Medical Communications

SECTION EDITOR

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Editorial

Anyone working in pharmacovigilance (PV) will already have spent many months working their way through the ever-changing updates and reforms to the Risk Management Plan (RMP), and the newly legislated RMP summary. Those not working in PV will probably also have heard all about it (if only through the tortured wails of their PV colleagues!).

To everyone's delight and amazement, we survived the pilot phase; consultation comments have been received and a new and improved version is imminent. We all eagerly await the revision of the RMP summary in particular: will the original concerns be addressed? Will we still be asked to produce a single document that can satisfy both professional healthcare providers and the general public in one fell swoop? Will the RMP summary achieve its aim of increasing transparency for the lay audience??

We will find out in time, I'm sure. But in the meantime, I'm delighted to present to you a really excellent article from Tiziana von Bruchhausen and Stefanie Rechtsteiner. Tiziana and Stefanie chart beautifully the evolution of, and challenges posed, conquered, and still to be undertaken, by the RMP summary guidance.

This article really should be called 'Everything you wanted to know about the RMP summary but were afraid to ask' and I will be printing it out and pinning it to my wall!

Enjoy.

Bestest.

Lisa

RMP public summary reloaded: Revision 2 of GVP Module V

Transparency in PV: why the RMP public summary was introduced

The European Medicines Agency (EMA) describes on its website how the agency has been aiming at and working towards increasing the transparency of its processes and decisions ever since its formation in the 1990s. The European Public Assessment Report (EPAR) was one of the first tools used to provide information on a medicine and its use. Striving for transparency and openness, the EMA decided to go beyond what is legally required, in order to provide as much information as possible to all interested parties. However, marketing authorisation holders (MAHs), investigators, and other stakeholders need to have the assurance that their intellectual property, as well as their personal and commercially relevant information and data, are protected. Therefore, the EMA needs to carefully balance data protection against transparency.[1]

Besides providing as much information as possible to other health authorities, MAHs, investigators, and healthcare professionals (i.e. medical experts), amongst others, the EMA also strives to better inform the general public, and thus a lay audience. This initiative translated into the RMP public summary (Part VI.2), which was introduced with the new GVP legislation in 2012. The agency's goal is to involve patients more and to provide them with all relevant information available for a specific medicine, and this, in the case of the RMP public summary, in a language tailored to patients' needs.

A long journey: how the RMP public summary has evolved over time

The past: first introduction

In 2012, the EMA launched its 'EU Pharma Package' (Regulation (EU) No 1235/2010 and Directive 2010/84/EU) and the accompanying transparency initiative, with

the goal of enhancing public information on processes around a medicine's authorisation, its efficacy, and safety. With this, the RMP as a whole underwent a major overhaul, and, additionally, the new concept of the RMP public summary (RMP Part VI.2) came into existence. A 1-year pilot phase for the publishing of the RMP summary started in March 2014 for medicines authorised under the centralised procedure. For many medicines the RMP summary has since been made publicly available on the EMA website, and is intended for regulators, industry, and healthcare professionals, as well as for patients.

With the new GVP format, the RMP was now a comprehensive document with a broad spectrum of information provided, including epidemiology, non-clinical and clinical data, as well as post-authorisation data, based on which safety concerns, pharmacovigilance activities, and risk minimisation measures could be identified.[2, 3] The RMP Part VI with the public summary offered the most important information on a medicine's safety profile in a short and summarised form. This new approach, incorporating the publicly available RMP summary (with its inherent difficulty of ensuring transparency and data protection at the same time), immediately became a topic that was widely discussed amongst all stakeholders, and still remains the focus of interest.

The present: Revision 1

The RMP template was updated in July 2013.[4] A first revision of the GVP Module V was released in April 2014, addressing feedback that had been received from various stakeholders and providing more clarity on various aspects, such as definitions and terminology for safety concerns and triggers for RMP updates.[5] However, Revision 1 of both documents, which is currently valid and the basis of all RMP writing, was a minor one. It did not include results from the pilot phase on RMP summaries, which had just started at that time.

In general, Part VI of the RMP supports the overall goal of transparent, concise, and high-level communication of all relevant data and information. Part VI consists of two main parts:

- Part VI Section VI.1 'Elements for summary tables in the EPAR' provides tabular overviews of the medicine's safety concerns and of the related pharmacovigilance and risk minimisation measures. These tables are copied from the main body of the RMP and incorporated in the CHMP assessment report as well as in the EPAR public assessment report at the time of authorisation;
- Part VI Section VI.2 'Elements for a Public Summary' provides lay language summaries that are also partly incorporated in the EPAR summary for the public (summary on treatment benefits). Additionally, Section VI.2 is published as a stand-alone document (referred to in this article as RMP public summary). The summaries in Section VI.2 provide information on the disease epidemiology, the treatment benefits, the unknowns relating to treatment benefits, and the safety concerns. For medicines with additional risk minimisation measures proposed or in place, a further summary in lay language informs the public about these measures.

The format of the RMP public summary aims at providing condensed, clear, and understandable information on elements of the RMP. However, this task is very challenging for medical writers, as the RMP is a long, complex, and quite technical document. As previously described,[3,6,7] the major challenge posed is to tailor the complex information on the most relevant aspects of the RMP to a heterogeneous audience, encompassing healthcare professionals, industry stakeholders, and patients/patient organisations, while ensuring correctness, accuracy, and clarity. This task is even more challenging in view of the word count constraints imposed by the guidance for most of the lay language overviews in the RMP public summary.

From a regulator's perspective, communicating the important risks of a medicine and the associated risk minimisation measures to the public represents, in itself, a form of risk minimisation and may additionally be a valuable tool for healthcare professionals and patients to support decisions for or against use of a medicine. For this reason, it is crucial that the target audience of the RMP public summaries is able to understand the complex benefit-risk information presented, which means taking into consideration the health literacy of the readership. For the RMP public summaries in their current format, medical writers normally aim at a literacy level of 11-12 years old or below.[3]

From guidance to real life The package leaflet (PL) and the EPAR summary present key information in lay language on the benefits and the risks of a medicine. The RMP public summaries intend to provide a context for the risk-benefit evaluation of a medicine and to complement the EPAR and PL by providing information on the safety concerns of a medicine and the related post-authorisation studies. The introduction of the RMP public summaries was generally perceived as a positive measure to improve transparent communication and to contribute to a more patient-centred drug development process. However, there are inherent limitations due to format, requirements, and lay language, which, in combination with the complex contents, lead to the following two questions:

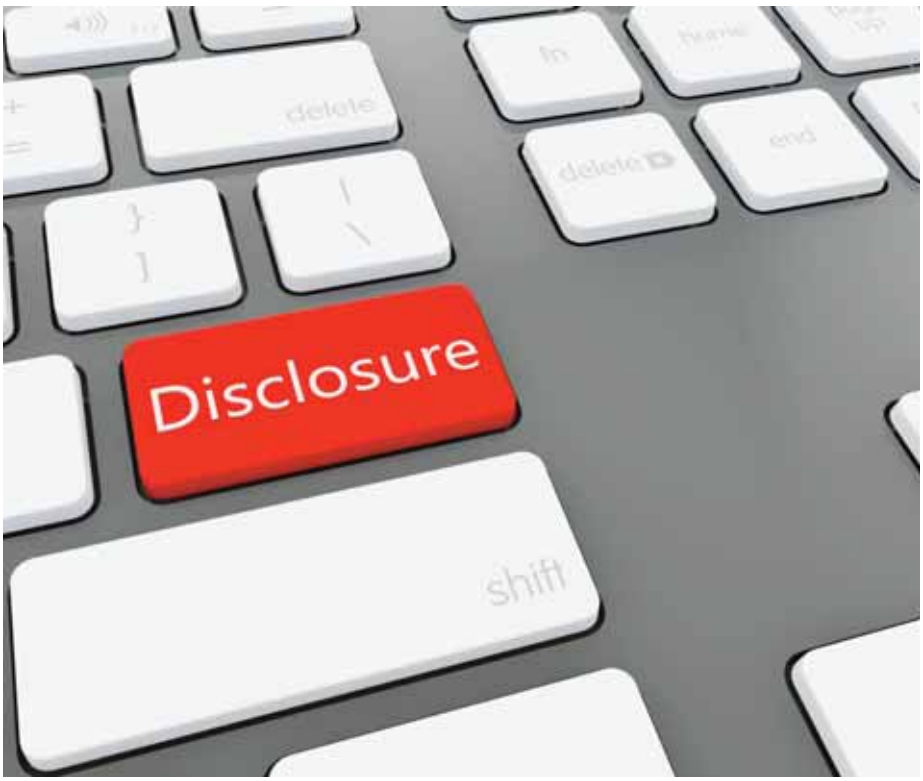
- how can the requirements and the format be adjusted to fulfil the needs of the targeted readership?
- is the lay public really the appropriate audience?

To explore the above questions, the EMA collected feedback from patients, healthcare professionals, and industry associations during the 1-year pilot phase on the RMP public summaries.

Industry feedback The industry welcomed the transparency initiative. However, the general perception of the industry was that, if the RMP public summary is mainly intended for patients, it should be improved and further adapted to meet the needs of this target audience. In particular, the suitability of the RMP public summary in its current format was critically questioned:[8]

- definitions for identified risks, potential risks, and missing information are not provided;
- there is no explanation on how the RMP public summary complements the SmPC, PL, and EPAR and what the differences are (e.g., important risks vs. side effects) between the concepts addressed in these documents;
- there are no explanations of pharmacovigilance and risk minimisation processes (post-authorisation plans, risk minimisation measures), with which the audience is not familiar.

In this context, RMP summaries containing numerous important risks and gaps in knowledge may lead to unjustified concerns and to the misleading perception that the product is more hazardous than it actually



is, and that the risks outweigh the benefits.

Patients' feedback The patients' feedback further challenged the RMP public summary format and language: in general, lack of clarity, context, and definitions were criticised, and the RMP public summary was considered to be hard for patients to understand due to its complex and technical contents. Moreover, among the public, knowledge and understanding of drug development, medicine safety monitoring, and health authority activities are generally limited. Therefore, it appears that the RMP public summaries are not perceived as a useful communication tool and do not effectively reach their target audience.[9]

In conclusion, despite the intention behind the lay language requirements, it is doubtful that the RMP public summary is indeed widely used. In addition, it does not provide the basic definitions to ensure understanding of the contents and of its relationship to the other publicly available documents. Therefore, it is questionable whether the RMP public summary fulfils criteria for effective, transparent communication.

The future: Revision 2

The objectives of the pilot phase on RMP public summaries were to confirm interest and usefulness for stakeholders, to confirm the target audience, to improve format and content based on the needs and expectations of the readership, and to streamline the process for preparation and update of the RMP public summaries.[8]

The pilot, which covered over 80 RMP public summaries, confirmed a wide interest from different audience groups and the need to improve format and contents to meet their demand and expectations. The main targets for the revision of the RMP public summary with regard to transparent communication are as follows:[8, 10]

- format, contents, and structure should be simplified with focus on the summary of safety concerns, risk minimisation measures, and planned post-authorisation development plan;
- while the PL and EPAR summary are the main primary source of information on benefits and risks of a medicine for patients, the RMP public summary should address an audience interested in additional background safety information provided in the PL;
- a plain language approach should be used; however, technical terms should not be avoided.

With Revision 2 of GVP module V, the RMP summary is now moving towards a rather professional audience and people seeking additional information, possibly with a slightly higher health literacy level. However, the RMP summary should still follow plain-language principles to facilitate readability by the general public:[11]

'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). It should contain the following information:

- the medicine and what it is used for;
- summary of safety concerns and missing information;
- routine and additional risk minimisation measures;
- additional pharmacovigilance activities.'[12]

The Revision 2 of GVP module V[12] and the RMP template[13] is a major one. The public consultation phase of this revision ended in May 2016; the publication of the final revision is expected in the third quarter of 2016. Although the revised RMP public summary considered many of the stakeholders' comments, it still does not seem to fully meet the needs of the diverse target audience. The contents of the revised RMP public summary are now very concise and limited to safety concerns, pharmacovigilance activities, and risk minimisation measures. The EPAR tables have been removed, as have the overviews on disease epidemiology and treatment benefits. Standard text has been proposed to define identified and potential risks, but not missing information. In addition, the definition of the 'importance' of a risk is still missing. Context is given with regard to the EPAR, the SmPC, and the PL; however, there is still no explanation about the difference between side effects/adverse events (terminology used in these documents) and important risks (terminology used in the RMP public summary). A definition has been provided for routine and additional risk minimisation measures as well as for routine pharmacovigilance activities, yet there is no explanation for additional pharmacovigilance activities

(post-authorisation studies).

In line with the objectives of template and process simplification, the proposed format of the RMP public summary maps the contents to the full RMP. This, however, gives the impression that its content is mainly taken verbatim from the body of the RMP. In this sense, the question then arises as to who should prepare the RMP public summaries in the new format: should it be the pharmaceutical company, or could it be the health authority when preparing the reader-friendly summaries?

The journey continues: open questions

Although Revision 2 of GVP Module V addresses many questions and concerns that were raised over the last two years, the following questions remain:

- the public summary is only available in English, which not everyone in the EU is able to understand. In addition, most people are likely not aware that an RMP summary, an RMP, or the EMA website exist, and therefore they do not have access to this information. Can the lay audience thus be reached at all with the RMP public summary?
- even if plain language is used, assuming the patients speak English, will they be able to understand the information provided and to consequently make appropriate decisions?
- does transparency require showing all details of the risk management process to an audience with low health literacy and no understanding of such processes?
- should the focus be shifted even more to patients' needs and readability, i.e. would user testing help to better meet patients' needs and to create a more reader-friendly document? Or should separate summaries be created for lay readers and expert readers?

Conclusions

In line with the transparency initiative and the efforts of the EMA to improve communication of clinical and safety information, the RMP public summary, four years after its first introduction, is currently undergoing a major revision based on feedback from all stakeholders. As a document that must address different needs and interests, and cover complex medical information, the RMP public summary has a major impact on how a medicine is perceived. Further interaction and exchange between all parties involved will likely be needed to reach the overall common goals: effective communication, transparency, and patients' safety.

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References

1. Transparency. European Medicines Agency [cited 2016 July 04]. Available from: http://www.ema.europa.eu/ema/ index.jsp?curl=pages/special_topics/ general/general_content_000526.jsp&mid=WC0b01ac0580789730
2. Von Bruchhausen T and Prechtel K. Pharmacovigilance medical writing: an evolving profession. Medical Writing 2015;24 (2):66-71.
3. Chamberlain-James L. Risk management plans – New challenges for a new era. Regulatory Rapporteur 2014;11(6):4-7.
4. Guidance on format of the risk management plan (RMP) in the EU – in integrated format. EMA/PRAC/613102/2015 Rev.2 accompanying GVP Module V Rev.1. European Medicines Agency; 2013 Jul 25 [cited 2016 Jul 04]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/11/WC500134650.pdf.
5. Guideline on good pharmacovigilance practices (GVP). Module V – Risk management systems (Rev 1). European Medicines Agency and Heads of Medicines Agencies; 2014 Apr 15 [cited 2016 Jul 04]. Available from: http://www.ema.europa.eu/docs/ en_GB/document_library/Scientific_guideline/2012/06/WC500129134. pdf.
6. Chamberlain-James L. Legislation and the lay audience: Challenges of communicating benefit and risk in the light of new regulations. Medical Writing 2015;24(4):195-9.
7. Prechtel K and Rechtsteiner S. Medical writing for two audiences – The RMP public summary. Medical Writing 2015;24(4):200-4.
8. Juan Garcia Burgos, EMA. Publication of Risk Management Plan (RMP) summaries: Analysis of the experience of the 1-year pilot phase. Lecture presented at PCWP meeting, 2015.
9. Raynor T. Does transparency in medicines information deliver benefits to patients? Lecture presented at DIA Euromeeting, Hamburg, 2016.
10. Caroline Voltz-Girolt, EMA. RMP template. 4th stakeholders platform – operation of EU pharmacovigilance legislation; RMP activities update session. Lecture presented at the 4th stakeholders platform, 2015.
11. Pharmacovigilance Risk Assessment Committee (PRAC). Minutes of the PRAC meeting on 11-14 January 2016. EMA/PRAC/92676/2016 Procedure Management and Committees Support Division [cited 2016 Jul 11] Available from: http://www.ema.europa.eu/docs/ en_ GB/document_library/Minutes/2016/03/WC500202623.pdf.
12. Guideline on good pharmacovigilance practices (GVP). Module V – Risk management systems (Rev 2) – draft for public consultation. European Medicines Agency and Heads of Medicines Agencies; 2016 Feb 24 [cited 2016 Jul 04]. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2016/02/WC500202424.pdf.
13. Draft guidance on format of the risk management plan (RMP) in the EU – in integrated format. EMA/PRAC/613102/2015 Rev.2 accompanying GVP Module V Rev.2. European Medicines Agency; 2016 Feb 29 [cited 2016 Jul 04]. Available from: www.ema.europa.eu/.../en_GB/document_library/Regulatory_and_procedural_ guideline/2016/02/WC500202373.doc.

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