

NOTICE

Our file number: 09-103644-626

Notice Regarding Implementation of Risk Management Planning including the adoption of ICH Guidance Pharmacovigilance Planning - ICH Topic E2E

Health Canada, as official observer to, and active participant in, the International Conference on Harmonisation (ICH), is committed to the adoption and implementation of ICH guidance. Health Canada, by this notice, is advising of its intent to implement Risk Management Planning, including adoption of ICH guidance E2E, *Pharmacovigilance Planning*¹, as part of an integrated risk management strategy supported by the necessary regulatory framework. In this regard, stakeholders will be consulted on the development of an enabling pharmacovigilance framework as part of broader consultations on the modernization of the *Food and Drugs Act* and *Regulations*, taking into consideration the importance of alignment with international requirements.

As an interim measure, Health Canada wishes to further advise that the European Medicines Agency (EMA) *Guideline on Risk Management Systems for Medicinal Products for Human Use*² and the *EMA Template for European Union Risk Management Plans (EU-RMP)*³, as amended in the attached Appendix, represents an acceptable approach to fulfilling requests by Health Canada for Risk Management Plans.

The key components to any Risk Management Plan (RMP) include:

- (1) a Safety Specification, which is a summary of the known important safety information about the health product and is a means to identify gaps in knowledge;
- (2) a Pharmacovigilance Plan, which is based on the Safety Specification and identifies and characterizes known or potential safety concerns; and
- (3) a Risk Minimization plan (RMinP), which provides proposals on how to minimize any identified or potential safety risk.

Health Canada will accept Risk Management Plans in other recognized formats (i.e. Risk Evaluation Management System), as long as they cover the elements described in the EU guidance. Appendix 1 to the Notice highlights suggested changes to the EMA Guideline on

¹ ICH E2E: Pharmacovigilance Planning document:
<http://www.ich.org/cache/compo/475-272-1.html#E2E>

² European Medicines Agency (EMA) Guideline on Risk Management Systems for Medicinal Products for Human Use:
<http://www.emea.europa.eu/htms/human/raguidelines/pharmacovigilance.htm>

³ Template for EU Risk Management Plan (EU-RMP)
<http://www.emea.europa.eu/htms/human/raguidelines/pharmacovigilance.htm>

Risk Management Systems in order to provide a Canadian context to submitted Risk Management Plans.

Risk Management Plans may be requested by Health Canada when they are considered relevant to decisions regarding the benefit to risk profile of a drug. If stakeholders have questions regarding whether or not it is appropriate to submit a Risk Management Plan to Health Canada, they are encouraged to start a dialogue early in the submission process (i.e. pre-submission meetings). In addition, stakeholders are requested to *clearly identify* at the time of screening whether or not a Risk Management Plan is included with a submission package.

Criteria which *could* be used to request a Risk Management Plan (RMP) include, but are not limited to:

- (1) any product containing a new active substance;
- (2) potentially those products with a significant change in indication;
- (3) those products which are new to a class for which a serious or potentially serious safety risk has been previously identified; or
- (4) on request of the regulator under circumstances where a safety risk has been identified such that the risk associated with the product is perceived to potentially outweigh its benefit².

Requests for such documents would involve pharmaceuticals, biologics and biotechnology-derived products for human use, within the scope of ICH⁴. Natural Health Products, Medical Devices and Veterinary Products are outside the scope of this interim implementation plan. Stakeholder consultations will inform future decisions regarding whether Risk Management Planning should be introduced as a possible regulatory tool for additional health product lines.

Background

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Pharmacovigilance planning has been recognized by the ICH through the finalization of E2E, the Guidance for Pharmacovigilance Planning for industry. Other regulatory jurisdictions, including the European Union and the United States have incorporated Pharmacovigilance and Risk Management Planning formally and informally in the submission process for drug review.

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International Conference on Harmonisation (ICH) Web site:
<http://www.ich.org/cache/compo/502-272-1.html#S6>

For any comments or inquiries related to this notice, please contact:

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For emails pertaining to this issue, please include the statement "Implementation of Risk Management Planning" in the subject line.

Appendix

Suggested changes to the EMEA Guideline on Risk Management Systems for Medicinal Products for Human Use in order to provide Canadian context

EMEA Guideline Section	Canadian Approach
Entire Guideline	Replace Summary of Product Characteristics (SmPC) with the Canadian Product Monograph (CPM).
Section 3: Legal Basis	Specific to the European Context: Not applicable in Canada
Section 4.1: Description of the risk management system	Refers to legislation requiring a description of the Risk Management System: Not applicable in Canada.
Sections 4.3.1 to 4.4	Requirements for EU-RMP in Europe; Processes regarding Central authorization: Not applicable in Canada.
Section 4.5.2.2 Populations not studied in the pre-authorization phase: Post-marketing experience	A discussion of post-marketing experience in the Canadian context should be presented.
Section 4.5.2.5: Epidemiology	The epidemiology of the medical condition in the Canadian population should be discussed.
Section 4.5.2.7 Additional EU requirements	All of these components should be included in the Canadian submission.
Section 4.6.1. Routine Pharmacovigilance	In the Canadian context this would involve: monitoring of Canadian adverse events from the Market Authorization Holder's database; reconciliation of such reaction with Health Canada's Canada Vigilance Database and routine pharmacovigilance of foreign reports.
Section 4.10 Marketing authorization	Refers to recommendations provided by the Committee for Medicinal Products for Human Use (CHMP): Not applicable in Canada.
Section 4.13 Submission of updated EU-RMP documents	Timelines for submission of updated RMP documents in Canada will be decided on a case-by-case basis until Health Canada and stakeholders gain experience in this area.