Towards Comprehensive Risk Management Planning: Health Canada's Proposed Approach

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Presentation Objectives

- Definitions
- The Current System
- International approaches
  - ICH
  - United States
  - European Union
- Health Canada's Proposed Approach

Definitions

Pharmacovigilance: the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

Risk Management System: a set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to medicinal products, and the assessment of effectiveness of those interventions.

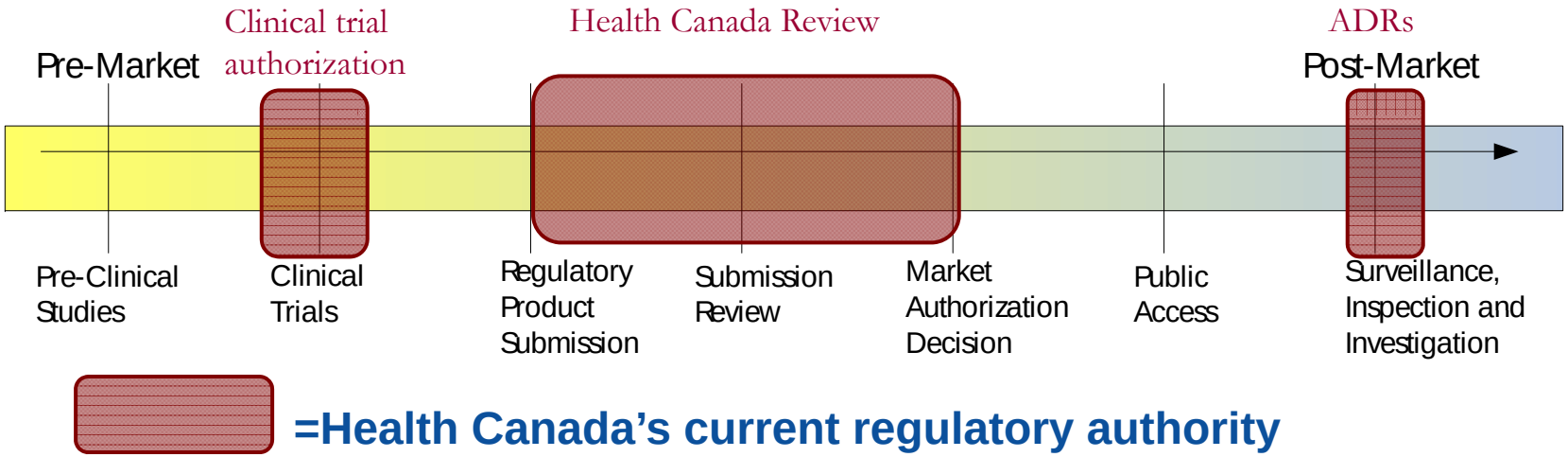
Definitions (cont.)

Risk Management Plan (RMP):

- A Safety Specification (summarizes important identified risks of a drug, important potential risks and important missing information)
- A Pharmacovigilance Plan (is based on the Safety specification and describes actions for safety concerns that have been identified)
- Risk Minimization activities (EU-RMP) (methods used to mitigate a risk once identified)

Current System: Licensing Model

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



=Health Canada's current regulatory authority

Current System: Integrated processes

Source

Scanning:
- Media
- Medical and scientific
- literature

Regulatory agency:
- Databases
- Warnings/Advisories

MAHs:
- Phase IV studies
- PSURs
- Registries

Health Canada:
- CanadaVigilance
- WHO – Vigimed
- TPD

Signal detection

Signal generation/ selection

Signal evaluation

Evaluation

Risk management

Risk Management Strategy

Risk communication

- **Public Advisory**
- **Health Professional Communication**
- **Notice to Hospitals**
- **Media**
- **CARN**
- **MedEffect/MedEffet**

Current System: Limitations

- Lack of follow-up on populations not studied in clinical trials
- Lack of authority to compel studies or other risk management strategies
- No systematic evaluation of risk management practice to determine effectiveness
- Limitations to our current sources of post-market data:
    - Spontaneous adverse reaction reports
    - Periodic Safety Update Reports (PSURs)
- Occasionally, we receive data from registries and epidemiological studies

International approaches to RMP

- ICH adopted the E2E guideline on Pharmacovigilance Planning in November 2004
- Europe and the US FDA implemented E2E and some form of Risk Management in 2005
- Both jurisdictions have legal authority to compel submissions and to levy fines for non-compliance

International approaches: ICH E2E

- Scope is to include:
  - New medicines for licensing and marketing
  - Biotechnology derived products
  - Significant modifications to existing medicines
- Guidance on good practice in design and conduct of post-marketing safety studies
- Components:
  - Safety specification
  - Pharmacovigilance plan
  - Annex on Pharmacovigilance methods

International Approaches: United States Food and Drug Administration

- November 2005:
  - Pre-marketing risk assessment
  - Good Pharmacovigilance and Pharmacoepidemiologic Practice
  - Development and Use of Risk Minimization Action Plans
- FDA Amendments Act (FDAAA): Risk Evaluation Mitigation Strategies (REMS)
- No published format for RiskMAPs or REMS
- Criteria for when a REMS is expected: "exceptional circumstances"

International Approaches: European Union

- 2005 developed "*Guidelines on risk management systems for medicinal products for human use*" including the European Union Risk Management Plan (EU-RMP), part of Volume 9A
- Provided both Guidance and a Template for RMP submissions
- Based on ICH E2E format:
  - Safety Specification
  - Pharmacovigilance Plan
  - Risk Minimization Plan (RMinP)

International Approaches: European Union (cont.)

- Application for new marketing authorization
  - New active substance
  - Biosimilar product
  - Generic product where problem found with innovator
- Significant change in authorization
  - New dosage
  - New route of administration
  - New indication
- On request of regulator
- On initiative of the Manufacturer for newly identified safety issue

Health Canada: status of Risk Managment Planning

- Health Canada is an observer to ICH and has committed to implement ICH guidance
- Health Canada currently receives and reviews RMP
- Need to adopt international best practices
- Necessary component of a comprehensive Product Vigilance Framework and product life cycle approach
- Need to provide guidance to industry on HC expectations

Health Canada's Proposed Approach

- Interim implementation (Notice posted on HC's website)
- http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/vigilance/notice_avis_rmp_pgr_e2e-eng.php
- drugs, biologics and biotech-derived products for human use
- Request in the EU-RMP format
  - One Canadian content exception: Section 4.5.2.2: Discuss post-market experience in the Canadian context
- Accept in other format (i.e.RiskMAP) if covers essential elements

FORMALIZES THE STATUS QUO

HC Approach: Interim implementation

- Need to establish resource-intensiveness for stakeholders and regulators
- Help establish best practice methods
- Refine criteria for submission
- Evaluate the benefits of implementing RMP
- Stakeholder Consultations

HC Approach: Criteria for RMP submission

- ***On Request*** when relevant to benefit/risk profile
- Could include but not limited to:
  - New active substances
  - Significant change in indication
  - Products new to class associated with a serious safety risk
  - On request: newly identified serious safety risk

HC Approach: Marketing status

- Interim implementation will not affect products already marketed unless:
  - A new serious safety issue is identified
  - There is a substantial change in indication that may be associated with a serious safety risk
  - A new serious safety risk is identified for a similar product in the class

  - Above are “could include but are not limited to”

HC Approach: Role of RMP

- Risk Management Planning will:
  - Improve monitoring of drugs post-authorization
  - Provide for better sources of post-market data
  - Enable assessment of effectiveness of risk mitigation strategies

- Risk Management Planning will not:
  - Lower safety standards for drug approval
  - Eliminate risk associated with therapeutic products

HC Approach: Remaining questions

- RMP for all products or only specific subset
- Set up timelines for feedback
  - US REMS: 18 months, 3 years and 7 years
- Determine format for feedback
  - PSUR
  - Specific RMP document
- Canadian guidance or international harmonization

Thank you

QUESTIONS ?