

# Risk Minimisation Through the Affiliate Lens

## Executive Summary

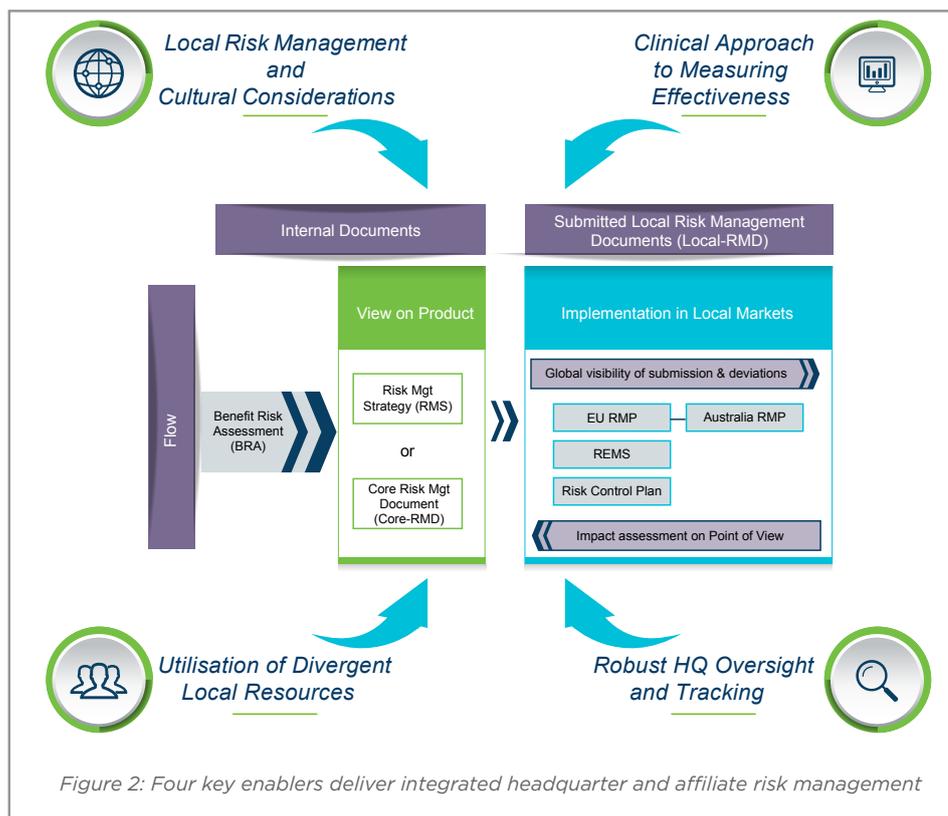
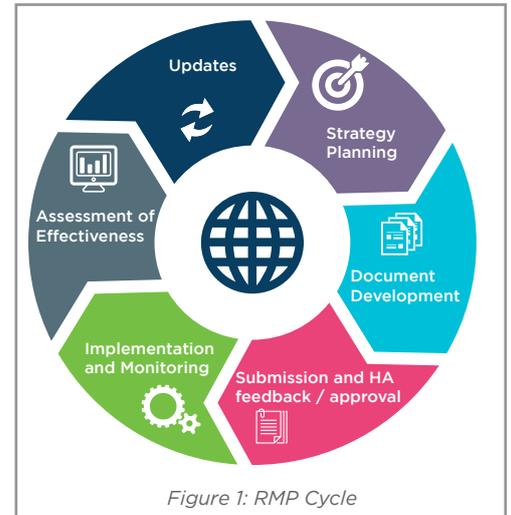
Navitas Life Sciences

### Risk Minimisation – the End Goal of Risk Management

Marketing authorisation holders (MAHs) are obligated to maintain a positive benefit/risk (B/R) profile for the products under their responsibility. The objective of risk management within pharmacovigilance (PV) is to ensure that the benefits of a medicine, or a series of medicines, exceed the risks by the greatest achievable margin.

### A Complex Global Regulatory Landscape to Navigate

All risk management documents (RMD) produced for Health Authorities (HAs) look to identify, monitor and minimise risk. The cycle of risk management reflects the steps an MAH should follow: the key is planning, informed action and structured assessment (Figure 1). The challenge an MAH faces is applying this cycle at the local level, where there are varying resources and local considerations. MAHs must balance the need to describe the risk minimisation measure (RMM) in sufficient detail to the authorities for approval while allowing sufficient flexibility to meet national requirements. Navitas see four key challenges and out of those, opportunities for local risk management success (Figure 2).



### Local Risk Management and Cultural Considerations

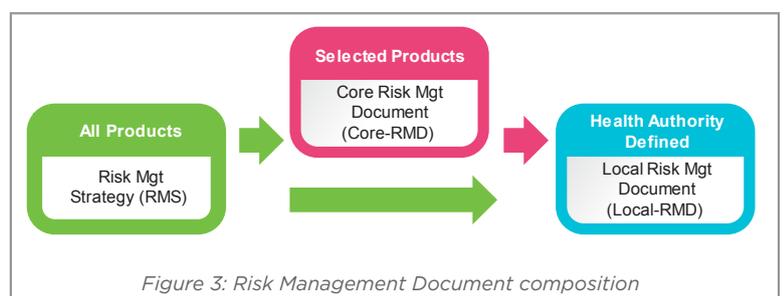
Development of a core risk management document (Core-RMD) is often the approach to address local requirements - there has been a trend to utilise the EU-RMP format as a point of departure which has caused challenges as the regulatory requirements and definitions differ country to country. A simple correction has been the use of the term Risk Management Document (RMD) instead of RMP. The RMD can be differentiated, with a Core-RMD that centres on what a company considers core risk management and Local-RMD which is a term for any local requirement such as REMS or EU-RMP. The challenge is ensuring that the global risk management position, Core-RMD, is maintained on an ongoing basis, informed by local regulatory intelligence and transferred into all Local-RMDs.

Through the development of a core position, industry can accommodate differences at the local level while ensuring a consistent global message and evaluation. The creation of an internal Risk Management Strategy (RMS) or a Core-RMD enables companies to maintain their 'core' while allowing

flexibility to adapt (Figure 3). The benefit of this is consistency in messaging, with the Core-RMP produced by taking the RMS and adding scientific depth. Therefore, all locally submitted documents use the RMS or the Core-RMD. This model emphasises the collaboration needed between headquarters and the local offices to successfully create and maintain RMDs.

### Utilisation of Divergent Local Resources

The right blend of local capacity and capability is pivotal, complicated by the fact that not every local office has the same resource model. The archetypal role of the affiliate as an operational hub and post-delivery service for Individual Case Safety Reports (ICSRs) is no longer viable. The demand on a Local Safety Officer has grown to include responsibilities to support functions such as Regulatory and Medical information. The cross functional nature of risk management activities drives the need for a cross-functional team approach (Figure 4).



The creation of a cross-functional team at the regional/local level is to provide input on feasibility and applicability of the global position (e.g. RMS). This team creates their local risk management plan and implements the activities described in the local-RMD. The core members are Local Safety, Local Regulatory Affairs, and Local Medical Affairs. The connection between local and global is achieved via a strong, continual communication channel and relationship between Local Safety and Global Safety.

## Clinical Approach to Measuring Effectiveness

The risk management cycle is not constrained to strategy and documents; outcomes matter and effectiveness assessment is key (Figure 5).

A specific and vital step is the implementation of risk management activities (RMA) and risk minimisation measures (RMMs); they are the actions described in the RMD. Companies should be taking a systematic approach to measuring effectiveness in a similar way to a clinical study. Referring directly to CIOMS IX, both the process (implementation) and outcome (minimised risk) should be assessed using a structured framework. As in Clinical, defining the primary points (success criteria) occur at design of the study. It is at the design step of the RMM that headquarters and local need to collaborate as the RMM must be locally relevant and feasible.

Assessing the outcome is another global-local activity as it relies on a baseline taken before implementation and then collaborating on whether the risk was minimised. As described by the EMA, "the ultimate measures of success of a risk minimisation programme are the safety outcomes..." (EMA, 2014b). One example of a safety outcome is measuring the frequency or severity of an adverse reaction.

Based on outcomes, headquarter and local teams assess the overall effectiveness of the RMM and decide whether the RMM is maintained, adapted, or ceased.

## Robust HQ Oversight and Tracking

Since all risks are ultimately minimised locally it is vital that an MAH has oversight of how the strategy is implemented - end-to-end tracking is essential. Investment in a system that allows an MAH to track risk management will offer both oversight and assurance that patients' safety is being enhanced. A new system is not necessarily required as many companies already have an electronic information system to store their RMD, such as SharePoint. Combining the use of SharePoint, business process management tools, workflow management tools, or an already established regulatory information management system can provide a strong tracking solution. This also provides the potential for visual dashboards.

## Path Forward

Maintaining the core risk management strategy while allowing flexibility for local variation is important. At the global level, having a team who coordinate using a single global risk management strategy (RMS) is the optimal setup at headquarters. This global team would not necessarily be new; likely, they exist through the Safety Management Teams (SMT) or Benefit Risk Teams (BRT) which many MAHs already have in place. This group set the core position and develop the global RMS. This setup is reflected at the local level, where a team similar in structure is formed for local RM to tailor documents and activities to the patient and geography. The natural handover is at the point where the Core-RMD or RMS is provided to the affiliates for local consideration. The local team structure ensures that departments are represented at a local level and by combining resources, experience, and tools, it achieves a higher level of cross-functional alignment and synergy. Finally, it is at the global level that a dashboard is utilised to monitor and maintain oversight, displaying the content of the RMS; overcoming the challenge faced in many RIMS of having easy, real-time access to the information they need.

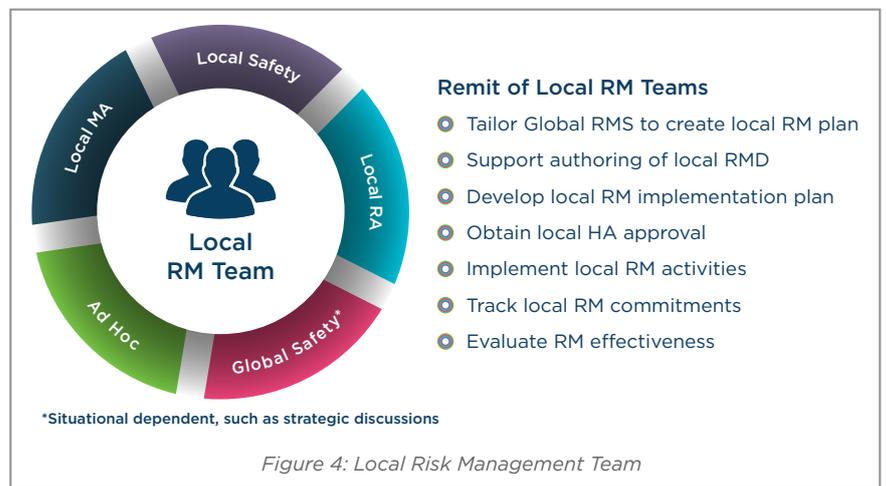


Figure 4: Local Risk Management Team

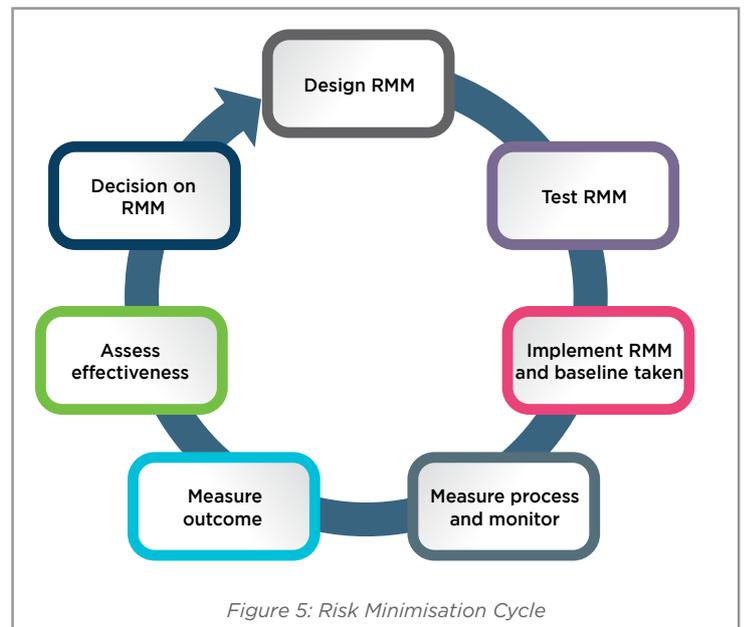


Figure 5: Risk Minimisation Cycle



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