Health Canada Santé Canada

Your health and safety…our priority. *Votre santé et votre sécurité… notre priorité.*

Planning for Our Future:

Federal Regulatory Post-Market Surveillance Strategy 2007-2012

Canada

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. We assess the safety of drugs and many consumer products, help improve the safety of food, and provide information to Canadians to help them make healthy decisions. We provide health services to First Nations people and to Inuit communities. We work with the provinces to ensure our health care system serves the needs of Canadians.

Published by authority of the Minister of Health.

Également disponible en français sous le titre Planifier l'avenir :
Stratégie de réglementation fédérale pour la surveillance après la mise en marché 2007-2012

This document is available on the internet at the following addresses:
www.healthcanada.gc.ca/medeffect or
www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/index_e.html

For further information, please contact:

Publications
Health Canada
Ottawa, Ontario K1A 0K9
Tel: 613.954.5995
Fax: 613.941.5366

Email: info@hc-sc.gc.ca

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2007.

This publication may be reproduced without permission provided the source is fully acknowledged.

Print: HC Pub: 1441
Cat#: H164-59/2007
ISBN: 978-0-662-05236-4
PDF: Cat#: H164-59/2007E-PDF
ISBN: 978-0-662-47231-5

Contents

Message from the Director General, MHPD

On behalf of the Marketed Health Products Directorate (MHPD), I am pleased to tell you about MHPD's important work and our objectives for the next five years. Since its inception in 2002, MHPD has:

- Established a strong monitoring and risk assessment capacity;
- Started to implement a new surveillance system for collecting and assessing adverse reactions; and
- Launched MedEffect Canada, MHPD's website for health product safety information and adverse reaction reporting.

Focussing on partnering, being proactive, and reaching out, MHPD's five-year plan includes many projects whose broad objectives are to:

- Enhance information sharing among partners and stakeholders;
- Increase international collaboration;
- Render timely and transparent regulatory decisions; and
- Increase public confidence and facilitate informed health product choices.

For updates on how we're doing, and to learn how you can help make health products safer, please visit the MedEffect Canada website often at www.healthcanada.gc.ca/medeffect.

Together we can improve health product safety!

Christopher Turner, MD, FRCPC

MHPD Management Team (l to r, standing): Heather Sutcliffe, Cindy Evans, Marc Berthiaume, Vicky Hogan (seated) Christopher Turner, Christiane Villemure

Together we can…

Your Health and Safety…Our Priority

As Canada's federal authority responsible for regulating health products and food, the Health Products and Food Branch (HPFB) evaluates and monitors the safety, quality and effectiveness of the thousands of human and veterinary drugs, vaccines, medical devices, natural health products and other therapeutic products available to Canadians, as well as the safety and quality of the foods they eat. HPFB's responsibilities include activities both before and after these products are authorized for sale in Canada. Before they can be authorized for sale, health products must demonstrate clear patient benefits relative to their potential risks. Following authorization, and in the light of additional information collected through use in the marketplace, "post-market surveillance," or "health product vigilance," as it is often called, ensures that the benefit/risk balance remains favourable. Currently, HPFB efforts are heavily weighted in favour of safety concerns, with minimal comparative effectiveness focus, though this weighting is expected to shift in future.

In early 2007 HPFB issued the *Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food* (www.healthcanada.gc.ca/hpfb-blueprint), which aims to modernize the Canadian regulatory system and affirm HPFB's role as an internationally recognized leader. In this document, HPFB recognized the paramount importance of moving toward a stronger post-market surveillance system, one that better generates, disseminates and responds to safety and effectiveness data for health products and food.

The Role of Post-Market Surveillance

Post-market surveillance is a fast growing field, due largely to the greater emphasis on health product safety monitoring in all major countries and to growing public interest in safety issues. Current vigilance practices originated in the 1960s when the Thalidomide incident generated calls for greater government drug oversight. With more than 22,000 pharmaceutical products, 42,000 natural health products and 50,000 medical devices on the market in 2007, the potential for adverse reactions continues to be a challenge, as is the potential for interactions among drugs, health products and food products. The demands for earlier access to new products puts more onus on post-market surveillance. Regulatory developments, increased international standardization and cooperation,

advances in access to information, and public expectations have all contributed to a need for more rigorous monitoring of marketed health products. The emerging concern about the effectiveness of products also has to be incorporated into HPFB's activities.

Since 2002, the Marketed Health Products Directorate (MHPD) within HPFB has managed post-market surveillance and disseminated health product safety information. Because post-market activities are also distributed among various other Branch partners, coordination is of prime importance for improving efficiency and consistency in the collection and analysis of post-market event information.

MHPD leads the coordination and implementation of consistent monitoring practices for all regulated marketed health product types (i.e., pharmaceuticals, biologics, vaccines, medical devices, natural health products, veterinary drug products and radiopharmaceuticals).

Since its creation, MHPD has been:

- Providing independent assessment and consistency in safety standards, methodologies, and messaging to stakeholders;
- Ensuring distinct resource use by dedicated post-market surveillance staff to optimize operational requirements and accountability;
- Enabling patients to take more responsibility for their health product decisions; and
- Putting increasing emphasis on post-market monitoring, review and risk management.

MHPD has an opportunity to add systematically to the available information to enable informed decision-making by patients and their health care providers. Attaining this goal requires a strategy, which this document outlines.

Toward a Stronger Post-Market Surveillance Program

Currently, the post-market surveillance program involves the collection, monitoring and assessment of adverse reactions to marketed health products and other data, as well as standard market intervention and communication procedures, along with associated policy development and business transformation activities.

As the Branch's focal point for post-market surveillance activities, MHPD:

- Conducts medical and other scientific assessments of the safety and therapeutic effectiveness of marketed health products;
- Works closely with other Branch directorates, offices and regions, the Department and the Public Health Agency of Canada;
- Employs a collaborative risk management approach to decision-making across all product classes aided by legislation, policy, science, communication, health promotion and education;
- Leads product advertising complaint assessment and coordinates relations with advertising pre-clearance agencies;
- Coordinates the dissemination of safety and risk information to health professionals and the public; and
- Participates in international fora (e.g., International Conference on Harmonization[2]) and shares information through memoranda of understanding with other countries.

[2] International Conference on Harmonization is a joint initiative involving both regulators and industry as equal partners in the scientific and technical discussions of the testing procedures required to ensure and assess the safety, quality and efficacy of medicines. The focus of ICH has been on the technical requirements for medicinal products containing new drugs. The vast majority of those new drugs and medicines are developed in Western Europe, Japan and the United States of America and therefore, when ICH was established, it was agreed that its scope would be confined to registration in those three regions. Canada is an observer to ICH and, where possible, applies their standards.

Because post-market activities are conducted across the branch, this strategy focuses not only on the role of MHPD; it also presents a Branch-wide approach to post-market surveillance.

MHPD is committed to creating a flexible and responsive organization for dealing with an ever-changing environment in which new health and safety risks can emerge despite the best efforts of agencies charged with risk prevention. The directorate plays a pivotal role in various projects, e.g., the development and renewal of regulations and legislation, the National Pharmaceutical Strategy, the Cost Recovery Initiative and the Office of Pædiatric Initiatives.

The Post-Market Surveillance Continuum

The post-market surveillance continuum comprises three principal phases:

- Information gathering, monitoring and processing;
- Signal detection and assessment; and
- Risk management and intervention.

This section contains descriptions of the continuum's three phases and associated information:

- Current and evolving business practices;
- Key stakeholders; and
- Opportunities for improvement.

Information Gathering, Monitoring and Processing

- Adverse events occur and information is gathered.
- Reports on adverse reactions are assessed for completeness.
- Data is entered into a computer system.
- Additional information is gathered from a literature scan, other regulatory agencies, the World Health Organization and companies.
- New risks are discovered with increased use of products in the marketplace.

Information Gathering, Monitoring and Processing

CURRENT PRACTICES

Heavy reliance on the mandatory reporting of adverse reaction (AR) data by industry and voluntary reporting by health care professionals and consumers

Focus to date has been on strengthening the AR reporting function and information sources:

- Opened seven new regional offices to assist in AR collection and promotion of reporting
- Expanding AR reporting outreach and education for health care professionals
- Addressing under-reporting by health care professionals
- Implementing a sophisticated system to better compile and process AR information
- Launched MedEffect Canada website in 2005
- Updating a 10-year-old guidance on how to report ARs

EVOLVING PRACTICES

- Efficient processes and communications for marketed health products that enable prompt interventions at point-of-care
- Capacity to compile information from various sources; shift to more data analysis
- Engaged health community, patients and consumers for reporting adverse events
- Strengthened mechanisms for obtaining external advice and public input

KEY STAKEHOLDERS

- Industry
- Health care professionals
- Hospitals
- Academic and research organizations
- Foreign regulators, provinces and territories
- Patients/consumers
- Canadian Agency for Drugs and Technologies in Health
- HPFB and MHPD medical and scientific staff

OPPORTUNITIES

- Under-reporting of ARs by health care professionals
- To optimize current level of use of foreign reports
- Proactive surveillance limited to pilots
- ARs processed manually due to outdated system
- Limited use of complementary information sources, e.g., therapeutic effectiveness and product utilization data

Signal Detection and Assessment

- Many information sources combine to create a signal, i.e., a suspicion that a connection exists between a product and reported adverse reactions.
- Assessment consists of the scientific/medical review of multiple data sources to analyse risks / benefits, considering risk profiles of therapeutic alternatives.

Signal Detection and Assessment

CURRENT PRACTICES

- Good capacity to detect and prioritize signals for domestic AR reports, severely limited by incomplete information and search limitations of an obsolete AR database
- Significant improvements in scientific assessment capability (including ad hoc review of periodic safety update reports [PSURs]), which is critical to boosting performance to an acceptable level
- Good quality standards applied to business processes and policies and the efficiency of the current environment

EVOLVING PRACTICES

- Capacity to analyse data efficiently from various sources, in different populations and for individual or groups of products
- Expertise, skills and resources readily available and assigned, based on risk priority
- Strengthened regulations to support requests that industry conduct post-market studies and more meaningful assessments of real-world benefits of products

KEY STAKEHOLDERS

- HPFB and MHPD medical and scientific staff
- Industry
- NGOs and government agencies and institutes
- Academic and research community
- Foreign regulators, provinces and territories

OPPORTUNITIES

- Capacity for systematic review of new information sources such as foreign AR data, PSURs, pharmacovigilance plans (PVPs), therapeutic effectiveness data or risk management plans
- Authority to request post-market studies or other data from industry
- PSUR requirement in Canada
- Current review processes in need of adapting for planned improvements, e.g., use of foreign reports in signal detection, PVPs, systematic PSUR submissions, risk management plans, all of which will generate more work
- Limited capacity in some areas of expertise
- Shortage of trained staff in health product monitoring, risk assessment and regulatory risk management

Risk Management and Intervention

- After safety risks have been identified, a risk management approach is defined, which may include interventions such as communicating risk information to health care professionals and the public, labelling changes, or recommending that a product be removed altogether from the market.
- Interventions are communicated broadly in the interests of transparency, increasing awareness and accountability.

Risk Management and Intervention

CURRENT PRACTICES

- A consistent, efficient and internationally recognized risk communication process
- Interventions limited by lack of regulatory authority
- MedEffect Canada website and e-notice usage increasing as vehicles for communicating risk information
- Regulatory oversight of advertising recently moved to criteria-based self identification of pre-clearance agencies
- 10-year old consumer advertising guideline for over-the-counter drugs and natural health products updated
- Canadian Adverse Reaction Newsletter published quarterly

EVOLVING PRACTICES

- Efficient communication processes for prompt interventions at point-of-care
- Effective outreach activities—aimed at both health professionals and the general public—for the right information at the right time to the right people
- Strengthened regulations to support more meaningful assessments of real-world risks and benefits of products

KEY STAKEHOLDERS

- HPFB/MHPD medical, scientific and communication staff
- Pre-clearance advertising agencies
- Disease and patient organizations
- Hospitals
- Public and consumers
- Health care professionals
- Industry

OPPORTUNITIES

- Limited authority to compel industry action (e.g., risk communications and labelling)
- More proactive risk management needed, as well as greater transparency with respect to the factors triggering risk communications and other interventions
- Improved communication needed with key partners, e.g., consumers and patients, health professionals, provincial and territorial ministries of health

Working Together

MHPD's five-year plan takes into account various internal exercises and focus groups conducted recently, as well as external fora such as the consultations on the Blueprint for Renewal, held late in 2006. To achieve its objectives, it will:

- Focus on an efficient and effective operation;
- Develop a specialized know-how and skill set among staff; and
- Adequately support structures for managing and reporting on post-market surveillance.

Mechanisms for strengthening post-market surveillance are also included in HPFB's *Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food* (www.healthcanada.gc.ca/hpfb-blueprint).

MHPD's strategy, which is closely aligned with the Branch's five-year plan, provides focus for achieving the desired states and helps prioritize workload and resources. Several high-level actions have been identified for each objective, which will be further defined in operational and project plans.

Core Values

MHPD's vision is to lead a post-market surveillance program that is at the forefront of regulatory science, promotes the safety and effectiveness of health products, and is recognized for its contributions to the health and safety of Canadians.

Guiding MHPD's work is a set of Health Canada core values:

- Leadership is required to coordinate policies, standards and actions commensurate with potential risks and respective of a product life-cycle approach. This will translate into a fair assessment of products, which will demonstrate that Health Canada is managing public safety in an unbiased, cohesive manner and will address calls for a greater federal role in incorporating therapeutic effectiveness data in marketed product assessments. This requires that MHPD take a leadership role in managing and coordinating post-market surveillance activities within HPFB.
- Sustainability necessitates that a proactive, progressive and comprehensive vigilance model be developed, one that capitalizes on its scientific capacity, international best practices and established information management principles and technologies.

- Strong stakeholder relations are the hallmark of an effective post-market surveillance program. The program's success resides in recognizing the various external stakeholders that make up the health care environment (shown in Figure 1), in the approach taken to integrate their various, sometimes opposed, opinions, and in the strength of the partnerships that form the basis of a collaborative, state-of-the-art product monitoring system.

* Canadian Agency for Drugs and Technologies in Health

Figure 1 – Post-Market Surveillance Stakeholders

MHPD will reach out to external stakeholders to include them in initiatives, solicit input, and communicate on post-market surveillance issues and changes. As an external consulting and communications 'arm' of MHPD's post-market surveillance program management, the Expert Advisory Committee on the Vigilance of Health Products (EAC-VHP) will soon be established.

Strategic Themes

MHPD's priorities focus on three strategic themes:

- Partnering: sharing information and work;
- Being Proactive: working toward sustainable post-market surveillance; and
- Reaching Out: strengthening HPFB's role as a more credible and efficient, and as a timely source of post-market safety information via the web and point-of-care.

The three themes have been developed into nine priorities, as shown below, and detailed in the following pages.

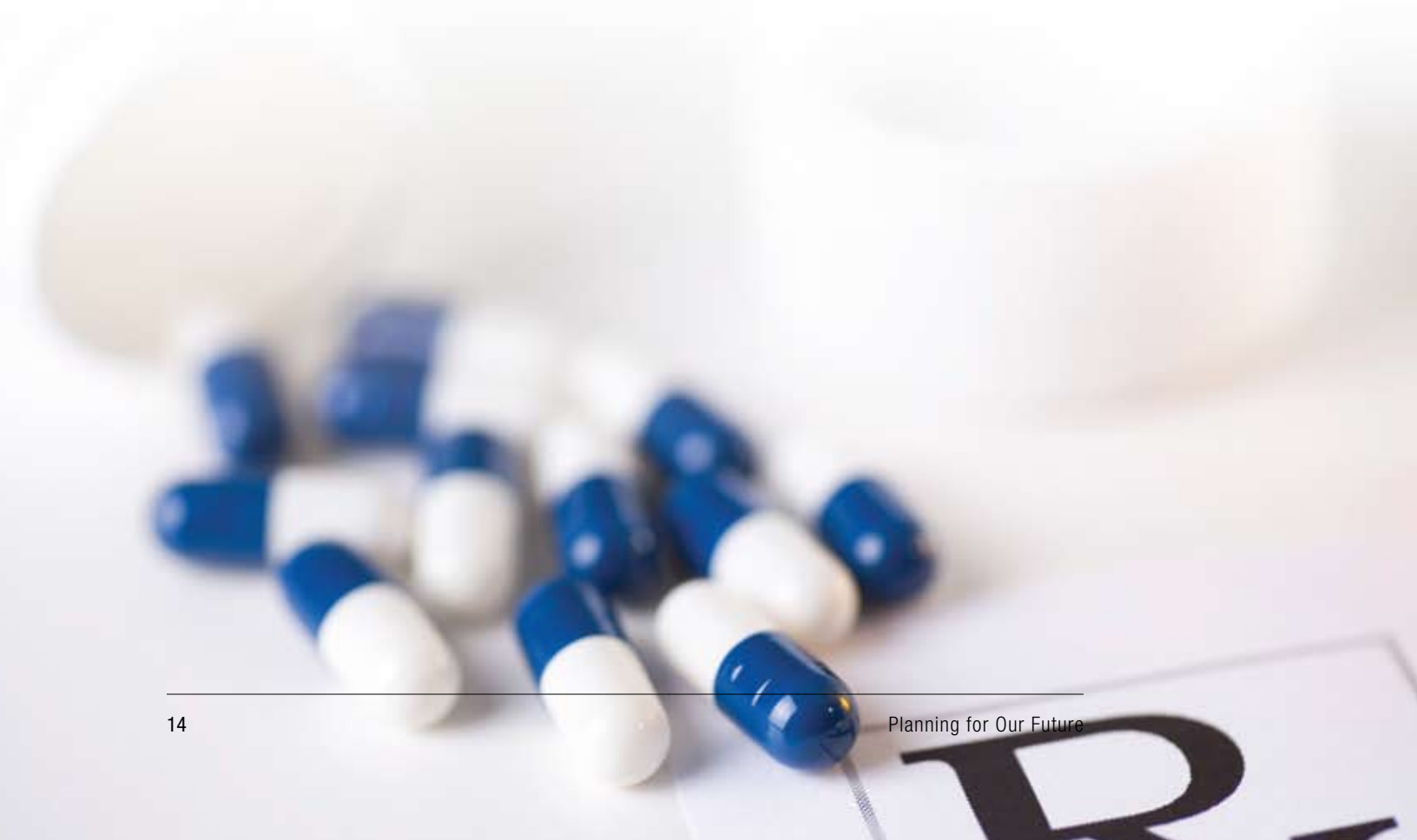
PARTNERING	BEING PROACTIVE	REACHING OUT
Develop current, and access new information sources (domestic and international) to increase AR reporting and expand data sources	Focus on higher risk products through standardized prioritization policies and optimize resources	Expand stakeholder engagement strategies for more efficient risk management and communication
Develop international partnerships for work sharing	Implement a post-market surveillance management framework that is standardized across product lines	Increase the breadth and effectiveness of communicating safety information through stakeholder collaboration
Strengthen external advice by establishing an EAC on Vigilance of Health Products, which will be integrated into the program's governance	Strengthen regulation of industry's monitoring responsibilities such as authority to request post-market studies (such as Phase IV clinical trials)	Obtain authority to require industry to take action with respect to risk communication and label changes

Partnering

This strategic focus is about building solid stakeholder relationships that capitalize on information, knowledge, and outputs of other organizations in Canada and abroad to better enable the Directorate to lead and coordinate post-market surveillance. By seeking, obtaining and systematizing information exchange and transfer across pre- and post-market areas and through external partnerships, MHPD will be able to "keep a pulse" on the environment and seize opportunities to build relationships, share resources, enhance communication and dialogue, influence and guide the development of new sources of information, and engage stakeholders early in the decision-making process.

Globally advances are being made in vigilance process and outputs in other countries. MHPD could capitalize on these by adopting or modifying them and entering into work sharing agreements.

Effective and efficient post-market surveillance requires timely access to good quality data and the capacity to process that data to detect meaningful signals. The availability of data will increase through partnering, international collaboration and increased awareness. The ability to gather and process the data is hindered, however, by technological limitations, and will require the development of robust information management systems.



Key Projects – Partnering

1. Develop current, and access new information sources (domestic and international) to increase AR reporting and expand data sources

CURRENT SOURCES

- Implement a new state-of-the art system to improve signal detection and AR data analysis

NEW SOURCES

- Develop proactive surveillance systems
- Investigate new sources of information through partnership with other organizations such as:
  - Common Drug Review
  - Canadian Pædiatric Society and the Canadian Patient Safety Institute
  - Other countries
  - Federal, provincial and territorial ministries of health
  - Canadian Institute for Health Information
  - Public Health Agency of Canada, Statistics Canada
  - Potential network of centers of excellence in research in real-world safety and effectiveness

OVERARCHING PLANS

- Implement an information management strategy to strengthen current information sources and enable the exchange of additional information and signal detection with external audiences
  - Implement electronic filing and receipt of information

2. Develop international and domestic partnerships for work sharing

- Implement work sharing through frameworks with other regulators / organizations
  - Conduct cross-walk of best international practices
  - Identify and approach foreign regulators and domestic organizations for work sharing and coordinated risk management actions

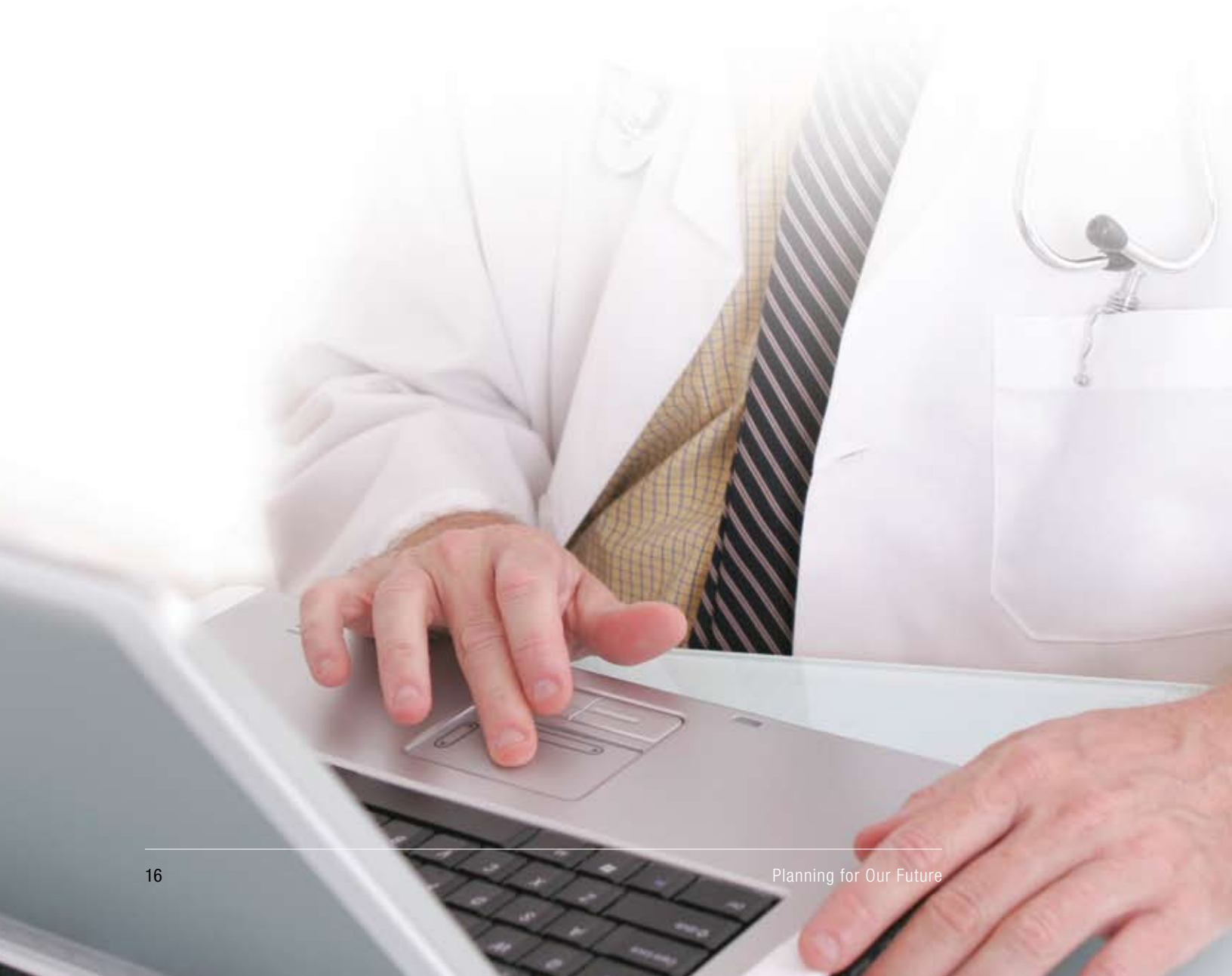
3. Strengthen external advice by establishing an EAC on Vigilance of Health Products, which will be integrated into the program's governance

- Establish a membership selection process-based on recently developed Branch standards – and create the EAC and initiate meetings
  - Integrate an accessible public communication channel for smooth functioning of the EAC

Being Proactive

This strategic focus pertains to greater emphasis on early, preventive actions and making the most of limited resources. It requires developing and implementing a risk-based approach to product monitoring to define and prioritize appropriate vigilance activities and information for each product line according to the product life cycle. It also requires that the role of therapeutic effectiveness in post-market surveillance be evaluated, and the applicability of vigilance activities to vulnerable populations be reviewed.

This can be done by prioritizing the products based on risk levels, focusing on activities that have added value, addressing relevant "at risk" populations and having an appropriate product monitoring framework and regulatory authorities. It will rely on benchmarking to identify best practices and leveraging work done in other countries.



Key Projects – Being Proactive

4. Focus on higher risk products through standardized prioritization policies and optimize resources

- Implement a transparent Branch-level risk management framework
  - Develop and formalize a standard method for prioritizing signals based on the type of product and its stage in the life cycle
  - Implement HR strategies to recruit highly qualified personnel and balance ongoing and emergency work
  - Implement performance tracking and reporting
  - Develop a comprehensive, scientific training and development plan for post-market surveillance staff
- Develop a capacity for systematically reviewing foreign data, which builds on the best international practices
- Conduct active surveillance in targeted vulnerable populations
  - Develop risk management practices for the pædiatric population

5. Implement a post-market surveillance management framework that is standardized across product lines

- Adopt recognized benchmarks and methodologies to build a post-market surveillance quality and management system
- Develop a systematic approach to PVP and PSUR review
- Integrate the use of therapeutic effectiveness in product monitoring
- Integrate the use of real-world safety and effectiveness data in benefit/risk assessment
- Integrate the use of drug and product utilization data in benefit/risk assessment

6. Strengthen regulation of industry's monitoring responsibilities, such as authority to request post-market studies

- Through the progressive licensing framework project, obtain authority to request industry to provide post-market studies and more meaningful real-world assessments of product benefits

Reaching Out

Effective post-market surveillance requires a well developed infrastructure to reach the right individuals with the right information at the right time.

All external stakeholders have a vested interest in post-market surveillance. This strategic priority will focus on engaging stakeholders in initiatives that improve risk management and communication. The focus will also be on maximizing and leveraging knowledge, skills and resources, as well as increasing awareness of MHPD and post-market surveillance.

Increasing regulatory authorities for industry to issue risk communications or make label changes is a mechanism of choice to ensure strengthening of industry's monitoring responsibilities.

Key Projects – Reaching Out

7. Expand stakeholder engagement strategies for more efficient risk management and communication
• Implement stakeholder relations framework and activities that facilitate stakeholder involvement
8. Increase the breadth and effectiveness of communicating safety information through stakeholder collaboration
• Increase registration to MedEffect Canada e-notice list and AR reporting – Promote the national surveillance program – Develop AR reporting educational programs • Increase effectiveness of risk communications – Develop targeted electronic notification processes – Formalize risk communication procedures and develop a risk management guidance document – Evaluate the effectiveness of risk management actions taken
9. Obtain authority to require industry to take action with respect to risk communication and label changes
• Through the progressive licensing framework, obtain authority to compel industry to issue risk communications and label changes

Looking Ahead

Our primary goal is to better protect the health and safety of Canadians. By **partnering, being proactive** and **reaching out,** MHPD will address new challenges to the health and safety of Canadians and keep pace in a rapidly changing environment.

As MHPD's post-market surveillance strategy is implemented, stakeholders can expect:

- To be consulted prior to the finalization of key post-market surveillance policies, regulatory changes, strategies and guidance documents;
- To be informed in a timely manner after safety risks have been identified, and decisions made, along with the rationale for the decisions;
- To have access to post-market surveillance strategic and business plans, as well as annual reports of activities;
- To communicate their questions and concerns to MHPD more easily.

In brief, the program will be characterized by:

- More cost-effective, efficient, proactive and transparent practices, based on sound risk assessment and prioritization; and a surveillance program that follows a product through its entire life cycle;
- Enhanced information sharing;
- Better informed and engaged health professionals and public;
- Stronger regulations and increased compliance;
- Greater public confidence in MHPD's post-market surveillance contribution to the health care system, and more informed choices.

Be sure to check our website this fall for the first-ever report on our activities. It will be a fact- and photo-filled retrospective of how far we've come in our first five years, as well as a sneak preview of early accomplishments in our strategy for the next five.

www.healthcanada.gc.ca/medeffect

Together we can improve health product safety!