Health Canada Santé Canada

# REGULATION AND BEYOND:

*Progress on Health Canada's Therapeutics Access Strategy*

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Canada

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## *Progress on Health Canada's Therapeutics Access Strategy*

## THE CHALLENGE

Therapeutic products ranging from pharmaceutical drugs, to vitamins, vaccines and medical devices, play an important role in the lives of Canadians, and in Canada's health care system. There are over 22,000 human drug products and 40,000 medical devices available on the Canadian market. Millions of people trust that the products available have passed Health Canada's rigorous safety standards and will help to deliver desired health outcomes.

Canada, as with all leading industrialized nations, is facing tremendous challenges as technology and science rapidly advance into exciting new opportunities that carry ever-more complex issues and rising costs. At the same time, Canadians are becoming more knowledgeable about managing their health, and expect timely and affordable access to the latest and greatest new therapies.

Improving Canadians' access to therapeutic products is a high priority for Health Canada. That includes looking at factors that affect access to medicines for Canadians once they are on the market, such as how medicines are prescribed, how they are used, and how much information is available about them.

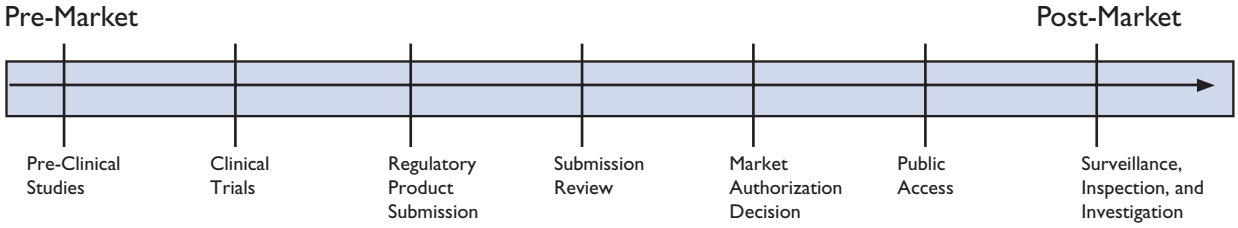
Access to therapeutic products is the result of a continuum, incorporating: pre-clinical and clinical trials; product submissions to Health Canada for regulatory review; the regulatory decision concerning market authorization; pricing; drug plan listing on federal/provincial/territorial formularies; and post-authorization surveillance, inspection, and investigation activities. Each part of the continuum engages a variety of different stakeholders such as: patients and consumers; health care professionals; research scientists; industry and academic institutions; pharmacies and hospitals; regulatory scientists; and policy decision makers.

In the 2002 Speech from the Throne, the government made a commitment to "speeding up the regulatory process for drug approvals to ensure that Canadians have faster access to the safe drugs they need, creating a better climate for research on drugs".

In 2000, 2003 and 2004, First Ministers of Health agreed to work together so that Canadians could continue to have access to new, appropriate, and cost-effective drugs. They set a number of priorities: optimal drug use; best practices in prescribing drugs; and better management of drug costs, including generic drugs.

Health Canada developed the Therapeutics Access Strategy (TAS), with partners and stakeholders, to help Canadians maintain and

*Figure 1*
**Access to Therapeutic Products in Canada**



improve their health, and to respond to these commitments. TAS supports Health Canada's efforts to ensure that human drugs and other therapeutic products are as safe as possible, accessible, of high quality, therapeutically effective, and used properly. TAS is also designed to make access both timely and cost–effective.

In the 2003 Budget, TAS received $190 million over five years; new investments that build upon a base of programs and people working together to achieve the vision.

During the spring and fall of 2003, Health Canada and the Public Policy Forum coordinated multi-stakeholder consultations to bring together consumer, patient, and industry groups to discuss and present perspectives on improvements to the regulatory system for therapeutic products to the Minister and Deputy Minister of Health. These sessions engaged stakeholders in developing the action plan for TAS. Deliberative materials and reports from the sessions are available at http://www.ppforum.ca/ow/ow_e_05_2003/Outcomes_Second_Multi-stakeholder_Session.pdf

A Secretariat has been set up to coordinate work under the strategy, and TAS is well into the second year of this five–year span.

TAS has three key objectives:

I. **To make pre-market regulatory decision-making more efficient, timely and transparent, while maintaining high standards of safety.** Through TAS, Health Canada will strive to meet review times that are in line with leading regulatory bodies throughout the world. To do this, we aim to wipe out the backlog of new drug submissions, consistently meet our performance targets for drug reviews, support better submissions, and improve our review practices and standards. And all of this will be done in a transparent way, making it easier for Canadians to understand the process.

II. **To pay greater attention to safety and therapeutic effectiveness once products reach the market.** Through TAS, Health Canada will improve its ability to monitor and influence the safe use of therapeutic products by Canadians. We will collect more information about how safe and effective products are, and make that information more available. When we make decisions, we will use more evidence about how effective drugs are, and we will help industry and others in the health system provide more and better information about any adverse reactions to drugs.

III. **To promote optimal drug use, including better practices in prescribing drugs, better management of products and drug plans, and making medicines more affordable.** Optimal drug therapy can help manage the growth of drug costs in Canadian public and private drug plans. Through TAS, Health Canada will ensure that Canadians continue to have access to therapies that are not only therapeutically effective but cost-effective as well. We will expand our knowledge about the links between how drugs are used and health outcomes, and improve the way drugs are prescribed. We will also take measures to manage drug costs and plans. The improvement of patented medicine price reviews, including how quickly they are done, is also a TAS goal.

TAS objectives complement one another and build on Health Canada programs that are already in place. The goals of TAS also include: being transparent; building public confidence and engaging Canadians; forging links across the health system; supporting innovative new therapies; and working together with other countries and international organizations. The TAS mandate supports a system that can both perform at its best and be sustained in the long run. TAS is both a vehicle and a symbol for change in the health care system.

TAS follows a two–track action plan, with work being carried out on both tracks at the same

time. Track I is designed to make immediate progress in meeting federal government commitments. The focus of Track II is to develop and implement a long–term plan, so that access to safe, effective, properly–used, and affordable therapeutic products is supported by a regulatory system that is both up–to–date and sustainable.

The following report outlines progress for implementation of TAS Track I initiatives.

- Section I and II provide details on steps made towards modernizing the regulatory regime to streamline the review process for therapeutic products, encourage better quality incoming submissions, and improve the efficiency, consistency, and transparency of regulatory decisions.
- Section III describes the activities that have taken place towards building a comprehensive post-market surveillance program.
- Section IV shows how Health Canada has been working with leading regulatory authorities in other countries to learn from best practices, and help reduce the risks and increase the benefits of therapeutic products that are available in Canada.
- Section V explains how the "real world" use of therapeutic products, including their prescribing, use, price and cost-effectiveness, is being improved upon through a variety of new initiatives.

# MOVING FORWARD

## I. Transforming the way we do busines

> "We need to define our role as a modern and innovative regulatory organization that contributes to the advancement of public health in Canada."
>
> **Diane Gorman**
> ***Assistant Deputy Minister,***
> ***Health Products and Food Branch***

A shrinking world, the pace of scientific and technological change, and the speed of innovation mean that the regulatory system must be ready to keep up –– to ensure that Canadians have timely access to new advances in health products, foods, therapies and health technologies, both from Canada and around the world.

This means taking a close look at how we regulate – everything from re-engineering our business processes to improving the way we handle conflicts. In the short term, we need to focus on how to move submissions through the review process faster, while still maintaining high standards of safety. The goal is a review system that is timely, consistent, predictable and of the highest quality.

### Setting and meeting performance targets:

The Speech from the Throne committed the government to speeding up the regulatory process for drug approvals so that Canadians have faster access to new drugs. One way to do this is to ensure review targets are met by using a consistent approach to submission reviews through project management.

***The goal:*** *To achieve review process improvements so that reviews can be completed within performance targets, through sound project management.*

***Highlights:***

- **Beating the backlog.** The Therapeutic Products Directorate (TPD) of the HPFB has dramatically reduced the backlog of new drug submissions. As of December 31, 2004, the Directorate had eliminated 67 per cent of the backlog for pharmaceutical submissions. This is the result of project management,

enhanced review capacity, new training tools and extended hours. Based on this progress, the TPD expects an increasing number of reviews to meet performance targets as the pharmaceuticals backlog is further eliminated.

- **Expanding our project management capacity and skills.** Sound project management improves the review process so that review teams can operate in a more effective and efficient way. Product submissions are now managed as "projects" in themselves, that are planned, coordinated and managed to meet performance targets.
- The TPD has created a number of new positions for regulatory project managers. Fifteen project managers are in place to coordinate and guide each submission through the entire review process.
- Other HPFB directorates, including the Biologics and Genetic Therapies Directorate (BGTD) and the Natural Health Products Directorate (NHPD) are now applying project management systems to their submission reviews. The BGTD has reduced its backlog by 22 per cent (as of December 31, 2004). Over 90 per cent of TPD and BGTD staff have attended a three-day project management training course, as part of a Competency-Based Project Management Training Program.

## Supporting quality submissions:

One way to reduce review processing times is to improve the quality of the applications. Guidance documents – information provided to industry to help them prepare their submissions – should be consistent, fully supported by the regulations and by international obligations, written in clear language, and used appropriately.

***The goal:*** *To provide quality guidance to industry involved in the review process.*

***Highlights:***

- Under the Good Guidance Practices Framework, a process "map" and standard operating procedures for developing guidance documents have been drafted. An extensive inventory of existing guidances has been established, and both TPD and BGTD have undertaken internal and external consultations as part of a needs assessment to prioritize where guidance documents are needed and/or require revision.

## Improving review practices and standards:

Health Canada reviewers depend on consistent and up-to-date review practices and standards to make the best decisions, and conduct the most efficient reviews.

***The goal:*** *To develop review practices and standards that support timely, predictable, consistent, and high quality reviews and reports.*

***Highlights:***

- **Introducing standard review templates.** TPD and the BGTD have developed new review templates and standard operating procedures for certain aspects of the review process. Clinical and quality components of the review process will now be in line with the International Conference on Harmonisation (ICH) Common Technical Document (CTD) format. The goal of the ICH is to harmonize guidelines and requirements for product registration. The ICH–CTD format makes it easier for product submissions to be filed in Canada and other countries at the same time. The United States, Europe, Japan and Australia all use this format.
- Guidance information for industry has been posted on the BGTD and TPD websites, so that most types of drug submissions filed in Canada can use the ICH–CTD format.

- Both TPD and BGTD have undertaken internal and external consultations to prioritize good review practices.
- **Introducing electronic submissions:** As of September 2004, the TPD and BGTD opened their doors to receive electronic drug submissions based on the ICH electronic CTD (eCTD) format. This capacity will help to make the review process more efficient. Draft guidance for industry on how to prepare drug submissions according to the eCTD format is now available on Health Canada's E-Review website.
- **Improved dispute resolution:** HPFB is setting up an Ombudsman Office. Working together with stakeholders, a Branch working group is now developing a transparent and consistent process to avoid or resolve disputes that arise during the drug submission process.

## Building expertise:

As the number of submissions increases or decreases, or when complex scientific issues call for drug or disease experts, the review process needs to be flexible, with the capacity to bring in special or additional expertise. This flexibility keeps the process timely, creates a ready source of expert knowledge, improves our knowledge base, and ensures that decisions are grounded in practice. In turn, this strengthens the quality and credibility of our decision-making.

***The goal:*** *To build flexible internal and external review capacity to cope with a changing environment.*

***Highlights:***

- **Recruiting expertise.** The TPD is developing a new contracting procedure that will allow greater flexibility and efficiency in securing external expertise in a timely manner. Pilot testing of a national inventory database of pre-qualified experts is underway to respond to immediate workload needs. Seven academic and professional organizations have indicated interest in review opportunities.
- **Building review capacity for natural health products.** On January 1, 2004, the Natural Health Products Regulations came into effect. To help stakeholders understand and meet these regulations, the NHPD has added review capacity and prepared comprehensive guidance documents. The guidance documents describe the standards of evidence for safety, efficacy and quality of natural health products, as well as how to prepare clinical, product and site licence applications. They also cover adverse reaction reporting, product monographs and good manufacturing practices. Good review practices have also been put into place for all aspects of the review process. Over 2004–2005, the NHPD anticipates having the review area fully staffed.
- **Expanding our partnerships.** To find new sources of expertise to provide advice on scientific and regulatory issues, the TPD is linking up with academic organizations such as the Canadian Society for Clinical Pharmacology, the Canadian Association for Population Therapeutics, and the Deans of Pharmacy.

## Enhancing science capacity:

Science capacity requires knowledge: people, processes and tools. Improving science capacity supports our efforts to achieve the highest, internationally recognized standards for safety and quality in regulatory decision-making.

***The goal:*** *To enhance the science, quality and credibility of regulatory decisions.*

***Highlights:***

- **Expanding scientific advisory bodies.** Scientific advisory bodies help develop the standards of evidence used in assessing the risks and benefits of drugs, and other therapeutic products. These standards are very important, as they affect decisions on whether or not products should be approved.

Advisory bodies also contribute to clinical and non-clinical guides, and offer advice on the safety of coexisting therapies. They may also offer their input on labeling, product monographs, package inserts and warnings. Scientific bodies may also discuss risk communications and post-market surveillance issues, identify new trends and technologies, and comment on specific submission issues.

Since 2003, the TPD has created six new scientific advisory bodies, including four scientific advisory committees: Human Reproductive Therapies; Oncology Therapies; Medical Devices in the Cardiovascular System; and Anti-Infective Therapies; as well as two scientific advisory panels: Hepatotoxicity; and Selective Serotonin Reuptake Inhibitors. For more information, including the Record of Proceedings, go to: *http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_activities_committees_e.html*

- **Proteomics analysis.** Special instruments are needed to identify proteins and determine their structure. Having these instruments enables faster analysis of protein structures in drugs and helps to deal with unusual conditions arising from new technologies. One example is genetically engineered therapies, where, for example, analysis of adverse reactions to flu vaccines might be required.

  The BGTD has upgraded the capacity for proteomics analysis in four of its research labs. The BGTD now expects to identify pathogens – disease-causing substances carried in the blood – at a rate 5 to 10 times faster than the old technology.

- **Improving lab information management.** Health Canada has launched an electronic Laboratory Information Management System (LIMS). This system, which is being set up throughout departmental labs, will improve laboratory testing, including testing for biologics.

- The BGTD has launched its LIMS pilot, which monitors samples and tracks lab testing activities, providing an inventory of information concerning testing for products that may present high risks. LIMS should be fully set up by 2005-06.

## An electronic environment:

Technology can increase the efficiency and speed of the entire review process. It can also reduce the burden on industry; allow greater collaboration between HPFB and its international regulatory counterparts; and support more timely access for Canadians to new drugs and information about therapeutic products on the market.

***The goal:*** *To develop technologies that support better processing of submissions from industry, create faster and more accurate automated workflows, foster information sharing in the system, and make it easier for stakeholders and the public to get information.*

***Highlights:***

- In support of improved submission management, since January 2004, the Natural Health Products Directorate has been able to electronically track and report on Product and Site Licence Applications as they progress through the submission review process.

- As part of HPFB's electronic review initiative, a pilot project is now under way to automate the procedure to support the receipt, review and final decisions on requests under the Special Access Program (SAP). The SAP allows health practitioners to gain access to therapeutic products that are not for sale in Canada. This program is used in emergency cases or when conventional therapies have failed, are unavailable, or are unsuitable to treat a patient.

- HPFB is also piloting an automated procedure to register, process and report on adverse drug reaction reports for clinical trials.

- As of September 1, 2004, TPD and BGTD were able to receive electronic drug submissions in eCTD format. A draft guidance document for the preparation of drug submissions in the eCTD format has been released.
- The electronic review initiative (E-review) is on target to be fully functional by March 2008. The maturity and capacity of products in the marketplace has been reviewed and has helped to further tailor long-term requirements which will include automated tracking, workflow management of submission information, and full electronic review capability across the Branch.

### IN 2005, WE WILL:

- **Further reduce the backlog in pharmaceutical drug submissions.**
- **Reduce the number of submissions going into backlog** and the length of time they stay there.
- **Meet performance targets 90 per cent of the time** for pharmaceutical new drug submissions by 2006, and for biologics and genetic therapies by 2007.
- **Apply performance improvements to all new drug submissions.** Regulatory project management will continue to be implemented, with the necessary planning, coordination and management of activities to achieve completion of reviews within performance targets. A comprehensive training program will be implemented for Regulatory Project Managers.
- **Launch a new Good Guidance Practices Framework.** The new framework will be tested through pilot projects involving the revision of existing, or development of new, guidance documents.
- **Implement review template and standard operating procedures for clinical evaluation in support of timeliness, consistency, predictability, and high quality reviews and review reports.** Guidance for reviewers on the use of product reports and information from other jurisdictions will be implemented through a pilot project.
- **Implement a global procurement strategy and create a database of external scientific experts.** We will also establish new scientific advisory committees and evaluate advisory bodies already in place. The new committees will include: (1) Neurological Therapies; (2) Metabolic and Endocrine Therapies; and (3) Musculo-skeletal Therapies. A Scientific Advisory Panel on Neuropathic Pain will also be set up. (Therapeutic Products Directorate.)
- **Continue to set up the electronic Laboratory Information Management System** (LIMS), including training. As part of the system, sample tracking, simple reports and summaries, manual data entry, data migration and instrument management will all be tested.
- **Upgrade lab equipment** to meet LIMS and Lab Accreditation needs. The Lab Accreditation plan will be set up and review staff will continue to be trained on Quality Management Systems ISO 17025. (Biologics and Genetic Therapies Directorate.)
- **Integrate the electronic Common Technical Document** into the new drug submission process, along with related guides for reviewers and industry. This is part of HPFB's ongoing efforts to encourage early filing of submissions by industry in Canada. As part of our progress towards achieving full electronic review (e-review) capacity, we will secure a vendor to tailor the long-term e-review solution (anticipated for phased-in delivery between 2006 and 2008).

## II: Involving the public in the regulatory process

> "Canadians want to be informed about, and engaged in, our processes. They want to know what we are doing, how we are doing it and why."
>
> **Diane Gorman**
> ***Health Products and Food Branch***

Regulating effectively in the public interest means that the views of citizens and stakeholders must be taken into account. This is especially true when both the benefits and the risks of scientific and technological advances in the health system are evolving so quickly. Governments, industry, health care professionals, and patient and consumer organizations all share responsibility for making the regulatory system work, and for being more open, transparent and accountable.

***The goal:*** *To strengthen the capacity of the Health Products and Food Branch (HPFB) as a transparent, open, responsive and accountable regulatory authority.*

### Providing better information:

Canadians manage their own health best when they can make decisions and choices based on reliable information about health products. Industry can work more efficiently and plan with confidence when they know they have consistent information on how and why regulatory decisions are made.

***Highlights:***

- **Improving drug information.** All new drugs approved for sale in Canada must have a product monograph. This written document describes the drug, explains its use, and provides other information so that it can be used safely and effectively, including the conditions under which it shouldn't be used. HPFB has revised the monograph format so that product information is organized into three categories: health professional; scientific; and a new section – consumer information. This new section will use plain language to tell Canadians, including health care professionals, what the medication is, how to use it and what the potential side effects are.

  Health Canada is looking into ways to make these product monographs more widely available to the public.

#### TRANSPARENCY IN THE REGULATORY PROCESS

HPFB is moving forward on many transparency initiatives, including:

- Product Monograph Project (new format and public availability)
- Summary Basis of Decision
- Notice of Compliance Database
- Science/Expert Advisory Committees
- Good Guidance Practices
- Continued stakeholder consultation in policy/regulatory development
- Publication of quarterly and annual performance plans
- Communications – e.g. fact sheets, news bulletins
- Association meetings/stakeholder meetings
- Increased meetings with sponsors during the submission process

- **Making decision-making more transparent.** In May 2004, as part of a pilot project, HPFB published information on how the decision was made to approve two new drug products and a medical device for the Canadian market. Known as a "Summary Basis of Decision" (SBD), this document explains the reasons for giving market approval to new drugs and medical devices, based on the scientific evidence, and a review of both the risks and the benefits.

In June 2004, Health Canada consulted with stakeholders to get feedback on the SBD format and how to improve it.

Canadian health professionals have frequently relied on product information from the United States or Europe, as there has been no similar information available in Canada. The SBD project marks the first time that both health professionals and the public have had access to "Made in Canada" information.

- **Improving accountability.** HPFB prepares quarterly and yearly Drug Submission Performance Reports used by industry and the public to understand how well the Branch is dealing with product submissions. The report is now being re-designed to improve the quality and usefulness of the information it provides.
- **Improving how we communicate safety information.** In 2004, HPFB published the results of a national opinion survey on key issues related to how well it communicates safety information on health products to Canadians. Health professionals and the general public were asked about health product safety, health risks posed by adverse reactions, as well as how aware and satisfied they were with new health product safety information. The survey results are being used to improve a variety of HPFB communications tools, including Dear Health Care Professional Letters, public advisories and warnings, and the *Canadian Adverse Reaction Newsletter*.

## Involving the public in what we do and how we do it:

Making better decisions requires the input of those who are impacted by them. Health Canada continues to involve the public in a broad range of activities, including policy development, reporting on adverse reactions and providing information about risks. Stakeholders want to be informed and involved. They want effective and appropriate opportunities to be heard, and they want Health Canada to be accountable for what it does with the advice it receives.

***Highlights:***

- **Forging stronger partnerships.** Members of HPFB's Advisory Committee on Management now include representatives from patient and consumer groups.
- In January 2004, the Best Medicines Coalition, an alliance of non-government health and advocate organizations, in association with HPFB, hosted the third **National Summit on "Patient Engagement in Canada's Health and Drug Review Reform."** Some 100 patient and consumer delegates from across Canada met with more than 30 representatives from government, voluntary associations and industry. During the Summit, HPFB reiterated its commitment to improve the transparency, openness and accountability of regulatory activities for patients and consumers.
- **Encouraging information-sharing and innovation.** A special panel was organized for Health Canada employees entitled: "Transparency and Openness in the Regulatory Process –– International Perspectives". The panel included the U.S. Food and Drug Administration, the Health Consumers' Council of Western Australia, and the National Consumer Council of the United Kingdom.
- As a follow-up to the Summit and special panel, HPFB and Health Canada's Office of Continuing Education coordinated a series of half–day employee workshops on "Patient and Consumer Involvement in the Review Process" in March/April 2004, to identify opportunities to expand patient and consumer engagement in the Canadian therapeutic products regulatory process.
- **Strengthening public involvement.** Following consultations with stakeholders across the country, HPFB has finalized a Framework for Public Involvement. The framework will, for

the first time, provide a consistent and coordinated approach to public involvement across the Branch, including benchmarks for success.

- **Ensuring a consistent policy approach.** A Branch policy has been drafted on recruiting, nominating, and recommending stakeholder representatives for scientific and expert advisory panels. The policy will be discussed in consultations with stakeholders.

### IN 2005, WE WILL:

- **Implement the new drug Product Monograph**, including a consumer information section. A plan to make the monographs more widely available to the public will be prepared.
- **Launch Phase I of the Summary Basis of Decision (SBD) project**, including the development, publication and website posting of SBDs for New Active Substances[1], and a subset of Class IV (high risk) medical devices.
- **Implement the Public Involvement Framework for HPFB.** Under the Framework, HPFB will develop a comprehensive program to get stakeholders involved. This includes creating a Branch policy on voluntary disclosure of information, establishing standard criteria for selecting stakeholder representatives and piloting new training curriculum that will better help the public participate in Branch expert advisory committees.

## III: Focusing on safety and effectiveness after products reach the market

Canadians share growing global concerns about the safety issues associated with therapeutic products, including the accessibility of information emerging from clinical trials.

As more and more complex health products become available to Canadians, the need to monitor the safety and effectiveness of these products once they are in use has never been more important or more challenging. By taking steps to generate more and better quality information on adverse events once clinical trials and products are approved, the regulatory system can promote safer product use. Ultimately, consumers and health care professionals will continue to have confidence in the health products on the market, and be able to make more informed choices and decisions about them.

Further, as therapeutic products become more numerous and costly, health care professionals, patients and consumers will need better information about how effective they are once they are on the market. This information will help to guide their decisions and ensure optimal drug use.

***The goal:*** *To provide better quality and more information to health professionals, consumers and patients on the safety and effectiveness of health products on the market.*

***Highlights:***

- **Offering "one-stop" product safety information.** Consumers and health care professionals have said they want a single, convenient way to report and receive information about the safety of health products on the market. The Marketed Health Products Directorate

1 New Active Substances are drugs that have never been approved for marketing in Canada before.

(MHPD) of HPFB is developing a single–window Internet portal, called MedEffect Canada, to meet this need. It will bring health product safety information into and out of Health Canada, gather information on adverse reactions and medication problems, and provide updated information on safe product use to the health care community and consumers.

- **Improving our capacity to receive adverse drug reaction information.** There are currently five Regional Adverse Reaction Centres across Canada. They receive adverse reaction reports directly from health care professionals and consumers, serving as the frontline of the Canadian Adverse Drug Reaction Monitoring Program. The program is being expanded with the addition of two new centres – one in Manitoba and one in Alberta.

  Standardized software for use by all Regional Adverse Reaction Centres is also being developed to consistently track adverse reaction reports across Canada.

- **Improving our access to international post-market safety information.** Working together with international organizations creates access to a larger pool of post-market safety information. It also means that we have more timely information and early warnings about emerging international safety issues, and the opportunity to develop our requirements in line with other regulatory authorities.

  The MHPD continues to be a key participant at International Conference on Harmonisation (ICH) meetings. Through a Memorandum of Understanding, MHPD is negotiating access to the U.S. Food and Drug Administration's (FDA) adverse reaction data. The MHPD is also looking into setting up an adverse event database that is compatible with ICH guidelines and would be capable of more complex analysis than the current Canadian Adverse Reaction Information System.

- **Improving drug safety information reporting.** HPFB's Inspectorate has designed a post-market inspection strategy to assess how well manufacturers have complied with the *Food and Drugs Act and Regulations*. These regulations govern the reporting of adverse drug reactions and any unusual failures in the efficacy of new drugs to Health Canada. Inspections started in September 2004.

- **Building our knowledge about therapeutic effectiveness.** HPFB is developing a new program to assess the therapeutic effectiveness of health products after they reach the market. Data has been acquired to conduct targeted, post-market assessments of the therapeutic effectiveness of health products. A task group consisting of a broad array of health system representatives has been formed to prepare recommendations to strengthen the evaluation of real world drug safety and effectiveness.

  The information generated, along with safety data and better communication to health care professionals and consumers, will support more informed decision-making by physicians and patients. That means better overall use of drug therapies in Canada.

### IN 2005, WE WILL:

- **Finalize and implement a post-market surveillance strategy.** HPFB will increase the capacity to generate, collect, detect, monitor, evaluate and disseminate timely, real-world evidence about safety and therapeutic effectiveness of drugs and other therapeutic products. Compliance and enforcement will be strengthened across the range of therapeutic products and activities, including clinical trials and serious adverse event reporting.

- **Launch the MedEffect Canada web site prototype.**

- **Consult with stakeholders and complete the planning for the establishment of new Regional Adverse Reaction (AR) Centres in 2005.** We will also standardize the information management and technology systems

found in the centres, as well as materials used to promote adverse reaction reporting.

- **Work closely with other countries, in particular the U.S., to share adverse reaction data, and explore new possibilities for upgrading reporting systems.** This will give Canada valuable information that supports our efforts to improve post-market monitoring and evaluation of therapeutic products.
- **Conduct post-market inspections** of up to 25 per cent of manufacturers under the HPFB inspection strategy.
- **Create a national vision for therapeutic effectiveness,** through MHPD and its partners.

## IV: Cooperating with international regulatory authorities

International regulatory cooperation can help address the challenges of industry globalization, including emerging threats to public health. Making good use of resources and knowledge from other agencies and governments also contributes to more informed, consistent and timely decisions. It can also lead to joint standards and practices, promote technological innovation, and ultimately, support greater access for Canadians to the latest in therapeutic products and methods.

***The goal:*** *To develop and strengthen relations with other regulatory authorities and international health organizations, in order to provide a more effective, efficient and informed regulatory program in Canada.*

***Highlights:***

- **Sharing information with international authorities.** HPFB has signed a number of international cooperative agreements designed to exchange regulatory information about therapeutic products. These include a Memorandum of Understanding (MOU) with the U.S. FDA, and one with Australia's Therapeutic Goods Administration. The MOUs will lead to greater collaboration on shared priorities.
- Since the signing of the MOU in November 2003, both the TPD and BGTD have had discussions with respective counterparts in the FDA. In May 2004, the BGTD visited the FDA's Centre for Biologics Evaluation and Research to identify a number of potential areas for joint projects. The TPD and the FDA's Centre for Drug Evaluation and Research (CDER) have jointly developed a framework for collaboration activities in product quality, bioequivalence and compliance. The TPD and CDER have also formed a North American Chemistry Manufacturing Controls Discussion Group with the first forum anticipated in 2005.
- During 2003 and 2004, HPFB continued its visiting experts program with the European Medicines Agency (EMEA). From January to April 2003, the TPD sent two senior review staff to the EMEA to conduct a three-month study of the EMEA's practices and procedures. In 2003, other reviewers from TPD, MHPD and BGTD also visited the EMEA to attend various scientific working sessions. These visits help the Branch to identify best practices and areas of mutual interest, resulting, for example, in collaborative work on a joint Health Canada-European Union draft quality guidance document on Inhalation and Nasal Products.

  The TPD also participates as an observer on the European Pharmacopoeia (EP) Commission and expert working groups. Both TPD and BGTD are similarly involved with various activities for the United States Pharmacopoeia (USP), including being observers to the Council of Experts and members of the USP Convention.

  Involvement in these forums supports increased standardization in the manufacturing of pharmaceuticals. A pilot project is currently underway to review reports prepared by the European Directorate for the Quality of Medicines (EDQM) in order to decide on official recognition of the

EDQM's Certificate of Suitability (CEP). Within the European Union, CEPs are used by manufacturers of pharmaceutical products in their applications for market access, to demonstrate compliance of the substance used with monographs of the EP. This leads to more efficient scientific reviews.

- **Streamlining submission requirements.** By participating in the International Conference on Harmonisation (ICH), the HPFB laid the groundwork for accepting submissions in the Common Technical Document format. ICH participants will be able to submit marketing applications to multiple countries at the same time, making new therapies available to Canadians much sooner.

### IN 2005, WE WILL:

- **Finalize an HPFB strategy for international regulatory cooperation.** TPD, BGTD and MHPD will implement respective international strategies, in line with branch and departmental frameworks.
- **Complete a parallel review pilot with Australia's Therapeutic Goods Administration** to study the similarities between the regulatory systems. The pilot, led by BGTD, is also expected to build mutual confidence, leading to work-sharing and other partnerships in the future.
- **Continue HPFB's Visiting Experts Program with the European Medicines Agency, and pursue joint activities with the United Kingdom's National Institute for Biological Standards and Controls (NIBSC).** The NIBSC develops and maintains a large proportion of international standards used for certifying biologics worldwide.
- **Continue joint activities with the FDA**, including expert visits, training, information sharing, scientific advisory bodies and reviewer forums.
- **Participate in ICH forums** as part of an ongoing commitment to harmonize regulatory standards, to strengthen access to safe, high quality and efficacious drug products.

## V: Supporting optimal drug therapies for Canadians

Health Canada, along with its provincial and territorial partners, has a critical interest in how drugs are used and prescribed in the real world, especially new drugs. In order to improve public access to effective and appropriate therapeutic products, TAS must take into account both pre–market and post–market influences that can affect this access. Post–market influences include prescribing practices and drug use, price, and cost–effectiveness.

***The goal:*** *To support access to cost-effective drug therapies for Canadians through better understanding and links between drug use, health outcomes and cost-effectiveness.*

***Highlights:***

- **Sharing information.** The start–up phase of the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) is now underway. COMPUS will be the Canadian centre for nationally–coordinated information and education on best practices in drug prescribing and use. It is housed in the Canadian Coordinating Office for Health Technology Assessment (CCOHTA).

  The first priorities of COMPUS will be in three prescribing areas, including: anti–hypertensives (used for the treatment of high blood pressure); proton–pump inhibitors (used for the treatment of gastrointestinal problems); and diabetes management. An advisory committee is in place, consisting of members from provincial and territorial health ministries, and federal drug plans. A series of consultation sessions across Canada started in October 2004, and are aimed at communicating COMPUS' role, processes and plans, as well as sharing ideas concerning the collection, evaluation and targeted interventions in support of evidence-based best practices.

- **Supporting best practices.** Health Canada created the Best Practices Contribution Program to help finance initiatives that assess and promote best practices in prescribing drugs, and using drug therapies. The Program has funded eight projects, with final products to be shared with COMPUS and other key stakeholders.
- **Expanding our knowledge about drug use and costs.** All public drug plans in Canada, with the exception of Quebec, participate in the National Prescription Drug Utilization Information System (NPDUIS), a database that stores information about individual prescription drug use and costs[2]. The Canadian Institute for Health Information has completed a business plan to expand NPDUIS. This will allow information from private drug plans to be analysed and provide links with other databases. The expanded scope of NPDUIS will provide valuable information to the health care system about the relationship between health outcomes, prescription drug use and costs.

  Work is underway to determine what kind of data is available and how to integrate private plan data into the NPDUIS. Creating linkages with health outcomes data is also being explored.
- **Forging stronger links between access and drug prices.** Health Canada's Health Policy Branch is studying non-patented drug prices. Recent studies from the Patented Medicine Prices Review Board (PMPRB) have shown that non-patented drug prices in Canada (including generics) are between 21 and 54 per cent higher than international median prices.

  To support policy development in this area, the Health Policy Branch has purchased a specialized database, going back five years, that provides quarterly drug use and price information from nine countries. The database will support intelligence gathering and help to establish research priorities.
- The PMPRB has drafted Standard Operating Procedures for the price review process and implemented operational improvements to strengthen its price review capacity to keep pace with the Common Drug Review[3]. As a result of these changes, an increasing number of new drugs are price-reviewed much sooner than compared with 2003. Price reviews are now based on the first 30 days instead of the first six months of sales data filed by the patentee.

### IN 2005, WE WILL:

- **Share best practices in prescribing drugs and using drug therapies** through collection, evaluation and targeted distribution of evidence-based information, strategies and tools, by COMPUS. We will also begin new projects under Health Canada's Best Practices Contribution Program.
- **Continue work on expanding NPDUIS,** including a review of additional prescription/claims data sources, an analysis of privacy issues and opportunities for data sharing.
- **Hold consultations on non-patented drug pricing**, in order to develop a solid policy option.
- **Conduct consultations to strengthen the price-review process** and enhance information used in price review (PMPRB).

2 The information in the database cannot be linked to the name of an individual.
3 This is a single common process for reviewing new drugs for potential coverage by public drug benefit plans in Canada.

# NEXT STEPS: TAS AND THE NATIONAL PHARMACEUTICALS STRATEGY

In October 2004, First Ministers adopted a 10-year plan on the Future of Health Care. Included in this plan, is a commitment by First Ministers to work together on the development and implementation of a comprehensive National Pharmaceuticals Strategy (NPS).

Both TAS and the NPS complement each other. TAS is strongly focussed on Health Canada's role in the pre-market regulation of therapeutic products and the NPS will be addressing the role of drugs in the health care system. The overall objective of TAS and the NPS is to improve Canadians' access to human drugs and other therapeutic products that are safe, of high quality, therapeutically effective, appropriately used, and accessible in a timely and cost-effective manner.

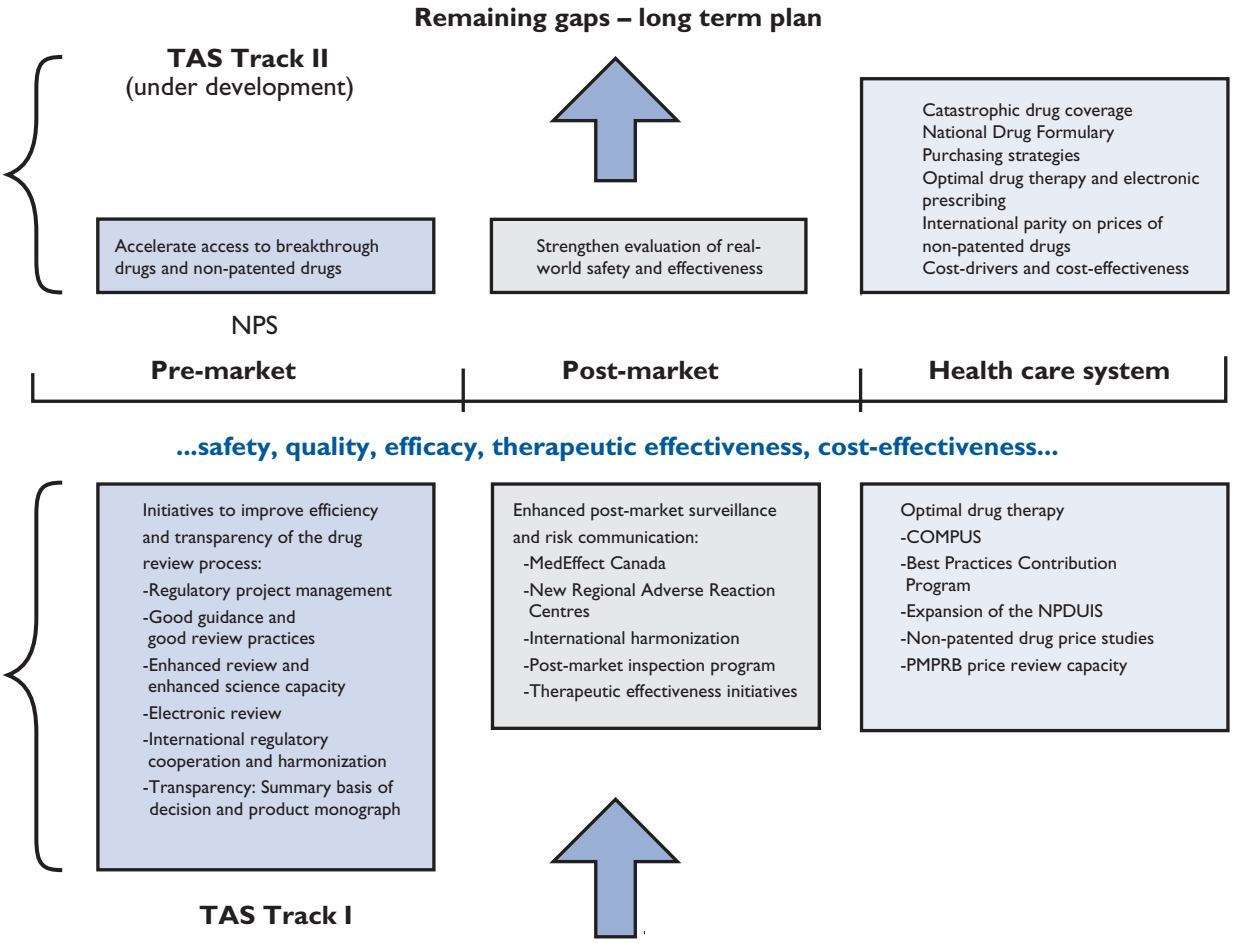
Health Canada will work with provincial and territorial counterparts to further the development and implementation of the NPS. In addition to influencing better prescribing and drug use, the NPS will support:

- development and costing of options for catastrophic pharmaceutical coverage;
- establishment of a common National Drug Formulary based on safety and cost-effectiveness;
- enhanced access to drugs and other therapies to address unmet therapeutic or public health needs;
- heightened monitoring and analysis of real-world safety and effectiveness information on drugs;
- influencing prescribing behaviour;
- electronic prescribing and further development of the Electronic Health Record;
- analysis of cost-drivers and cost-effectiveness, including Drug Plan Management Best Practices;
- accelerated access to, and international parity on, prices of non-patented drugs; and
- purchasing strategies to obtain best prices for Canadians for drugs and vaccines.

Health Canada is committed to staying accountable to our stakeholders and to Canadians on what we are achieving. We also want to ensure that our objectives remain relevant and responsive.

- The TAS Secretariat will coordinate quarterly and annual financial and performance reports. Based on experiences gained from the first years of TAS, a comprehensive performance measurement framework will be designed, with a focus on results.
- In 2005, the work completed in the first 18 months of TAS will be evaluated. We will look at whether TAS has made progress in achieving its intended results by studying how resources were used, and reviewing the infrastructure, tools, processes and structures that have been put in place. The evaluation will also include an analysis of the overall design of TAS and the links between objectives, along with recommendations on where TAS design and delivery can be improved.
- HPFB will examine its current performance metrics for review times, to find out if Canada's approach is comparable to other leading regulators. It will also look at ways to best communicate this information, and consider alternative reporting schemes based on this analysis.
- Health Canada will continue to develop and set up a long–term plan for TAS, so that access to safe, effective, properly–used and affordable drugs and therapeutic products is supported by a regulatory system that is both up–to–date, and sustainable.
- A long term funding strategy to support the review process and sustain performance improvements will be developed, including a new "external charging", or cost recovery, regime.

## Access to Drugs: A Long Term Plan




# GLOSSARY

*These plain language definitions are intended for general understanding and are not necessarily the formal definitions used by Health Canada, or those that appear in legislation or regulations.*

**Adverse reaction**: any undesirable effect of a health product. This can range from a minor effect such as a skin rash, to a life–threatening one, such as liver damage.

**Bioequivalence**: a high degree of similarity in the rate and extent of absorption into the systemic circulation of two comparable pharmaceutical products from the same dose, that are unlikely to produce clinically relevant differences in therapeutic effect, or adverse effects, or both.

**Biologic**: a therapeutic product that has biological origins, such as a vaccine.

**Biologics and Genetic Therapies Directorate (BGTD)**: the regulatory authority in Canada that is responsible for ensuring the safety, quality and efficacy of all biologics and radiopharmaceuticals for human use in Canada.

**Clinical trial**: a scientific study, using a test population, designed to test the safety and efficacy of drugs and therapeutic products in humans.

**Common technical document (CTD)**: a common international format that may be used by drug sponsors to submit information supporting new drug applications to regulatory authorities for review. The United States, Europe, Japan, Australia and now Canada all use this format.

**Common Drug Review**: a single common process for reviewing new drugs to assess potential coverage under Canadian public drug benefit plans, established in September 2001 by federal, provincial and territorial Health Ministers.

**Drug**: any substance used in the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state, and in restoring, correcting, or modifying organic functions in humans or animals.

**Drug review process**: drugs are only approved for sale in Canada once they have gone through the drug review process. Drug applications are carefully reviewed by scientists in the Health Products and Food Branch of Health Canada. These scientists assess the safety, efficacy and quality of a drug. If the benefits of the drug outweigh the risks, the product is given a licence to be marketed in Canada.

**Effectiveness**: whether a drug achieves its desired effect in the real world.

**Efficacy**: whether a drug has the ability to bring out the intended beneficial effects in an ideal world – with no interactions with other drugs or diseases.

**Generic products**: products that offer the same medicinal properties as the original brand name drug, without a brand name, and not protected by a trade-mark (patent).

**Guidance documents**: manuals, policy interpretations, guidelines and other texts that support a better understanding of regulations, and how to participate in the review process.

**Health Products and Food Branch (HPFB)**: a science–based organization within Health Canada that regulates products, including pharmaceuticals, radiopharmaceuticals, biologics and genetic therapies, medical devices, natural health products, veterinary drugs and food, as required by the *Food and Drugs Act and Regulations*.

**Inspection**: an independent evaluation, conducted by an objective, unbiased inspector, or inspection team, to assess an establishment's compliance against set standards or regulations.

**International Conference on Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use -ICH)**: a global project dedicated to reducing duplicate testing of new medicines, to make better use of resources, safeguard public health and avoid unnecessary delays in making new medicines available.

**Marketed Health Products Directorate (MHPD)**: the Canadian regulatory authority responsible for coordination and consistency of post-approval surveillance and assessment of signals and safety trends concerning all marketed health products.

**Medical Devices**: any article or instrument used in the diagnosis, treatment, mitigation, or prevention of a disease, disorder, or abnormal physical state, and in restoring, correcting, or modifying organic functions in humans or animals. Devices also include those used in the prevention, diagnosis and care of pregnancy.

**Natural Health Products**: drugs that include vitamins, minerals, traditional medicines, medicines made from plants, bacterium and fungus, probiotics, amino acids and essential fatty acids (such as Omega-3). *Also refer to definition of drug.*

**Natural Health Products Directorate (NHPD)**: the Canadian federal authority that regulates

the safety, quality and efficacy of natural health products for human use in Canada.

**New drug submission**: the formal process of applying for market approval of a new drug product. A new drug is any drug that has not been sold in Canada for sufficient time, and in sufficient quantity, to establish its safety and effectiveness under use or its recommended conditions for use.

**Performance metrics**: how performance is measured, based on specific target goals.

**Pharmaceuticals**: mostly synthetic products made from chemicals. Pharmaceuticals include prescription and non-prescription drugs, disinfectants, as well as low risk products such as sunscreens, antiperspirants and toothpaste.

**Post–market surveillance**: the process of tracking drugs and other therapeutic products already approved and on the market, to assess signals and safety trends once they are in use among a wider population.

**Product monograph**: all medicines approved for sale in Canada must have a product monograph. This written document describes the drug, explains its use, and provides other information so that it can be prescribed and used safely and effectively.

**Quality**: an accepted standard of production methods and manufacturing facilities, including the premises, equipment, in-process controls, as well as tests during fabrication, packaging and labeling, to ensure consistent results in final products that are safe, efficacious, pure and stable.

**Radiopharmaceuticals**: a pharmaceutical or biological that contains a radioactive entity. Radiopharmaceuticals are primarily used for various imaging functions but can also be used in a therapeutic capacity.

**Regulatory process**: the entire process by which the safety, efficacy and quality of drugs and other therapeutic products is ensured. This includes the review process prior to approving drugs for sale, tracking drugs once they are on the market, and communicating information on the risks and benefits of medicines.

**Risk**: chance of harm, a health hazard. All therapeutic products that offer benefits are accompanied by risks. Although risks can be controlled and managed, they cannot be fully eliminated. Risk varies by product and changes through the product life cycle. The definition of risk within the context of safety, quality and efficacy of therapeutic products continues to develop globally, and through international harmonization initiatives.

**Risk communication**: the exchange of information about health risks between experts, other interested parties and the public.

**Safety**: is the relative risk of harm. Safety is aimed at defining the type, level and scope of adverse events, reactions and hazards that can be balanced against the benefits of a health product, so that an appropriate risk/benefit assessment can be developed and an appropriate therapeutic index for a health product can be established.

**Summary basis of decision (SBD)**: a public document that outlines, in technical language, the scientific and benefit/risk-based decisions that factor into Health Canada's decision to grant market authorization for a drug or medical device. The documents include regulatory, quality (chemistry and manufacturing), efficacy and safety considerations.

**Therapeutic**: designed to cure or restore health.

**Therapeutic Products Directorate (TPD)**: the Canadian federal authority that regulates the safety, quality and efficacy of pharmaceutical drugs and medical devices for human use in Canada.