be learned from other jurisdictions and best practices to be applied to the Canadian context.

In closing, Dr. Peterson thanked participants for their contributions and continuing efforts in assisting and advising Health Canada to ensure improved health outcomes for all Canadians.