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Periodic Safety Update Report (PSUR) Review Project

Workshop on New Directions in Postmarket Surveillance of Pharmaceuticals & Other Health Products: Improving Patient & Product Safety

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Canada

Agenda:

- **What is a PSUR?**
- **Where do PSURs fit in the Product Vigilance Framework?**
- **Current and Future Legislative Authority for PSUR Submission**
- **PSUR Review Project Drivers**
- **PSUR Review Project - Key Objectives**
- **Project Status Update & Next Steps**



Here's a snapshot of the topics that will be discussed today...

What is a PSUR?

- PSURs present the worldwide safety experience of a therapeutic product at defined times post-authorization, in order to:
 - report all the relevant new safety information
 - relate these data to patient exposure
 - summarize the market authorization status of the product in different countries and provide updates on regulatory changes in other jurisdictions
 - indicate whether changes should be made to the product information (product monograph)
 - create periodically the opportunity for an overall safety re-evaluation and conclusion on the safety profile of a product





I do remember mentioning possible side effects.



Development of ICH E2C Guidelines for PSURs

- 1992 proposal for harmonization of periodic safety reporting from Market Authorization Holders (MAH) to regulators
- 1996 The International Conference on Harmonization (ICH) published a guideline (ICH E2C) on “Periodic Safety Update Reports for Marketed Drugs”. Health Canada committed to the implementation of ICH guidelines
- 2002 ICH E2C addendum published



PSURs – General Principles

- General principles include :
 - one report for one active substance
 - prepared every six months or at multiples of 6 months
 - the Company Core Safety Information forms the basis for determining whether an ADR is listed or unlisted
 - safety data should cover only the period of the report with the exception of:
 - regulatory status information
 - data on serious unlisted Adverse Drug Reactions (ADRs)
 - late-breaking information



Content of a PSUR...

1. Introduction
2. Worldwide market authorization status
3. Update of regulatory authority or MAH actions taken for safety reasons
4. Changes to reference safety information
5. Patient exposure



... Content of a PSUR

6. Presentation of individual case histories
7. Studies
8. Other information
9. Overall safety evaluation
10. Conclusion



Objectives of a PSUR Review

- The objectives of a PSUR review are:
 - to monitor that the product's labelling is up to date with respect to the new safety information presented in the PSUR
 - to monitor the market authorization holder's compliance with Good Pharmacovigilance Practices with respect to that product
 - to assess the need for regulatory intervention due to safety reasons



PSUR Review Model – Level I and II Reviews



Current Legislative Authority for PSURs...

C.01.016(2) of the Food & Drugs Regulations requires that “ The manufacturer shall, on an annual basis and whenever requested to do so by the Director, conduct a concise, critical analysis of the adverse drug reactions and serious adverse drug reactions to a drug referred to in subsection (1) and prepare a summary report in respect of the reports received during the previous twelve months or received during such period of time as the Director may specify.”



... Current Legislative Authority for PSURs

C.01.016(3) Where, after reviewing any report furnished pursuant to subsection (1) and any available safety data relating to the drug, the Director considers that the drug may not be safe when used under the recommended conditions of use, the Director may, for the purpose of assessing the safety of the drug, request in writing, that the manufacturer submit

(b) a summary report prepared pursuant to subsection (2).



Current Legislative Authority for PSUR Submission

- C01.016 authority to require an annual summary report – this regulation is quoted when ever MAHs are requested to provide an Annual Summary Report
- Regulatory letter asks that the MAH submit the Annual Summary Report in the format of a PSUR
- Majority of MAHs comply however, there is currently no legislative authority to REQUIRE that Market Authorization Holders (MAHs) submit PSURs in E2C ICH format



Future Legislative Authority for PSUR Submissions

- **Power to require information:**
 - to ensure that information necessary for the ongoing evaluation of the benefits and risks of therapeutic products can be obtained when needed
 - necessary to address those circumstances that would not be already addressed through the terms and conditions of an authorization or licence
 - corresponding regulations would permit the Minister to specify the types of information that is being requested (including PSURs) along with how the information should be submitted, to whom it should be delivered and by which date.



PSUR Review Project Drivers

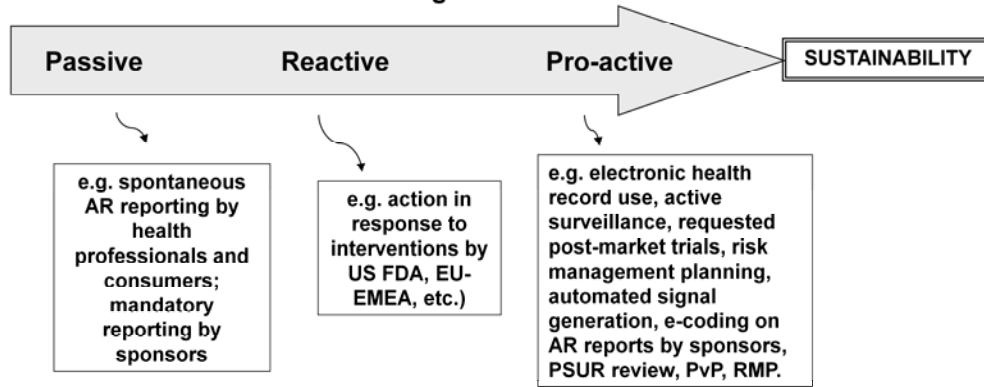
- Blueprint for Renewal II aims to modernize Canada's regulatory system for health products and food by:
"Moving towards a stronger post-market surveillance system"
- MHPD is moving towards using the following risk tools in the life cycle management of health products:
 - Pharmacovigilance Plans (PVPs)
 - Risk Management Plans (RMPs)
 - Periodic Safety Update Reports (PSURs)
- Health Canada has committed to implement ICH E2C (November 1996) and its addendum (February 2003)



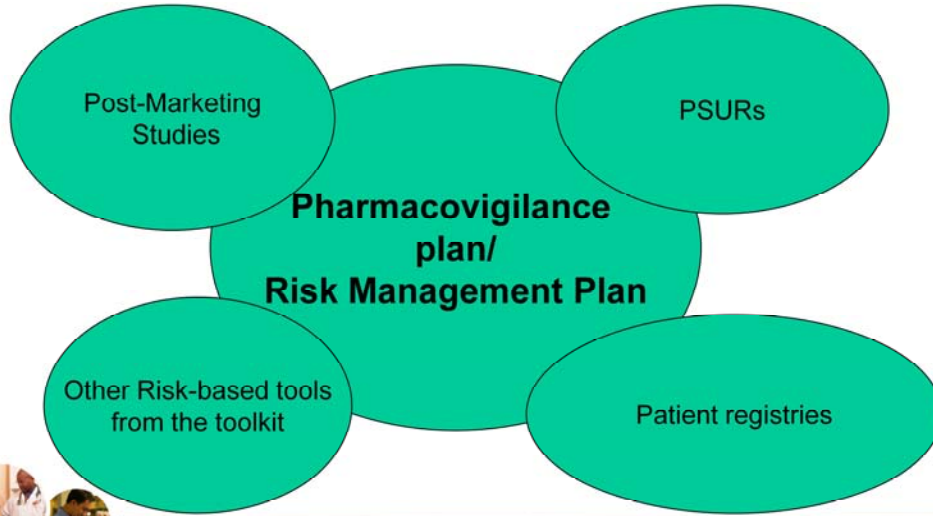
The lack of balanced and objective information, in vaccine advertisements to consumers, in terms of risks/benefits associated with the use of the product (i.e. no information regarding potential side effects, contraindications in certain populations, unknown duration in immunity, other limitations, etc.), is the driver that lead to the analysis of the issue. The ultimate goal is to verify that we are taking all the necessary measures to have accurate and balanced vaccine advertisements that are meaningful to consumers, so that they can make informed decisions about their health.

PSUR Review Project Drivers

Post-Market Surveillance/Health Product Vigilance



Where do PSURs fit in the Product Vigilance Framework?



Where do PSURs fit in the Product Vigilance Framework?

- **Health Canada is currently working to define how the various risk evaluation tools will be used to evaluate the ongoing safety of health products throughout their life cycle to ensure that :**
 - the new product vigilance frameworks integrates the use of the various risk tools used in pharmacovigilance in a logical and systematic way
 - the integrated approach taken to evaluate product safety focuses on the products with the greatest risk and/or unknown risk
 - a high productivity to workload ratio is achieved for the resources invested



PSUR Review Program Project – Key Objectives

- Key objectives of a PSUR review program in Health Canada include:
 - to provide the opportunity for an organized and systematic structure for the review of PSURs
 - to ensure that PSURs reviews are assigned and conducted based on the potential risk of a product (i.e. with priority given to highest or unknown risk associated with health products)
 - to ensure an efficient allocation of resources
 - to improve the capacity for Health Canada to conduct ongoing assessment of MAHs ability to manage the safety of their products
 - to bring Health Canada in line with the use of international standards in pharmacovigilance practices.



Project Status/Update...

Current Project Status:

- PSUR review templates and SOPs for Level I & II reviews have been finalized and approved by PSUR-Task Force and MHPD Management Committee
- The design of the PSUR Tracking system (in DSTS*) has been completed and signed off
- Risk Tool Screening Section staffing actions:
 - Project Leader has been hired
 - Staffing of the Risk Tool Screening regulatory officer - in progress
- DocuBridge and DSTS* training of MHPD staff in progress:
- Second monitor for all PSUR reviewers have been ordered



* Drug Submission Information System

...Project Status/Update

Next Steps:

- Develop regulatory letters to be sent to Market Authorization Holder (MAH) e.g. Confirmation of Receipt; Notice of Deficiency, Intent to Conduct a Comprehensive Review, Outcome of Comprehensive Review, etc.
- Seek senior management's approval of recommended option for the PSUR Review Program & work process flow
- Prepare a Communications Plan
- Send *Notice of Intent* to MAHs to inform them of Health Canada's intention to implement a PSUR Review Program (targeted time frame: Fall 2009).



Questions / Comments...





PROFESSIONNELS DE LA SANTE HEALTH PROFESSIONALS
INCIDENT REACTION DATABASE BASE DE DONNEES DES EFFETS INDIVIDUELS



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**ELEMENTS OF DISCUSSION REGARDING
THE PRODUCT VIGILANCE
TRANSFORMATION TOPICS PRESENTED
TODAY**

Facilitator: Vicky Hogan, Health Canada



PROFESSIONNELS DE LA SANTÉ HEALTH PROFESSIONALS
BASE OF KNOWLEDGE BASE OF KNOWLEDGE

PRODUCT VIGILANCE IN CANADA

- 1) Based on the information provided to you in the presentations you heard today, what role do you now or could you in the future play in product vigilance in Canada?
- 2) Are we missing any elements in our development of product vigilance?
- 3) What might be the greatest challenges for Health Canada? What might be the greatest challenges for stakeholders?

