Medical writing for two audiences – The RMP public summary

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Abstract

With the introduction of the new EU Legislation in 2012, RMP requirements have changed significantly, triggering content- and process-related changes. An RMP is written as part of a submission dossier and is submitted for assessment to the EMA. The most important information is outlined in Part VI of the RMP, which forms the basis for the summary that is subsequently published on the EMA website. For medical writers the task of writing for expert and lay audiences at the same time poses new challenges.

Keywords: Risk Management Plan (RMP), RMP summary, Lay audience, EMA website, RMP Part VI

Introduction

New challenges have evolved for medical writers with the introduction of the 2012 'EU Pharma Package' (Regulation (EU) No 1235/2010 and Directive 2010/84/EU) and the transparency initiative, which follows the EMA's decision to better inform the public about the processes around medicine authorisation and evaluation of a medicine's safety.[1] One of these challenges is writing the public summary in Part VI of the European Risk Management Plan (RMP). This summary is made publicly available on the EMA website for regulators, industry, and healthcare professionals, as well as for patients, i.e. a lay audience. To author Part VI of the RMP thus means to serve two masters: while the information provided must be medically accurate and convey all relevant information needed for a medicine's authorisation, it should at the same time be written so that it can be understood by a lay reader.

The RMP, and especially its publicly available summary, have become one of the 'hot topics' in the pharmacovigilance world, and a large number of questions have arisen. Many of these questions are related to the content of the public summary (please also refer to the article by Lisa Chamberlain James in this issue of *Medical Writing*, pp.195–199), but also to the new RMP process that had to be established. This process needs to allow for transparency on the one hand, and data protection on the other hand.

In this article, we briefly touch on the EMA RMP guidance, templates, and useful reference documents (see Table 1). We look at the RMP structure, explaining how the relevant pieces of information from the individual modules and parts merge into an overall summary in Part VI. And we discuss the purpose of Part VI of the RMP, its main data and information sources, the functions involved in its creation, and the main difficulties the writer faces. Once the RMP is submitted to the EMA, the assessment procedure starts, and with it the review of the public summary, which is detailed in the last part of this article.

Table 1: Infobox showing useful information sources

- 'EU Pharma Package' – Regulation (EU) No 1235/2010 and Directive 2010/84/EU[1]
- EMA RMP webpage,[4] including:
  - GVP Module V – Risk management systems (Rev 1)[3]
  - EMA RMP template[5]
  - Q&A on RMP summary[9]
- EMA webpage: public summary examples[6]
- PRAC website[7]
- CHMP website[8]

Guideline requirements and RMP structure

As described in the June 2015 issue of *Medical Writing*,[2] the RMP provides a detailed description of a medicine's safety profile and the measures to prevent or at least minimise the risks that a medicine has. The regulatory basis of the RMP is Good Pharmacovigilance Practices (GVP) Module V–Risk

Management Systems.[3] With its modular structure, the RMP touches various sources of information and stages of drug development. In each of the RMP modules, a conclusion needs to be drawn, stating whether safety concerns were detected. In the RMP parts that follow the safety evaluation, the related pharmacovigilance activities and risk minimisation measures are described.

The RMP is a comprehensive document that provides the reader with an abundance of information on, among other topics, epidemiology, clinical and non-clinical data, limitations of the clinical trial programme, and post-authorisation data. All of this provides the basis for the identification of safety concerns, pharmacovigilance activities, and risk minimisation measures. RMP Part VI summarises in an abridged form the important information compiled in the complete RMP and thus provides the essence of the medicine's overall safety profile.

RMP Part VI – RMP summary

In the EMA template, Part VI is split into two segments. The first one contains 'Elements for Summary Tables in the EPAR' (European public assessment report) and includes tables from Module SVIII and Parts III, IV, and V. The second segment, 'Elements for a Public Summary', provides short summaries (50 to 300 words, depending on the number of indications) on several topics as detailed below. Figure 2 shows which modules and parts

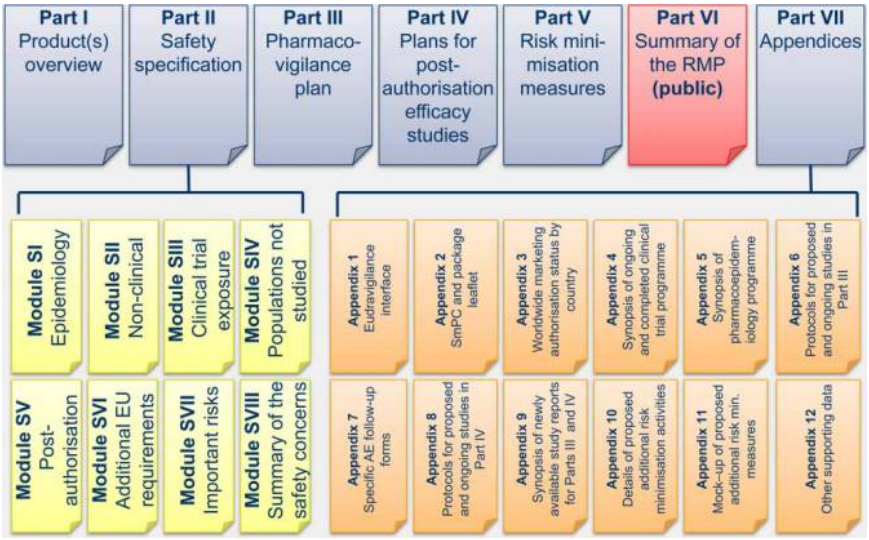

Figure 1: The Risk Management Plan[3].

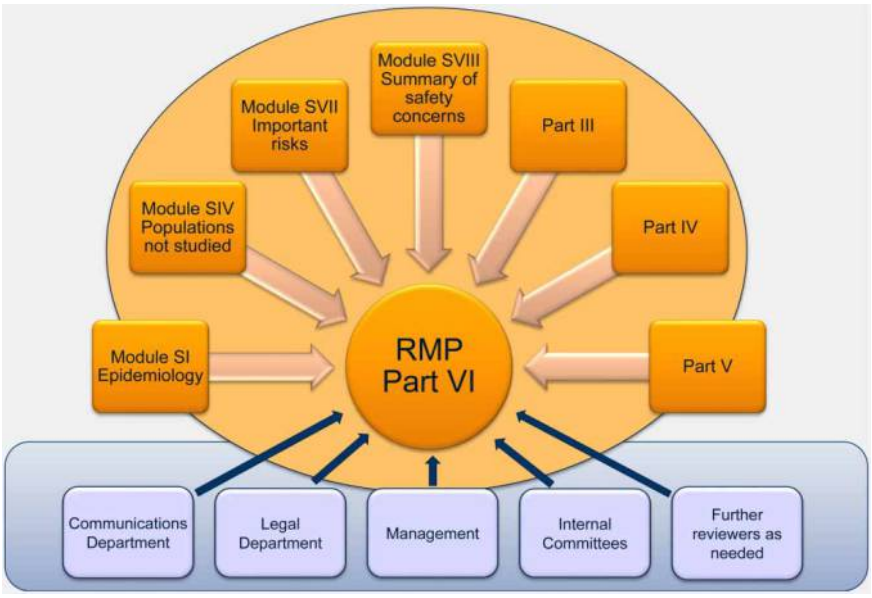

Figure 2: RMP Part VI: Public summary.

form the basis for Part VI, and which functions are involved in the creation of Part VI.

Once the RMP is approved, this second segment is used by the EMA as the basis for the RMP summary that is published on its website. Therefore, lay wording is required. The purpose of the public summary is twofold: it is supposed to summarise all relevant information for regulators, and at the same time should make the medical context, benefits, unknowns, and, most importantly, safety concerns clear to the lay reader. With a single text, the writer therefore needs to reach two different audiences with very different needs: experts and lay readers. To achieve this can be a challenge in regulatory writing, since conveying correct and exact medical information can prove difficult if medical terminology is to be avoided. This is especially true if the word count is limited, meaning that explaining medical terms or using both medical and lay terms is not an option.

In addition to writing the RMP summary for two different audiences, the writer also serves as an 'interface' between the expert functions that contribute to the RMP summary and the lay readership. In most cases, the content provided by the expert functions needs to be 'translated' into lay language. Due to this, the writer is often caught between two antipodal positions: the expert contributing to the RMP is often concerned that important medical information will get lost with the use of lay language and may thus be reluctant to omit medical terms, whereas the EMA requirement is to use lay language to make the information also accessible to the general public.

The requirements and detailed instructions for RMP Part VI can be found in GVP Module V and in the EMA template on the EMA RMP webpage.[3–5] More and more medicines now have published RMP summaries, examples of which can be found on the EMA website.[6]

How do the EPAR summary, PL, and RMP summary connect?

Patient-friendly documents such as EPAR summaries and the package leaflet (PL) are already available from the EMA. The EPAR summaries explain for lay people what the medicine is, how it works, how it has been studied, what it is used for, what the benefits and risks are, and why and how it was approved. In other words, the EPAR summary explains the scientific and regulatory context of the medicine. Tables from the first segment of RMP Part VI feed into this EPAR summary.

The PL contains instructions for the patient on the actual use of a medicine, i.e. how to take it properly (e.g. administration, dosage), anticipated side effects, etc. The PL therefore places the medicine in the context of everyday use and daily medical practice.

The RMP summary provides yet another angle on the medicine and further enhances transparency and public access to relevant information. It introduces the concept of 'risks' related to a medicine, which is not covered in the EPAR summary or the PL. The RMP summary, EPAR summary, and PL thus complement each other and provide a complete picture of a medicine's safety profile.

The RMP summary is written in lay language and summarises the information in the RMP, which is a long, complex, and partly very technical document. The RMP summary is intended for readers who would like to know more about the risks related to a medicine, in the context of the benefits of the medicine, and how these risks are handled. It includes the following:

- a brief overview of epidemiology (i.e. how common the disease is and which parts of the general population are affected by it)
- a summary of the treatment benefits (based on the main studies conducted)
- a description of the unknowns of treatment benefits (populations not studied)
- a tabular summary of the important risks and how they are managed
- a tabular overview of missing information which needs to be collected
- any additional measures to be taken as required as part of the marketing authorisation
- a list of planned studies to provide more information on the safety and benefits of the medicine
- a tabular overview of updates to the RMP

How RMP Part VI is turned into an RMP summary – The process at the EMA

In a 1-year pilot phase, the EMA started publishing RMP summaries in March 2014 for medicines authorised under the centralised procedure. The proposed target audiences are professional stakeholders as well as members of the public. Eventually all centrally authorised medicines will have a public RMP summary.

The RMP is part of the marketing authorisation application submitted to the EMA for assessment. During the assessment process, the RMP is reviewed

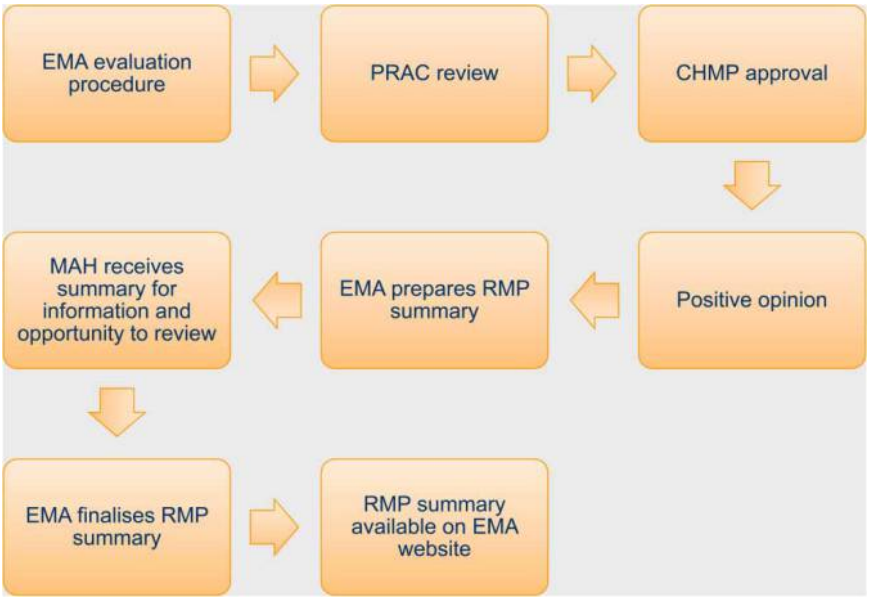

Figure 3: How Part VI is turned into the RMP summary.

by the Pharmacovigilance Risk Management Committee (PRAC)[7] and approved by the Committee for Human Medicinal Products (CHMP)[8] before a positive opinion is issued in favour of marketing authorisation. After the positive opinion has been issued, the EMA transfers the relevant information from Part VI of the approved RMP to the EMA RMP summary template and revises the text according to agency style, format, and naming conventions. The marketing authorisation holder (MAH) then receives the RMP summary and is given the opportunity to review it with a focus on content-related issues only. This review step is short (a few days) and the MAH should be prepared for a quick turnaround. The MAH should also consider whom to include in this short review. For example, it might be advisable not to include the entire multidisciplinary team that contributed to the RMP but rather the relevant Part VI authors only (e.g. drug safety, epidemiology, medical, regulatory) and to add representatives from legal and communications departments, as well as management. After this step, the MAH returns consolidated comments to the EMA, which then finalises the RMP summary for release on its website. The RMP summary is now publicly available.

However, the RMP summary will always be subject to change. In contrast to the other documents in the submission dossier, the RMP is a living document that is updated continuously throughout the life cycle of a medicine. Over time, knowledge about the benefits, risks, and overall safety profile of a medicine will increase and the RMP will be updated to reflect the current status. So whenever there are significant changes to an RMP (i.e. a change in the benefit-risk profile) the RMP summary will be updated as well.

Present and future challenges

Apart from the challenges in writing the RMP summary, there are unanswered process-related questions, as is expected for a new procedure:

- At the moment, the publication of RMP summaries applies only to medicines authorised under the centralised procedure. Nevertheless, Part VI is needed for all RMPs, regardless of the authorisation procedure. Currently, no detailed guidance is available for medicines authorised under other procedures (mutual recognition, decentralised, and national) and information on national publication strategies (if in place at all) is sparse. Also, the template text provided by the EMA is tailored to centrally authorised medicines and is not always suitable for the other authorisation procedures and the MAH depends on feedback from national authorities on local requirements and whether deviations from the EMA template text are permitted or even required.
- An official lay term glossary and style guide for Part VI, available to all MAHs in order to write the lay texts for the RMP summary, would be helpful.
- Due to the transparency initiative, RMPs can be requested by third parties. Therefore,

data protection needs to be carefully considered when writing the RMP and especially Part VI (e.g. patient identifiers should not be used).
- As GVP Module V is currently under revision and feedback from the pilot phase is still being analysed, changes to the RMP in terms of content, process requirements, and target audience can be expected.
- As mentioned above, the EPAR summary, PL, and RMP summary provide different perspectives on a medicine's safety profile. However, the differences in these three documents' concepts (e.g. the distinction between side effects and risks) might not be obvious to the lay audience.
- Although the RMP summary is to be written in lay language with a focus on patients, it is still a very technical document and is not very reader-friendly. For instance, lay audiences will not be familiar with the definitions of 'risk', 'important risk', 'potential risk', 'identified risk', etc. Also, the public summary is only available in English, which not everyone in the EU/EEA is able to understand. In addition to the language barrier, there is an 'information barrier': most people are not aware that an RMP summary, an RMP, or even an EMA website exists and thus simply do not have access to this information.

Conclusion

With the implementation of the EU Pharma Package in 2012, RMP content and process requirements have changed. Since then, both regulators and MAHs have gained experience on the RMP as a whole and the RMP summary in particular. Nevertheless, open questions remain and the new RMP process is still evolving. Medical writers will thus continue to face the challenge of meeting the needs of all stakeholders and working in a dynamic and transforming environment.

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