The new EU RMP guidance and template in daily pharmacovigilance practice
What's new, why, and how to deal with it

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Regulatory background:

The session addressed the major revision (Revision 2) of the Guidance on EU risk management plans (RMPs): the Good Pharmacovigilance (PV) Practice Module V (published by the EMA in March 2017) and the related RMP template update, as well as their impact on the daily lives of PV medical writers.

Speakers:

The speakers were *Val Simmons*, MB BS FFPM and *Sven Schirp*. Val Simmons, the European Qualified Person for PV (QPPV) at Eli Lilly, has more than 30 years' PV experience and has been a member of various working groups, including the European Federation of Pharmaceutical Industries and Associations PV Expert Committee. Sven Schirp, the Head of Global Pharmacovigilance Writing at Boehringer Ingelheim, has been active in PV since 2009 and presented on risk-benefit at the 3rd EMWA Symposium in 2015. The ESS PV session was moderated by Tiziana von Bruchhausen, PhD, EMWA President, Chair of the EMWA PV Special Interest Group, and Senior Global PV Writer at Boehringer Ingelheim.

Key takeaways:

Val Simmons – who was closely involved in Revision 2 – clarified that there was an industry need for more focused RMPs. Before the revision, RMPs sometimes included a high number of safety concerns (i.e., important identified risks, important potential risks, and missing information) and ran over 1000 pages ("the RMP had lost its way"). The concept of an important risk has not changed with the revision, but has been revisited and explained in line with ICH principles. The revised guidance clarifies what RMPs should focus on with regard to the safety concerns, strengthening a risk-proportionate approach. To illustrate these principles, Val presented the following explanation (kindly provided by the QPPV of Astra-Zeneca):

- **signals:** petty thieves who want to be criminal, although very few succeed;
- **adverse drug reactions (ADRs):** adequate evidence to be sentenced for causal relationship, sometimes only based on circumstantial evidence;
- **risks:** the damage (broken window or nose) caused by the ADR;
- **important risks:** more severe vandalism, where probation and/or a rehabilitation programme are deemed necessary.

Val gave several examples to illustrate the differences among the concepts above. If the clinical outcome (the risk, e.g. infection caused by the ADR neutropenia) is a clinically relevant change severe enough to impact the benefit-risk, then this risk is important. Val also provided tips for the practical implementation of these principles in RMPs and shared the following rules of thumb:

- while discussing the benefit-risk impact in the RMP (Module SVII.3), it will become clear whether a risk is important;

- either a safety concern is important enough to conduct additional risk management activities, or it is not important enough to be included in the RMP.

Sven Schirp – who has broad experience with RMPs and their assessment – discussed the impact of Revision 2 on the RMP global management: the more stringent approach in the definition of safety concerns may lead to differences in the list of safety concerns between EU RMPs and global periodic safety update reports (PSURs).

Regarding the practical implementation of the revised format, Sven analysed the impact on the PV writer throughout the RMP sections in the Revision 2 template, discussing which information or data need to be newly provided or revised. Sven's rule of thumb for PV writers was to advise their teams to use common sense while updating RMPs, e.g. not to generate new data for products that have already been on the market for a long time only for the sake of the revised template. He advised writers to provide transparent justifications for empty sections and to cross-reference to previous procedures, to help the assessor understand how sections were populated.

Sven also advised RMP authoring teams to carefully consider the potential impact on other documents when introducing changes in the RMP. If safety concerns are removed, added, or reclassified in the EU RMP based on the Revision 2 guidance, this will impact RMPs submitted to other countries and the benefit-risk profile in the PSUR, which is a global document.

Comments and discussions:

Val and Sven gave interactive presentations, sharing their opinions and providing practical tips for PV writers. The participants asked various questions on the implementation of the revised guidance. One participant confessed to feeling motivated to return to his desk and apply the tips he'd learnt.

The key message of the session was that converting an RMP to Revision 2 format is not a simple matter of condensing and copy/pasting; the need for a critical review of the safety profile of the product offers the opportunity to remove safety concerns as appropriate. However, the impact of the changes in the list of safety concerns needs to be carefully discussed within the authoring teams. A deep understanding of the principles and requirements of Revision 2 is essential to re-focus the RMP and to effectively plan risk minimisation measures. PV writers should properly train RMP authors at the RMP kick-off meeting.

The session was well received. Conference participants could further talk with the speakers during an informal PV lunch roundtable discussion.