



Health  
Canada

Santé  
Canada

*Your health and  
safety...our priority.*

*Votre santé et votre  
sécurité...notre priorité.*

# Workshop on Post-Market Drug Safety & Effectiveness

Federal Drug Regulatory Process  
May 22, 2008

**Cindy Evans**

**Therapeutic Effectiveness and Policy Bureau  
Marketed Health Products Directorate**



Canada 

## Presentation Outline

- Context for the federal drug regulatory process.
- Current situation and emerging challenges.
- Issues concerning how can Health Canada make optimal use of post-market data on safety and effectiveness to support decision-making in the regulation of drugs.



# Health Product Vigilance: Canadian Post-Market Context

Currently:

- Over 20,000 therapeutic drug products (excludes medical devices) including prescription and non-prescription drugs, and disinfectants approved for use in Canada.
- Approximately 42,000 natural health products on the Canadian market (most are over the counter and self-care products and available in pharmacies and health food stores).
  - 14,000 currently have had pre-market review.
  - 6,480 have been licensed.
- More than 81,000 licensed medical devices.



# Post-Market Surveillance or Health Product Vigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other health product related problem.

This definition encompasses the use of pharmaco-epidemiological studies (ICH).



# Health Canada Post-Market Risk Management

Sources of Information



**Risk Identification**



**Risk Assessment**



**Risk Mitigation**



# Post-Market Signal Detection, Prioritization & Assessment

Approaches to prioritize signals are based on:

- International best practices
- SNIP Criteria\*

Strength: *Is this a strong signal?*

- are there many cases? are there good cases descriptions? is there good evidence of causality?

Newness: *Is the signal new?*

- unidentified / unlabelled? change of frequency? change of severity? new risk factors? Time interval since product marketed?

Important: *Is this an important issue?*

- Are cases serious (WHO definition) ? severe? sustained? who and how many could be affected? Is product used widely? Used by special populations?

Potential for prevention: *Can the risk be reduced?*

- Revise indications? add contraindications? strengthen warnings? inform public / professionals? suspend or revoke?

\*Waller PC, Lee EH. Responding to drug safety issues. *Pharmacoepidemiol Drug Safe* 1999; 8: 535-552



# Post-Market Signal Detection, Prioritization & Assessment

Signal classified as:

– **High priority**

- Serious\*, unknown and/or unlabelled.
- If confirmed, intervention likely.

– **Medium priority**

- If confirmed, potential shift in benefit/risk.

– **Low priority**

- ADR already known or partially labeled.
- Related to potential confounders.
- No evidence of an urgent safety problem.

\*Serious: a noxious and unintended response to a drug<sup>1</sup> or NHP<sup>2</sup> that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, that causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death

<sup>1</sup>*Food and Drug Regulations*, Part C, Division 1, General (C.01.001), C.R.C., c. 870.

<sup>2</sup>*Natural Health Products Regulations*, Interpretation, C.R.C., SOR/2003-196.



# Post-Market Signal Detection, Prioritization & Assessment

## Considerations:

- Critical analysis taking into account all available scientific and regulatory information (consultation with internal experts and with other regulators).
- Consideration of uncertainties impacting the risk assessment.
- Recommendations made based on sound science, including causality assessments.
- Causality assessments using WHO algorithm (certain, probable/likely, possible, unlikely, unassessable).
- Determines the strength of association between the product and the adverse reaction (AR).



## Post-Market Risk Management

- Regulatory request for safety information from market authorization holders.
- Withdrawal of product license.
- Risk communication.
- Product recall.
- Changes in pre-market assessment or requirements (e.g., cautionary labelling).



## Data Sources in Signal Detection, Prioritization & Assessment

- Reports of adverse reactions (AR) or lack of efficacy.
- Periodic Safety Update Reports (PSURs).
- Registries.
- Epidemiologic studies.
- Clinical trials/studies.
- Risk communications (Foreign jurisdictions).



## Data Sources in Signal Detection, Prioritization & Assessment (cont'd)

- Scientific literature.
- Industry.
- International organizations.
- Foreign regulatory jurisdictions.
- Organizations providing evidence-based reviews of safety & effectiveness.
- Databases & other data retrieval resources.
- Other Health Canada programs.



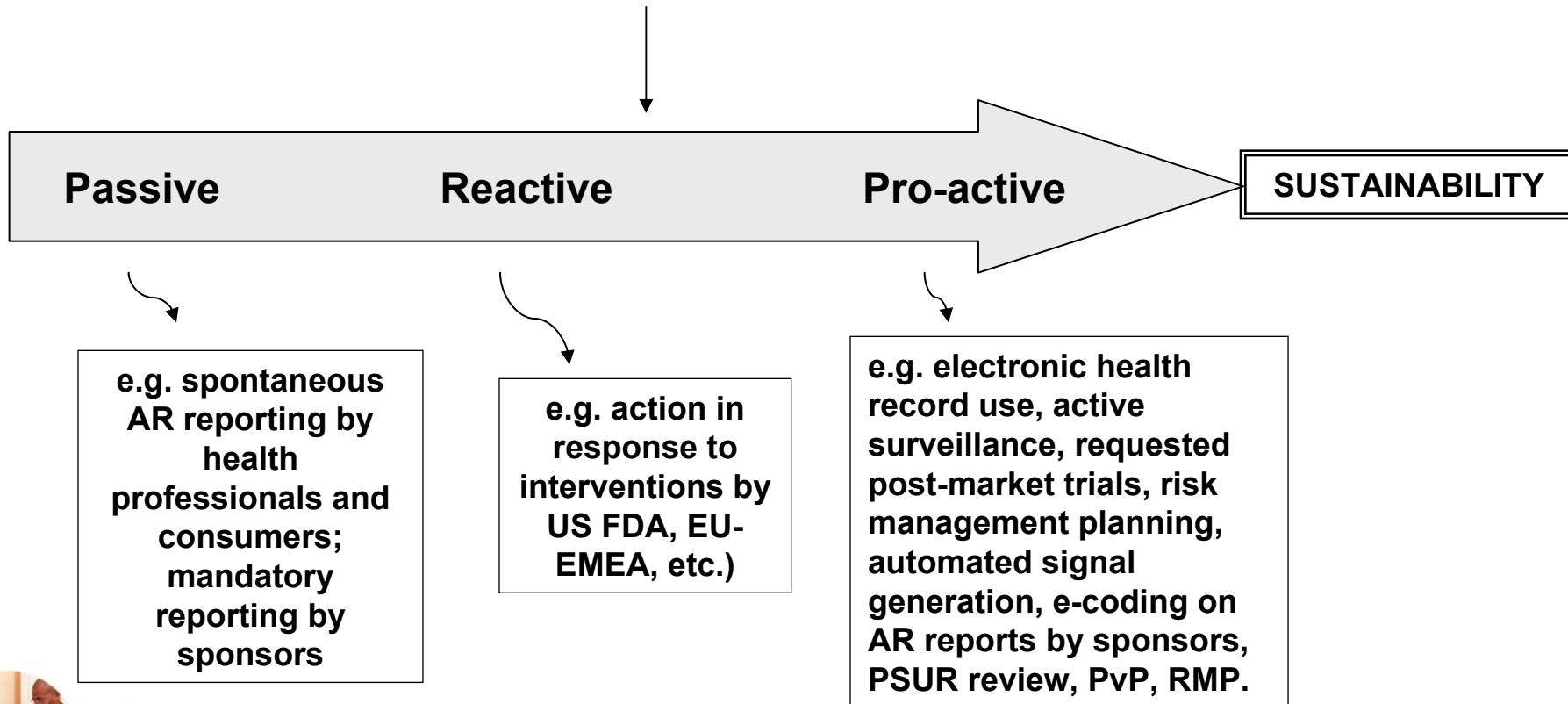
## Emerging Opportunities

- Moving from a passive to a more proactive system of post-market surveillance in Canada.
- Increased emphasis on the consideration of the effectiveness (benefits) as well as the risks of drugs.
- Proposed enhancements to a life-cycle approach in the regulation of drugs in the post-market phase.
- Proposal for research network to generate post-market data on safety and effectiveness.

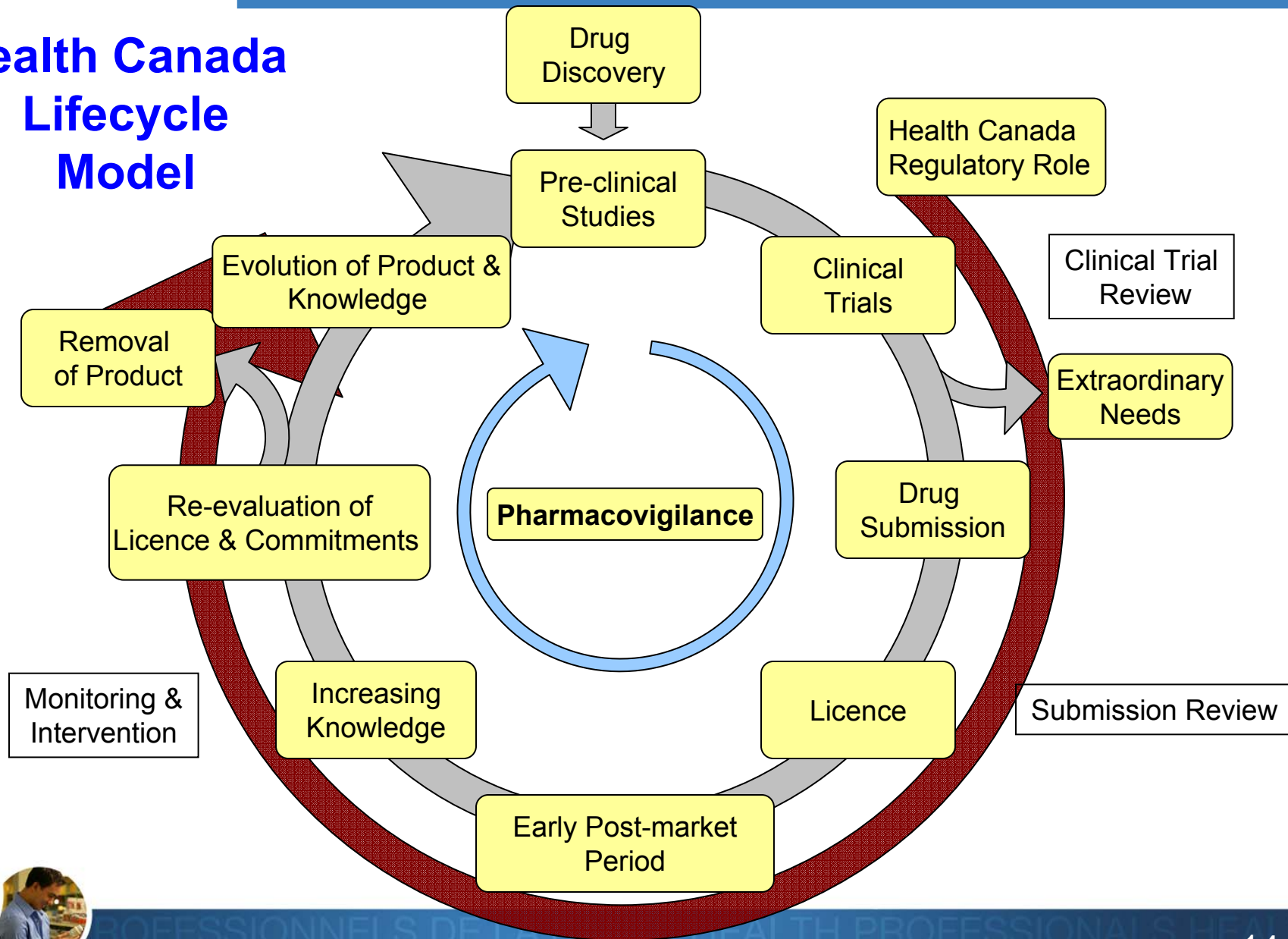


# Future Direction: Moving from Passive to Proactive

## Post-Market Surveillance in Canada



# Health Canada Lifecycle Model



## Post-Market Surveillance - Challenges

Making the optimal use of post-market data on safety and effectiveness to support decision-making in the regulation of drugs:

- Examining the best ways to utilize current real world data types and sources in the post-market signal detection, prioritization, and assessment processes.
  - the most useful sources of information.
  - the most informative types of data/studies.
- Considering the robustness of available datasets for use in the various regulatory decision-making steps.



## Post-Market Surveillance - Challenges

Making the optimal use of post-market data on safety and effectiveness to support decision-making in the regulation of drugs:

- Integrating data on therapeutic effectiveness into the risk management decision-making process.
  - operationalizing (types; timing; critical review).
  - level of evidence to inform or impact decision-making.
- Contemporaneous assessment of safety and therapeutic effectiveness.



## Post-Market Surveillance - Challenges

Making the optimal use of post-market data on safety and effectiveness to support decision-making in the regulation of drugs:

- Using research networks to fill gaps in evidence on the “real world” safety and effectiveness of drugs.
  - Evidence generated leads to improved post-market decision-making.
  - Improved identification and coordination of research needs.
  - Ensuring timeliness for incorporating data into the post-market regulatory decision-making process.
  - The “focus” of post-market research to fill data gaps.
    - the balance between data generation on health risks and therapeutic effectiveness.



## Post-Market Surveillance – Keys to Success

- Collaboration of external third parties.
- Pooling of data from various sources.
- Strategic partnership development, collaboration with other regulators.
- Strong prioritization capacity to optimize resources.
- Data of sufficient quality/robustness to support regulatory decision-making.





# Efficacy & Effectiveness\*

## Efficacy:

The extent to which an intervention produces a beneficial result **under ideal conditions**.

## Effectiveness:

The extent to which a specific intervention, when used **under ordinary circumstances**, does what it is intended to do.

\* Cochrane Collaboration

