Drug Safety at Health Canada

Presentation to CADTH

Kimby N. Barton
Director, Bureau of Cardiology, Allergy and Neurological Sciences and Chair, Health Portfolio Risk Management Planning WG
April 16, 2012
Caveat statement

The opinions expressed in this presentation are those of the presenter and do not necessarily reflect those of the Government of Canada.
Presentation Objectives

• Evolution of safety models at HC
• Pre-approval safety assessment
  – Links to MHPD and CDR
• Health Product Vigilance and safety assessments
• Current drug safety at HC
• Future Directions
Historic System: Licensing Model

- Point-in-time approach
- Discrete, defined Health Canada involvement in lifecycle

= Health Canada’s current regulatory authority
Progressive Licensing Model

Pharmacovigilance and Risk Management

- Drug Discovery
- Pre-Clinical Studies
- Pre-Submission Meeting
- Clinical Trials
- Pre-Submission Meeting
- Drug Submission
- Licence
- Early Post-Market Period
- Ongoing Reporting of New Information
- Re-Evaluation of Licence and Commitments
- Evolution of Product and Knowledge
- Removal of Product

- Industry
- Health Canada
- Pharmacovigilance Regulator, Industry, Health Professionals, Public

Monitoring and Intervention
Clinical Trial Review
Submission Review

Safety assessment: Pre-approval

- Safety data from clinical trials
- Post-market data from other jurisdictions (where available)
- Adverse drug reactions assessment
- Risk Management Plan Review
  - Joint process between pre-market Directorates and MHPD
  - Focus on identified and potential risks and populations not studied in trials
- Sharing of safety information with CDR for products meeting specific criteria (i.e. CDR priority review)
- Formulate overall Benefit/Risk assessment
  - Recommend for NOC or not
Health Product Vigilance Activities

Marketed Health Products Directorate

“Partner” Health Products Directorates

Rx & Devices

Therapeutic Products Directorate

BIOLOGICS

Biologics & Genetic Therapies Directorate

NHPs

Natural Health Products Directorate

HPFB Inspectorate

Marketed Pharmaceuticals and Medical Devices Bureau

Marketed Biologicals, Biotechnology and Natural Health Products Bureau

Therapeutic Effectiveness and Policy Bureau

Marketed Health Products Safety and Effectiveness Information Bureau (Canada Vigilance database)

Bureau of Strategic Initiatives and Planning

Office of Risk Management & Science
Health Product Vigilance is composed of three major activities:

- **Market Authorization**: Adverse events occur and information is gathered. Reports are assessed for completeness and assigned medical terminology. New risks are discovered with increased use of product in real world. Information is compiled from literature scans data from other regulatory agencies, companies etc.

- **Signal Detection and Evaluation**: Many information sources combine to create a signal: a suspicion there is a connection between a product and reported adverse reactions. Evaluation consists in the scientific/medical review of multiple data sources to analyse risks and benefits, considering risk/benefit of therapeutic alternatives.

- **Risk Management (Interventions)**: A risk management approach is defined which may include interventions such as: product recall, labelling changes, communicating risk information to health care professionals and the public. Interventions are normally communicated broadly as a mechanism to show accountability.
1. Sources

**Scanning:**
- Media and scientific literature

**Int. Regulatory Agencies:**
- Databases
- Warnings/Advisories

**Manufacturer:**
- Post-market studies
- Periodic Safety Update Reports

**Health Canada:**
- Adverse reaction reporting
- Pre-market safety information

**Drug Safety & Effectiveness Network**

2. Signal identification

- Signal Detection
- Prioritization
- Evaluation

3. Risk mitigation

- Risk Mitigation Strategy
- Risk communication
- Other regulatory actions:
  - Market withdrawal, labelling change, recall

**Health Product Vigilance Process Overview**

- Public Advisory
- Health Professional Communication
- Notice to Hospitals
- Media
- Cdn Adverser Reaction Newsletter
- MedEffect/MedEffet
- Its Your Health
Continuous Improvements to Health Product Vigilance

- The MedEffect™ Initiative
- C.0.016 Amendment
- Risk-prioritized Periodic Safety Update Report (PSUR) regulatory review pilot (ICH E2C)
- Implementation of Risk Management Planning (ICH E2E)
- Developmental Safety Update Reports WG (ICH E2F)
- Development of Signal Detection Working Groups within MHPD
  - Industry identified safety issues (MAHSI-WG)
  - Foreign agency identified safety issues (SIFA-WG)
  - Safety issues identified through literature review
  - CanadaVigilance based safety issue identification
Continuous Improvements to Health Product Vigilance (2)

• International Collaboration
  – Quadrilateral with TGA, SwissMedic, Singapore’s HSA and Health Canada
  – 4-way Pharmacovigilance Teleconference with US FDA, TGA, MedSafe NZ, Singapore’s HSA and Health Canada
  – Participation at European Union Pharmacovigilance Working Party meetings (EU-PhV)
  – Foreign review pilot project
• Ongoing Council for International Organizations of Medical Sciences representation (CIOMS VIII, IX)
• Drug Safety and Effectiveness Network (DSEN)
• Evaluating Effectiveness of Health Product Risk Communications (EERC) Initiative
• Periodic Benefit Risk Evaluation Reports (PBRER) (ICH E2C (R2))
12

Product Vigilance and Benefit-Risk Management Cycle

1. Gather and Process Information
- Voluntary / Mandatory adverse reaction reporting
- Safety studies
- Product usage tracking
- Patient registries
- Medication incident reporting
- Environmental scanning
- Database searching
- Compilation and consolidation of data
- Sharing information between governments and regulators
- Standardization of terminology

2. Monitor and Evaluate
- Optimal understanding of a product’s benefit/risk profile
- Integrating knowledge on real world safety and effectiveness
- Periodic analysis of safety information
- Evaluation of safety reports
- Data assessment (e.g. clinical)
- Signal identification, assessment, prioritization
- Benefit-risk assessment
- Compliance monitoring
- Assessing outcomes
- Determining best practices

3. Managing Risks
- Optimal health outcomes
- Planning and revision of vigilance and risk management
- Communication of safety information
- Revision of authorization (e.g. terms and conditions, naming, labelling & packaging)
- Integration of best practices
- Informed decision-making
- Compliance and enforcement

A range of risk management principles and product vigilance methods are applied throughout the product life cycle to support Health Product Vigilance and Benefit-Risk Management.
Future Direction: Moving from Passive to Proactive

Health Product Vigilance in Canada

- **Passive**
  - e.g. spontaneous AR reporting by health professionals and consumers; mandatory reporting by sponsors

- **Reactive**
  - e.g. action in response to interventions by US FDA, EU-EMEA, etc.

- **Pro-active**
  - e.g. electronic health record use, active surveillance, requested post-market trials, risk management planning, automated signal generation, e-coding on AR reports by sponsors, PSUR review

**SUSTAINABILITY**
Acknowledgements

• My Yen Yu
• Jason Berg
• Bruce Wozny
• Nashwa Irfan
• Vicky Hogan
Questions/Comments?
### Where are we heading?

<table>
<thead>
<tr>
<th><strong>Now (January 2010)</strong></th>
<th><strong>Future (March 2014)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Product Vigilance mostly focused around a single information source (AR facing under-reporting)</td>
<td>Comprehensive and timely information from various sources supported by engaged stakeholders and state-of-the-art IM/IT</td>
</tr>
<tr>
<td>Limited post-market regulatory authorities</td>
<td>Strengthened regulation of MAH vigilance responsibilities through increased authorities</td>
</tr>
<tr>
<td>Passive system mostly reacting to events</td>
<td>Pro-active and transparent system using risk-based management, vigilance framework and life-cycle approach</td>
</tr>
<tr>
<td>Health Product Vigilance isolated from broader health system</td>
<td>Health Product Vigilance a visible, full partner in health care system evidence gathering resulting in information, advice, work sharing and improved reach</td>
</tr>
<tr>
<td>Health Product Vigilance is one of several HPFB functions</td>
<td>Integrated, transparent and synergistic program (product line) approach supported by horizontal policies and transformative initiatives</td>
</tr>
</tbody>
</table>
The MedEffect™ Canada Initiative

• Launched in August 2005
• Intent is to integrate the communication and promotion efforts of all Post-Market Surveillance programs and activities
• It aims to:
  – Provide centralized access to new safety information about marketed health products in an easy to find, easy to remember location;
  – Address the requirement to make it as simple and efficient as possible for health professionals and consumers to complete and file adverse reaction reports; and
  – Help increase awareness about the importance of AR reports in identifying potential risks associated with certain drugs or health products.
• It is the public interface for the entire Post-Market Surveillance program.
• It works to improve accountability, public confidence, stakeholder relations, effective communications and outreach through the use of:
  – Audience-friendly, clear and consistent messaging
  – Use and seamless integration of multiple mediums and platforms
  – New technologies and approaches to address changes in ways our audiences obtain information and communicate with their government.
HC-CDR joint reviews pre-approval

- Must meet specific criteria (substantial improvement or no other drug)
- Savings of $2.5 million
- Ongoing communication between CDR and HC
  - Share clarifaxes
  - CDR attends sponsor meetings (often teleconferences)
  - HC can attend CEDAC meeting as observer
- Sharing of safety information
- Maximizing use of expertise
- Better awareness of the complementary roles (not duplicative)
- Increased transparency
- Quicker access post NOC
HC-CDR joint reviews pre-approval

Criteria:

- The new drug is effective for the treatment of an immediately life-threatening disease or other serious disease for which it offers substantial improvements in clinically important outcome measures of effectiveness, safety, tolerability, and/or quality of life compared with other available therapies in Canada, or for which no comparable drug is marketed in Canada; or

- the new drug, if listed by all CDR participating drug plans, has the potential to result in combined annual savings to the drug plans of at least $2.5 million, based on the manufacturer’s list price.
HC-CDR process (2)

- Information sharing occurs throughout the process:
  - Manufacturer provides Clarifaxes – initial and ongoing
  - HC reviewers meet with the CDR reviewers (teleconference/in person)
  - CDR-HC Pre-PM negotiation meeting
  - CDR attends PM negotiation meeting
  - Ongoing dialogue between CDR and HC during review
  - Manufacturer informed of dialogue through CDR web reports
  - HC attends the CEDAC meeting as observer
HC-CDR process (3)

- Maximizing use of limited expertise across the Market Access Continuum
- Potential for better awareness of the complementary roles (not duplicative)
- Common understanding by industry about differences in assessments
- Increased transparency
- Potentially quicker access to publicly funded medications post NOC