EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Q&A on RMP updates for centrally authorised medicinal products

8th industry stakeholder platform - operation of EU pharmacovigilance legislation

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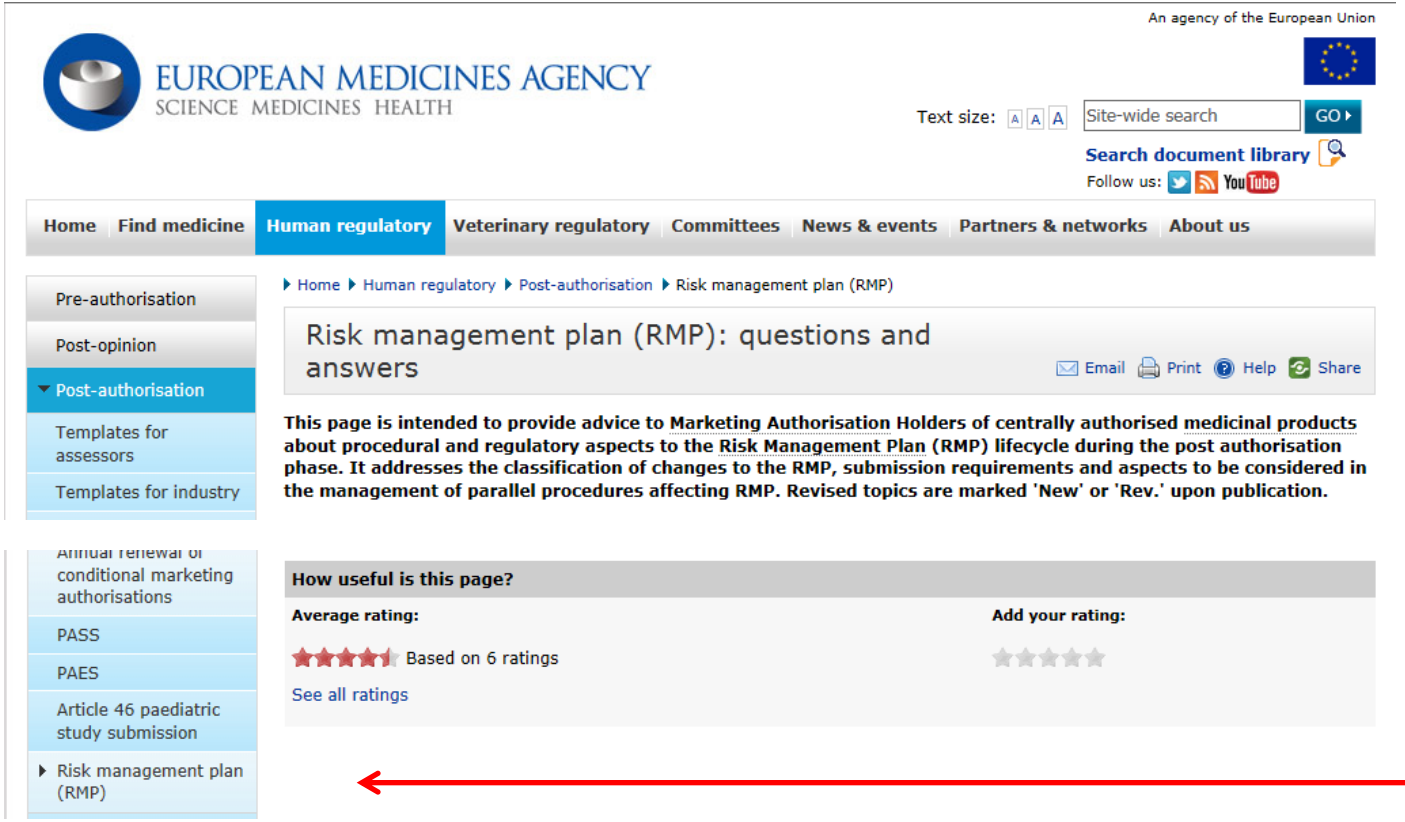
New Post-Authorisation Guidance module on RMP updates



When should I submit an RMP (update)?

- Strictly speaking, whenever any element of the RMP is affected
- In case of a significant change to the safety profile, typically
  - New dosage form or new route of administration
  - New manufacturing process for biotechnologically-derived medicinal products
  - New indication (or significant change to current indication)
  - Clinically important changes to PI (e.g. new contraindication or warning/precaution for use)
  - New additional risk minimisation measures (or changes to existing ones)
  - Updates to Annex II conditions, PhV plan studies or PAES
- At the request of the Agency

When is my RMP update a stand-alone variation?

- As a general rule, when submitted on its own
- Common scenarios
  - In follow-up to changes recommended in a prior procedure
  - In follow-up to PSUR when RMP was not allowed to be submitted with the PSUR
  - To introduce changes to studies in the pharmacovigilance plan (sometimes in follow-up to a protocol assessment in a post-authorisation measure (PAM))

What if I don’t submit an RMP (update)? – Pending updates

- If not submitted but warranted, an RMP update may be requested during assessment
  - The RMP update should normally occur within the procedure
  - In certain cases, the changes may be submitted as part of a subsequent RMP update
- Similarly, in case of submitted RMP update and upon request of further changes during the assessment
  - The finalisation of the RMP update should normally occur within the procedure
  - In certain cases, the changes may be submitted as part of a subsequent update
- Pending updates create a backlog upon implementation

Which variation classification will apply for my RMP updates?

- Type II variation C.I.11.b
  - New RMP
  - Changes to Annex II conditions (except isolated change in final due date)
  - Changes to safety concerns
  - Changes to category 3 studies (except isolated change in final due date)
- Type IA variation C.I.11.a
  - Previously agreed changes including the actual wording and no linguistic review for PI
- Type IB variation C.I.11.z **(no default RMP changes under this category)**
  - RMP submission not qualifying for type II or IA variation
  - Isolated changes in final due dates
  - Changes previously agreed without pre-agreement of the actual wording

Which changes can be included in an RMP update without the need for an additional variation?

- Minor administrative changes
- Update to new template
- (non-clinical/clinical/post-marketing) Exposure information
- Changes to category 4 studies
- **Any minor change which would, on its own, only trigger a type IA or IB variation**

Can I group my RMP updates?

- RMP update in multiple variations does not suffice in principle to prompt grouping of them
- It is likely that the variations may fulfill the grouping criterion of 'making sense to assess together' (e.g. clinical safety variations **but not** non-clinical and clinical safety variation)
- Grouping should not delay implementation of important changes (typically, extension of indication should not be grouped with safety variations)
- Multiple major (type II) variations can be combined into a **grouped** variation
- Multiple minor (type I) variations can be combined into a **single** variation

Handling of proposed changes - example

Submission of a final study report for a category 3 study in the RMP via a type II variation C.I.13 with consequential and/or other updates of the RMP, such as:

Deletion of this study in the RMP – no need for separate variation since related to the main application;

Addition of a safety concern in the RMP following request from the PRAC as part of a PSUR assessment – minor change (previously IB variation);

Changes to the due dates for the provision of the final study reports for 2 category 3 studies in the RMP – minor changes (previously 2 IB variations);

Update of the RMP with new data on the clinical trial exposure – minor change.

=> Single type II variation C.I.13 (previously 1 type II variation C.I.13 and 3 type IB variations C.I.11.z).

Submission requirements

- Parallel RMP submissions: combined highlighted version acceptable at submission and during the procedure, but clean version (only accepted changes) will be requested at Opinion
- Submission requirements: RMP highlighted version (working document), Clinical Overview
- Updated RMP submission with closing sequence: not acceptable unless reviewed during the procedure
- Inclusion of progress reports/interim results from PhV plan studies: generally unnecessary
- Annex 1 (Product Information) of the RMP submission to Eudravigilance: within 30 days from CHMP Opinion or EC Decision (whichever is the latest outcome)