Questions and Answers

Role of Health Canada and the Risk Management Plan in the Product Lifecycle
Information Session for Stakeholders

Q1. What is a Risk Management Plan?

A Risk Management Plan (RMP) is a document created by the manufacturer of a drug product and submitted to regulatory agencies, such as Health Canada, for review. RMPs often consist of a core document produced for international regulators, plus country-specific information, for example, in the form of a Canadian-specific addendum. An RMP describes a set of important safety risks and uncertainties, along with activities and interventions designed and intended to characterize and minimize those risks and uncertainties. The objective of an RMP is to ensure that the benefits of a particular health product outweigh the safety risks by the greatest achievable margin, and thus maximize positive patient outcomes. RMPs are normally updated during the life cycle of the product.

- A Pharmacovigilance Plan details how the risks will be further characterized and monitored through the conduct of pharmacovigilance activities.

  Routine pharmacovigilance activities, such as the reporting of adverse reactions and the preparation of annual adverse reaction reports by the manufacturer, are conducted for all drug products. When a specific risk or uncertainty needs better characterization or closer monitoring, additional measures such as clinical trials, post-authorization safety studies or patient registries may be put in place. Health Canada periodically reviews reports prepared by the manufacturer that describe the occurrence of adverse reactions after market entry, and determines if the risk/benefit balance has changed and if additional regulatory actions are warranted.

- A Risk Minimization Plan focuses on specific measures and tools to minimize the safety risks, and also focuses on the evaluation of the effectiveness of these measures.

  Routine risk minimization is usually accomplished by the inclusion of risks associated with a drug product in its Canadian Product Monograph. Additional risk minimization measures are considered when the labelling of the risks alone is not sufficient to mitigate them. Examples of additional risk minimization measures may include:

  - Brochures for healthcare professionals and/or for patients (and caregivers)

  Brochures for healthcare professionals and/or for patients provide additional information on specific safety risk(s). They may also provide advice on the early recognition and management of these risks and can also address important considerations regarding the use of the product.

  - Checklists

  Checklists are a tool that can be used where a number of steps or actions are needed prior to prescribing and/or administering a product.

  - Patient Alert Cards

Patient Alert cards are generally used when it is desirable to have the patient carry information about their medication and associated safety risks, at all times. They may be shared with healthcare professionals other than the patient's regular care team if an emergency arises.

- Risk Communications

The aim of a Risk Communication is to communicate rapidly to a specific audience (such as healthcare professionals important information about of a safety risk associated with a product, for which certain actions on their part should be taken.

- Pregnancy Prevention Programs

Pregnancy Prevention Programs (PPPs) include several interventions that are aimed at reducing the exposure during pregnancy to a given health product with established or potential teratogenic effects. The objectives of the PPP are to ensure that patients are not pregnant when initiating treatment with the product, and do not become pregnant while under treatment or shortly thereafter.

- Controlled Distribution Programs

Controlled Distribution Programs aim at controlling access to a health product, through the implementation of a set of requirements that need to be fulfilled prior to a product being prescribed or dispensed to optimize its safe use (e.g., laboratory testing). Outside of the scope of Risk Management Plans, manufacturers have made operational decisions related to specific distribution approach for their product.

Health Canada is keeping abreast of new, innovative means to share key safety information with healthcare professionals and patients. Health Canada will review any educational tool proposed by a Sponsor within an RMP, to determine whether it will effectively communicate key safety information regarding the important risk in question to the target audience, to mitigate its occurrence. Measures evaluating the effectiveness of the educational tools proposed should also be included by the Sponsor in the RMP.

Q2. Why are Risk Management Plans important for me as a healthcare professional (HCP)?

The main objective of the Risk Management Plan (RMP) is to identify how risks will be minimized and monitored to ensure that the benefit of a particular drug used in the treatment of patients outweigh the risks.

Specific elements of the RMP are designed for either healthcare professionals or patients. For example, these elements may include Brochures for healthcare professionals and/or for patients (and caregivers), Checklists, Patient Alert Cards and Risk Communications.

These materials help healthcare professionals in the prescription and administration of prescribed products. They also assist with patient education and help ensure that products are used correctly. Furthermore, they alert patients to potential early evidence of serious adverse events, and therefore serve a purpose in minimizing safety risks. Programs such as Pregnancy Prevention are implemented by manufacturers very selectively when the risk of serious adverse outcomes are of particular concern. Healthcare professionals' involvement in these programs are particularly important. For example, it ensures that important patient data are collected to inform patient safety. The safety data gathered through these programs are also used to help evaluate their effectiveness.

Q3. Why do some risk minimization measures include educational materials for HCPs?

The intended objective of educational materials is to raise awareness to specific important risks or on important considerations regarding the use of the product (therapeutic monitoring, product handling, and administration). They may also focus on the early recognition and management of adverse reactions. Educational materials may be helpful for encouraging discussions between healthcare professionals and patients in relation to the safety concerns and RMM when the objectives of RMM cannot be reached with labelling alone.

Q4. How are educational materials reviewed prior to them being available for HCPs and patients?

Educational materials are proposed by the Sponsor (sometimes in response to issues raised by Health Canada) and then reviewed by Health Canada to determine if they adequately communicate the key safety information to the intended audiences, and are appropriate at mitigating the risk in question.

Health Canada encourages manufacturers to submit all educational materials directed at Canadian healthcare professionals and patients to the Pharmaceutical Advertising Advisory Board (PAAB) for review.

Q5. Where can I find information about actual Risk Management Plans?

While detailed information regarding RMPs and their components is not currently available on the Health Canada website, there are different ongoing initiatives to address this information gap and increase transparency.

- The Health Canada Drug Product Database provides high-level information on additional risk minimization measures included in the product's RMP, if any, on the same webpage as the link to the Canadian Product Monograph of a given drug product.

- The Health Canada Summary Basis of Decision for a specific drug product also includes information on the approved RMP, if any.

- New, more agile regulations are being developed to better support the oversight of drugs, both before and after market entry. As part of these regulations, measures to increase transparency of RMPs are being considered. A draft of these regulations may be published in Canada Gazette Part I as soon as October 2022, for public consultation.

Q6. What are the differences between Risk Management Plans and Patient Support Programs?

Patient Support Programs or Patient Assistance Programs are developed by the manufacturer and are positioned as a service to support patient care. Specific services may include physician and patient support through coordination of drug distribution, appointment scheduling, call centres for assistance with health insurance questions and reimbursement support, nursing services, and pharmacy services.

Unlike the Risk Management Plan (RMP), Patient Support Programs are not requested nor reviewed or overseen by Health Canada and are not considered additional RMMs since their primary objective is not the mitigation of risks.

However, a sponsor may independently decide to implement a Patient Support Program which integrates some components of the RMP. For example, adverse reaction data collection is sometimes done through Patient Support Programs. The distribution of Educational materials aimed at minimizing risks can also be done through Patient Support Programs.

From Health Canada's perspective it is important that any measure that is essential for risk minimization be accessible to healthcare professionals and patients, whether they are part of a Patient Support Program or not.

Q7. Why is the Risk Management Plan important to Health Canada?

When a drug is first approved, its safety profile is not considered fully characterized. Information pertaining to the severity and frequency of some safety risks, their potential to lead to negative clinical outcomes, or information pertaining to the use of the drug in more vulnerable patient populations may not be available from clinical trials. The RMP ensures a plan is in place to further monitor these risks during the product's life cycle, and mitigate them. It also supports safe access to health products for which there are important potential or known safety concerns that may have a direct impact on the benefit-risk profile of the drug in question, and therefore constitutes an important factor in the decision to approve or keep a drug on the market.

Q8. How is the selection of additional measures done?

For a drug to receive and maintain marketing authorization in Canada, its benefits must outweigh its risks. Health Canada uses the label as a primary tool to communicate information related to safety risks with drugs.

When it is found that describing an important safety risk in the product labelling is not sufficient to raise awareness about this risk, the use of additional measures (described above) is considered as a means to prevent its occurrence or minimize its severity. The manufacturer is responsible for selecting and designing additional risk minimization measures, subject to review by Health Canada.

The selection of appropriate additional measures should follow a risk-based approach, and must be aligned with the intended objectives of the intervention. This approach takes into account the seriousness and probability of the safety risk(s), the intended population, impact on the health care setting and clinical practice, feasibility with regard to implementation, anticipated effectiveness to prevent the risk(s), degree of clinical management required, and the need for timely patient access. A given risk or set of risks may be addressed by using a variety of risk minimization measures, and a single risk minimization measure may address more than one risk or set of risks that need to be mitigated.

The specific operational requirements implemented for more stringent risk minimization measures, such as the selection of preferred pharmacies that can enrol in the program or the training of pharmacists, are usually decisions made by the manufacturer, without the oversight of Health Canada.

Q9. What is the review process for a Risk Management Plan?

Risk Management Plans are typically included as part of a New Drug Submission (NDS), as discussed with Sponsors prior to the submission of a NDS, and further recommended based on certain criteria outlined in the Guidance Document on the Submission of Risk Management Plans and Follow-up Commitments. Risk Management Plans are reviewed by Health Canada in parallel with the rest of the NDS, which includes the review of non-clinical and clinical safety and efficacy data, as well as quality and manufacturing information, among other topics.

The RMP, including any additional measures the manufacturer intends to take to monitor or mitigate risks and uncertainties, may be considered by Health Canada in deciding whether to authorize sale or allow the continued sale of a product.

Additional information on the Management of Drugs Submissions and Applications can be found here.