AGENZIA ITALIANA DEL FARMACO

Tutela Ricerca e Sviluppo per la Salute

ICSRs

Risk Management Plan Assessment

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Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	x	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	x	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	x	☐	☐	☐ optional
2. Consultancy for a company	x	☐	☐	☐ optional
3. Strategic advisory role for a company	x	☐	☐	☐ optional
4. Financial interests	x	☐	☐	☐ optional
5. Ownership of a patent	x	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	x	☐	☐	☐ optional
7. Investigator	x	☐	☐	☐ optional
8. Grant or other funding	x	☐	☐	☐ optional
9. Family members interests		X	☐	☐ optional

*Laura Galatti, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (25.03.2015) and published on the Official Journal of 15.05.2015 according to EMA policy /626261/2014 on the handling of the conflicts of interest for scientific committee members and experts.

N.B. I am not receiving any compensation except for the daily allowance

The Italian Pharmacovigilance System – some legal background (1)

European legislation

- Regulation 1235/2010/EU (02 July 2012)
- Directive 2010/84/EU (21 July 2012)
- Implementing regulation (EU) 520/2012 (10 July 2012)
- Guideline on good pharmacovigilance practises (GVP)

National legislation

- D.Lvo 219/2006 (and its updates) – community code on medicinal products for human use
- D.M. 30/04/2015 – rules, duties and responsabilities of different stakeholders
- Law 24 November 2004, n 326 – AIFA institution
- Standardized Operative Procedure (SOP) available in AIFA – guarantee coherence and quality within processes carried out

The Italian Pharmacovigilance System – main roles and duties (1)

- **Reporter**: sending of ICSRs to the local PV responsible (paper forms or on-line reports through Vigifarmaco)

- **Local PV Responsible**: ICSRs management in the database (entry, updating, deletion), feedback to the report, answers to MAHs' requests, dissemination of information to healthcare professionals, analysis of local data

- **Regional PV Centers**: regional coordination of PV activities, support to LRPV in the ICSRs management, quality control and data coding, causality assessment, data analysis, partecipation to signal dection, educational activities

The Italian Pharmacovigilance System – main roles and duties (2)

- **Regions**: to realise active PV projects, to provide usage data, information and training to healthcare professionals

- **Pharmaceutical companies**: transmitting ICSRs directly to EV, limited access to the ICSRs in the National Pharmacovigilance Network

The Italian Pharmacovigilance System – main roles and duties (4)

AIFA

5. Transmit the reports of suspected ADR, electronically, to the EV database

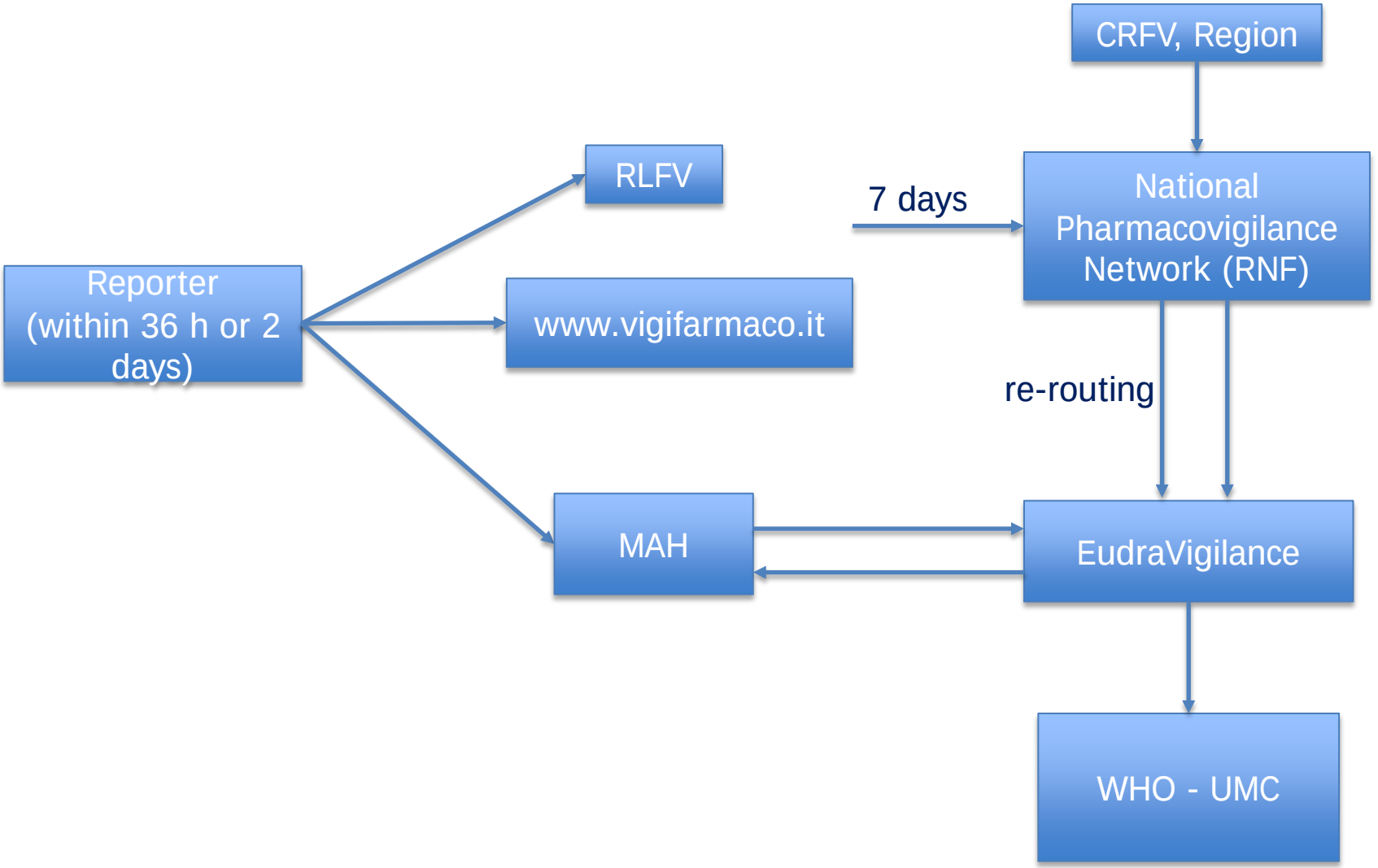
5. Encourage patients, doctors, pharmacists and other health professionals to report suspected ADRs

5. Facilitating patient in reports ADRs by offering them paper and electronic reporting forms

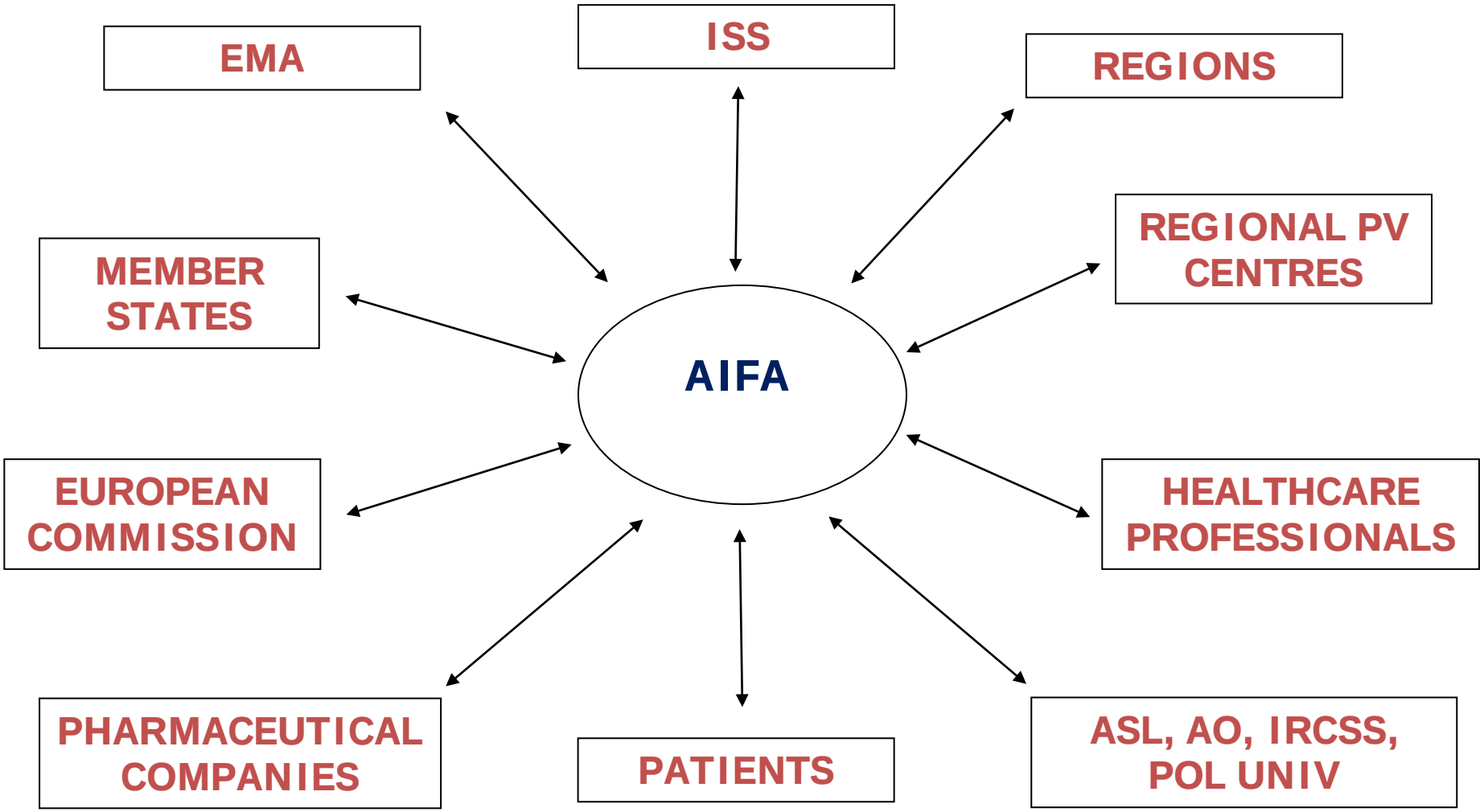
5. Provide the public with timely important PV information

5. Update the web portal and link it to the EMA web portal

How to report ADRs – reporting flow



The Italian Pharmacovigilance System - Stakeholders (1)



RMP

References:

GVP Module V- Risk Management system (Rev 2)

Other references:
-Guidance on format of the RMP in the EU – in integrated format

-Guideline on good pharmacovigilance practices (GVP)
Annex I - Definitions (Rev 3)

Aim of a Risk Management Plan (RMP)

Generally, a medicinal product will be associated with adverse reactions and these will vary in terms of severity, likelihood of occurrence, effect on individual patients and public health impact.

However, not all adverse reactions and risks will have been identified at the time when an initial marketing authorisation is granted and some will only be discovered and characterised in the post-authorisation phase.

The aim of a risk management plan (RMP) is to document the risk management system considered necessary to identify, characterise and minimise a medicinal product's important risks.

Aim of a Risk Management Plan (RMP)

The RMP contains:

1. the identification or characterisation of the safety profile of the medicinal product, with emphasis on important identified and important potential risks and missing information, and also on which safety concerns need to be managed proactively or further studied (the ‘safety specification’);
2. the planning of pharmacovigilance activities to characterise and quantify clinically relevant risks, and to identify new adverse reactions (the ‘pharmacovigilance plan’);
3. the planning and implementation of risk minimisation measures, including the evaluation of the effectiveness of these activities (the ‘risk minimisation plan’).

Definitions

Identified risk (1)
An untoward occurrence for which there is adequate evidence of an association with the medicinal product of interest. Examples include:
• an adverse reaction adequately demonstrated in non-clinical studies and confirmed by clinical data;
• an adverse reaction observed in well-designed clinical trials or epidemiological studies for which the magnitude of the difference compared with the comparator group, on a parameter of interest suggests a causal relationship;
• an adverse reaction suggested by a number of well-documented spontaneous reports where causality is strongly supported by temporal relationship and biological plausibility, such as anaphylactic reactions or application site reactions.
In a clinical trial, the comparator may be placebo, active substance or non-exposure.

Definitions

Identified risk (2)

The RMP should focus on the important identified risks that are likely to have an impact on the risk-benefit balance of the product. An important identified risk to be included in the RMP would usually warrant:

- Further evaluation as part of the pharmacovigilance plan (e.g. to investigate frequency, severity, seriousness and outcome of this risk under normal conditions of use, which populations are particularly at risk);
- Risk minimisation activities: product information advising on specific clinical actions to be taken to minimise the risk, or additional risk minimisation activities.

Definitions

Important Identified risk (examples)
If an adverse reaction which is an important identified risk for an active comparator occurs at a similar or higher frequency with the new medicinal product in a clinical trial, this suggests that the adverse reaction may also be an important identified risk for the new medicinal product.

Definitions

Important Identified risk (examples)

For a medicinal product on the market for years, drug-induced liver injury was identified as a new adverse reaction after a referral procedure and considered to have a major impact on the benefit risk. Warnings in section 4.4. of the SmPC have been implemented and the recommendation to perform regular liver function tests have been added to the SmPC as a precautionary measure in the post-marketing period. “Hepatotoxicity” or a similar term should be classified as an important identified risk.

Definitions

Important Identified risk (examples)

Neutropenia of ≥ grade 3 and serious infections with fatal outcome were observed in clinical trials prior marketing authorisation of an oral “first-in-class” medication. Regular blood counts are recommended, according to the SmPC, to minimise the risk of serious infections. As oral medications are very likely to be used in an out-of-hospital setting and it is unclear whether this risk minimisation will be effective, “serious infections” should be included as an important identified risk.

Definitions

Potential risk

An untoward occurrence for which there is some basis for suspicion of an association with the medicinal product of interest but where this association has not been confirmed . Examples include:

• non-clinical toxicological findings that have not been observed or resolved in clinical studies;

• adverse events observed in clinical trials or epidemiological studies for which the magnitude of the difference, compared with the comparator group (placebo or active substance, or unexposed group), on the parameter of interest raises a suspicion of, but is not large enough to suggest, a causal relationship;

• a signal arising from a spontaneous adverse reaction reporting system;

• an event known to be associated with other active substances within the same class or which could be expected to occur based on the properties of the medicinal product.

Definitions

Potential risk

From the potential risks of the medicinal product, the RMP should address only the risks that are undesirable clinical outcomes and for which there is scientific evidence to suspect the possibility of a causal relationship with the medicinal product, but where there is currently insufficient evidence to conclude that this association is causal. The important potential risks to be included in the RMP are those important potential risks that, when further characterised and if confirmed, would have an impact on the risk-benefit balance of the medicinal product. Where there is a scientific rationale that an adverse clinical outcome might be associated with off-label use, use in populations not studied, or resulting from the long-term use of the product, the adverse reaction should be considered a potential risk, and if deemed important, should be included in the list of safety concerns as an important potential risk. Important potential risks included in the RMP would usually require further evaluation as part of the pharmacovigilance plan.

Definitions

Important Potential risk (examples)

A treatment has been proven effective only in adults (e.g. because the disease is very rare in children and, therefore, data in children could not be gathered and the medicinal product is likely to be ineffective or unsafe in this population). However, a high risk of off-label use in children related to the absence of effective and safe treatments in this patient population has been identified post-marketing. The potential safety harm to children resulted from the likely off-label use should be discussed in the RMP, a safety concern in the form of an important potential risk related to the specific safety concern should be considered, and paediatric post-marketing safety studies may therefore be a suitable pharmacovigilance activity, despite the restricted indication in adults.

Definitions

Important Potential risk (examples)

Based on the characteristics and the mechanistic properties of a medicinal product, abuse of a medicinal product is possible and would lead to significant consequences such as addiction and death from overdosing. Nevertheless, abuse has not yet been observed. Risk from abuse/misuse should be listed as an important potential risk.

Definitions

Important Potential risk (examples)

Based on the characteristics and the mechanistic properties of a medicinal product, abuse of a medicinal product is possible and would lead to significant consequences such as addiction and death from overdosing. Nevertheless, abuse has not yet been observed. Risk from abuse/misuse should be listed as an important potential risk.

Definitions

Missing information

Gaps in knowledge about a medicinal product, related to safety or use in particular patient populations, which could be clinically significant.
It is noted that there is an ICH definition for important missing information, which is: critical gaps in knowledge for specific safety issues or populations that use the marketed product .
The change of the EU term, to name this concept “missing information” rather than “important missing information”, is to be clear that in the EU a marketing authorisation cannot be granted if there are unacceptable gaps in knowledge, a marketing authorisation shall be refused if the quality, safety or efficacy are not properly or sufficiently demonstrated.

Definitions

Missing information

Missing information relevant to the risk management planning refers to gaps in knowledge about the safety of a medicinal product for certain anticipated utilisation (e.g. long-term use) or for use in particular patient populations, for which there is insufficient knowledge to determine whether the safety profile differs from that characterised so far. The absence of data itself (e.g. exclusion of a population from clinical studies) does not automatically constitute a safety concern. Instead, the risk management planning should focus on situations that might differ from the known safety profile. A scientific rationale is needed for the inclusion of that population as missing information in the RMP.

Definitions

Missing information (examples)

Patients with severe renal impairment were excluded from clinical trials, and the medicinal product is not contraindicated in this population; if the pharmacokinetic profile may be different in the excluded population (based on knowledge of the pharmacokinetic profile or the known mechanism of action) further data collection/ studies in such population are considered warranted. The safety concern should be classified as missing information “use in patients with renal impairment”;

Definitions

Missing information (examples)

A medicinal product is initially approved for treatment of adults and, subsequently, it is approved for treatment of the same disease in children based on a small clinical study in children (e.g. deferred paediatric development for selected age groups/indications). The approval is justified based on an extrapolation to the adult experience, both in terms of efficacy and safety. There are no specific safety concerns in children, as compared to the adult population. However, long-term safety data have not been studied at all in this population. In such case, ‘long term safety in children’ may be included as missing information. As limited data have been available at the time of marketing authorisation, a paediatric PASS should be considered as a suitable method of collecting post-approval safety data in children.

Principles

The RMP is a dynamic document that should be updated throughout the life cycle of the product(s). This includes the addition of safety concerns where required, but also, as the safety profile is further characterised, the removal or reclassification of safety concerns.

It may be that important potential risks can be removed from the safety specification in the RMP (e.g. when accumulating scientific and clinical data do not support the initial supposition, the impact to the individual has been shown to be less than anticipated resulting in the potential risk not being considered important, or when there is no reasonable expectation that any pharmacovigilance activity can further characterise the risk), or they need to be reclassified to 'important identified risks' (e.g. if scientific and clinical data strengthen the association between the risk and the product).

Principles

Given the overall aim of obtaining more information regarding the risk-benefit balance in certain populations excluded in the pre-authorisation phase, it is expected that as the product matures, the classification as missing information might not be appropriate anymore once new data become available, or when there is no reasonable expectation that the existing or future feasible pharmacovigilance activities could further characterise the safety profile of the product with respect to the areas of missing information.

Overview of the RMP parts and modules

Part I	Product(s) overview
Part II	Safety specification
Module SI	Epidemiology of the indication(s) and target population(s)
Module SII	Non-clinical part of the safety specification
Module SIII	Clinical trial exposure
Module SIV	Populations not studied in clinical trials
Module SV	Post-authorisation experience
Module SVI	Additional EU requirements for the safety specification
Module SVII	Identified and potential risks
Module SVIII	Summary of the safety concerns
Part III	Pharmacovigilance plan (including post-authorisation safety studies)
Part IV	Plans for post-authorisation efficacy studies
Part V	Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)
Part VI	Summary of the risk management plan
Part VII	Annexes

Overview of the RMP parts and modules

The amount of information, particularly in RMP part II, should be proportionate to the identified risk and the potential risk, and will depend on the type of medicinal product, its risks, and where it is situated in its life cycle.

Where applicable, the information in the RMP should provide an integrated overview/discussion focusing on the most important risks that have been identified or are anticipated based on pre-clinical, clinical and post-marketing data presented in other modules of the eCTD. Any data included in the RMP should be consistent with other sections of the dossier. Links or references to relevant sections of the non-clinical and clinical overviews and summaries should be included in the RMP.
The RMP is part of the scientific dossier of a product and as such should be scientifically based and should not include any element of a promotional nature.

RMP part II "Safety specification"

The purpose of the safety specification is to provide an adequate discussion on the safety profile of the medicinal product(s), with focus on those aspects that need further risk management activities.

It should include a summary of the important identified risks of a medicinal product, important potential risks, and missing information. It should also address the populations potentially at risk (where the product is likely to be used i.e. both as authorised and off-label use), and any outstanding safety questions that warrant further investigation to refine the understanding of the risk-benefit balance during the post-authorisation period.

The safety specification forms the basis of the pharmacovigilance plan and the risk minimisation plan.

Product	Part I	Part II								Part III	Part IV	Part V	Part VI
		SI	SII	SIII	SIV	SV	SVI	SVII	SVIII				
0. Full MA application	√	√	√	√	√	√	√	√	√	√	√	√	√
1. Generic product	√							‡	√	√	*	∫	√
2. Informed consent product	√	√	√	√	√	√	√	√	√	√	√	√	√
3. Hybrid product	√	†		†				†	√	√	√	∫	√
4.a. Fixed combination product – new active substance	√	∓	∓	∓	∓	∓	∓	√	√	√	√	√	√
4.b. Fixed combination product – no new active substance	√		†	†				‡	√	√	*	∫	√
5. Well established medicinal use product	√							√	√	√	√	√	√
6. Biosimilar product	√		√	√	√	√	√	√	√	√	√	√	√

√ = applicable/relevant

‡ = relevant only if "originator" product does not have an RMP and its safety profile is not published on CMDh website

* = relevant only when a PAES was imposed for the "originator" product

∫ = statement of alignment of safety information in PI is sufficient

† = requirements based on risk proportionality principle, addressing new data generated or differences with the "originator" product

∓ = focus on the new active substance

RMP part II “Safety specification”

For generic medicinal products the expectation is that the safety specification is the same as that of the reference product or of other generic products for which an RMP is in place. If discrepancies exist between approved RMPs for such products, then the applicant is expected to propose and justify the most appropriate safety specification for their product. Exceptionally, the applicant for a new generic medicinal product may add or remove safety concerns compared with the safety profile of the reference product if this is appropriately justified (for example, when there is a more up to date understanding of the current safety profile or when there are differences in product characteristics compared with the reference product, e.g. there is a risk associated with an excipient present only in some of the products containing the same active substance).

RMP part II, module SVII “Identified and potential risks”

This RMP module should provide a focused discussion on the identification of important identified and important potential risks, and missing information (i.e. safety concerns). The following safety topics derived from specific situations/data sources are thought to be of particular interest for the risk identification discussion in module SVII, and should be discussed when they lead to risks of the product:

- potential harm from overdose,
- potential for risks resulting from medication errors
- potential for transmission of infectious agents
- potential for off-label use
- important risk common to other members of the pharmacological class
- important risks related to identified and potential pharmacokinetic and pharmacodynamic interactions. Important risks derived from interactions should be included as a safety concern
- risks in pregnant and lactating women
- effect on fertility
- Risks associated to disposal or administration
- Paediatric safety issue.

RMP part II, module SVIII “Summary of the safety concerns”

In this RMP module, a list of safety concerns should be provided with the following categories:

- important identified risks;
- important potential risks;
- missing information.

This list should be reported also in the Overview and in the Public Assessment Report.

RMP part III “Pharmacovigilance plan (including post-authorisation safety studies)”

- The purpose of the pharmacovigilance plan in part III of the RMP is to present an overview and discuss how the applicant/marketing authorisation holder plans to further characterise the safety concerns in the safety specification. It provides a structured plan for:
- the investigation of whether a potential risk is confirmed as an identified risk or refuted;
- further characterisation of safety concerns including severity, frequency, and risk factors;
- how missing information will be sought;
- measuring the effectiveness of risk minimisation measures.

RMP part III “Routine pharmacovigilance activities”

- Routine pharmacovigilance is the primary/minimum set of activities required for all medicinal products as per the obligations set out in DIR and REG. Signal detection, which is part of routine pharmacovigilance, is an important element in identifying new risks for all products.

- This RMP section should describe only the routine pharmacovigilance activities beyond adverse reaction reporting and signal detection.

Specific adverse reaction follow-up questionnaires

- Where an applicant/marketing authorisation holder is requested, or plans, to use specific questionnaires to obtain structured information on reported suspected adverse reactions of special interest, the use of these materials should be described in the routine pharmacovigilance activities section and copies of these forms should be provided in RMP annex 4.

RMP part III “Additional pharmacovigilance activities”

- The applicant/marketing authorisation holder should list in this RMP section their planned additional pharmacovigilance activities, detailing what information is expected to be collected that can lead to a more informed consideration of the risk-benefit balance.
- Additional pharmacovigilance activities are pharmacovigilance activities that are not considered routine. They may be non-clinical studies, clinical trials or non-interventional studies. Examples include long-term follow-up of patients from the clinical trial population or a cohort study to provide additional characterisation of the long-term safety of the medicinal product.

RMP part IV “Plans for post-authorisation efficacy studies”

- This RMP part should include a list of post-authorisation efficacy studies (PAES) imposed as conditions to the marketing authorisation or when included as specific obligations in the context of a conditional marketing authorisation or a marketing authorisation under exceptional circumstances. If no such studies are required, RMP Part IV may be left empty.

RMP part V “Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)”

Part V of the RMP should provide details of the risk minimisation measures which will be taken to reduce the risks associated with respective safety concerns.

Routine risk minimisation activities

Routine risk minimisation activities are those which apply to every medicinal product. These relate to:

- the summary of product characteristics;
- the labelling (e.g. on inner and outer carton);
- the package leaflet;
- the pack size(s);
- the legal status of the product.

Even the formulation itself may play an important role in minimising the risk of the product.

RMP part V “Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)”

Routine risk minimisation activities

Summary of product characteristics (SmPC) and package leaflet (PL)

Both materials provide routine risk minimisation recommendations; however, there are two types of messages the SmPC and PL can provide:

- routine risk communication messages: usually found in section 4.8 of the SmPC or section 4 of the PL; these messages communicate to healthcare professionals and patients the undesirable effects of the medicinal product, so that an informed decision on the treatment can be made;

- **routine risk minimisation activities recommending specific clinical measures to address the risk:** usually found in sections 4.2 and 4.4 of the SmPC but can also be found in sections 4.1, 4.3, 4.5, 4.6, 4.7 and 4.9, and sections 2 and 3 of the PL; warning and precaution messages and recommendations in the SmPC will include information on addressing the risk of the product

RMP part V “Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)”

Additional risk minimisation activities

Additional risk minimisation activities should only be suggested when essential for the safe and effective use of the medicinal product. If additional risk minimisation activities are proposed, these should be detailed and a justification of why they are needed provided. The need for continuing with such measures should be periodically reviewed.

Where relevant, key messages of additional risk minimisation activities should be provided in RMP annex 6 – Details of proposed additional risk minimisation activities.

Examples:

Healthcare Professional and Patient/Carer Guide

Healthcare Professional training material

Patient diary

Patient alert card

Pregnancy prevention programmes

RMP part VI “Summary of the risk management plan”

A summary of the RMP for each authorised medicinal product shall be made publicly available and shall include the key elements of the risk management plan. Part VI of the RMP shall be provided by the marketing authorisation applicant/holder for medicinal products which have an RMP, regardless of whether they are centrally or nationally authorised in the EU.

The audience of RMP summaries is very broad. To ensure that the summary can satisfy the different needs, it should be written and presented clearly, using a plain-language approach. However, this does not mean that technical terms should be avoided. The document should clearly explain its purpose and how it relates to other information, in particular the product information (i.e. the SmPC, the PL and the labelling).

The summary of the RMP part VI should be consistent with the information presented in RMP part II modules SVII, SVIII and RMP parts III, IV and V.

The relationship between the risk management plan and the periodic safety update report

The primary post-authorisation pharmacovigilance documents for safety surveillance are the RMP and the PSUR. Although there is some overlap between the documents, the main objectives of the two are different and the situations when they are required are not always the same.

Regarding objectives, the main purpose of the PSUR is retrospective, integrated, post-authorisation risk-benefit assessment whilst that of the RMP is prospective pre-and post-authorisation risk-benefit management and planning. As such, the two documents are complementary.

Risk management plans with initial marketing authorisation applications

Product	Part I	Part II								Part III	Part IV	Part V	Part VI
		SI	SII	SIII	SIV	SV	SVI	SVII	SVIII				
0. Full MA application	√	√	√	√	√	√	√	√	√	√	√	√	√
1. Generic product	√							‡	√	√	*	∫	√
2. Informed consent product	√	√	√	√	√	√	√	√	√	√	√	√	√
3. Hybrid product	√	†		†				†	√	√	√	∫	√
4.a. Fixed combination product – new active substance	√	∓	∓	∓	∓	∓	∓	√	√	√	√	√	√
4.b. Fixed combination product – no new active substance	√		†	†				‡	√	√	*	∫	√
5. Well established medicinal use product	√							√	√	√	√	√	√
6. Biosimilar product	√		√	√	√	√	√	√	√	√	√	√	√

√ = applicable/relevant

‡ = relevant only if "originator" product does not have an RMP and its safety profile is not published on CMDh website

* = relevant only when a PAES was imposed for the "originator" product

∫ = statement of alignment of safety information in PI is sufficient

† = requirements based on risk proportionality principle, addressing new data generated or differences with the "originator" product

∓ = focus on the new active substance

New applications under Article 10(1), i.e. “generic”

RMP part II: there are 3 situations possible:

1. The originator product has an RMP: RMP modules SI-SVII may not be applicable. Module SVIII should include the summary of the safety concerns, in line with the originator product. If the applicant considers that the available evidence justifies the removal or the change of a safety concern, then data in module SVII should also be included to address the safety concern and detailing the applicant’s arguments. Similarly, if the applicant has identified a new safety concern specific to the generic product (e.g. risks associated with a new excipient or a new safety concern raised from any clinical data generated), this should be discussed and the new safety concern detailed in module SVII.

New applications under Article 10(1), i.e. “generic”

RMP part II: there are 3 situations possible:

2. The originator product does not have an RMP but the safety concerns of the substance are published on the CMDh website9. The elements under point 1 above should be followed. If more than one list of safety concerns published on CMDh website apply for the same active substance, the applicant should justify the choice of proposed safety concerns in module SVIII.

New applications under Article 10(1), i.e. “generic”

RMP part II: there are 3 situations possible:

3. The originator product does not have an RMP and the safety concerns of the substance are not published on the CMDh website: Full modules SVII and SVIII should be included in the RMP. Module SVII should critically analyse available relevant information (e.g. own pre-clinical and clinical data, scientific literature, originator product’s product information) and propose a list of important identified and potential risks as well as missing information.

Risk management plans updates

An RMP update is expected to be submitted at any time when there is a change in the list of the safety concerns, or when there is a new or a significant change in the existing additional pharmacovigilance or additional risk minimisation activities. The significant changes of the existing additional pharmacovigilance and risk minimisation activities may include removing such activities from the RMP.

A medicinal product can only have one “current” approved version of an RMP. If several updates to the RMP are submitted during the course of a procedure, the version considered as the “current” approved RMP for future updates and track-changes purposes shall be the one submitted with the closing sequence of the procedure.

Conclusion

- The RMP is a dynamic document that should be updated throughout the life cycle of the product(s).

- Appropriate parts of the safety specification should be included, important (outstanding) issues should be discussed, the safety specification should provide a true reflection of the safety concerns (e.g. important identified risks, important potential risks and/or missing information) with the medicinal product, all safety concerns from the safety specification should be covered in the pharmacovigilance plan and the risk minimisation measures should be appropriate and assessed in terms of effectiveness .

- Harmonization of the RMPs for the same active substance is recommended.

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Thank you!