4th meeting of the CIOMS Working Group WG XIV on Artificial Intelligence in Pharmacovigilance

12 April 2023

Virtual meeting

Meeting Minutes

Overview:

Summary

The CIOMS WG XIV on AI in PV held its 4th meeting virtually on 12 April 2023. The writing teams presented their chapter drafts, and the WG agreed to meet face-to-face in June to review the updated drafts.

Minutes of discussion

1. Opening and welcome

Hervé le Louët, CIOMS President, welcomed the WG members and chaired the meeting. He confirmed that the next meeting will be hosted by Takeda in Zurich and emphasised the importance of the meeting in the light of prevalent discussions about Artificial Intelligence.
Lembit Rägo, CIOMS Secretary General, added his words of welcome and chaired the meeting. For a list of participants, see **Annex 1.**

The meeting agenda was adopted.

2. Progress updates on chapter drafts

All draft materials presented are available in the WG private member area.

Chapter 1-3. Introduction, landscape and scope

- Walter presented the Chapter 1-3 draft outline, and the following only represents the discussion points raised after the presentation.

- The introductory section of the document considers the different interests and perspectives of various stakeholders, acknowledging both common and distinct aspects.
- Adjustments to the chapters may be needed as the rest of the chapters are finalised.
- The team acknowledges that the focus is much broader than just signal detection and welcomes additional input and perspectives from the WG on the draft outline.
- Lembit encouraged all chapter teams to send their work, even preliminary drafts, to be added to the password-protected section of the website to enable all members to review and feedback.
- He added that chapter leads are welcome to communicate to avoid redundancies and overlaps, but a comprehensive review to eliminate overlaps will be more effective once the complete draft is available.

Chapter 4. Guiding principles

- Beth gave the Chapter 4 team presentation, and the following only represents the discussion points raised after the presentation.
- The team discussed the importance of longevity for the guideline, considering the rapid advancement of technology.
- It was suggested to balance the document's depth by starting at a high level in each of the chapters, and then progressively delving into more detailed content. This structure will ensure value for all readers, from those seeking a broad understanding to those desiring more detailed information.
- To ensure cohesion throughout the document, all chapters should approach their respective subjects from a similar perspective. All are welcome to suggest the best strategies.
- The WG is conscious of the timing of the document's publication due to significant international interest in the topic. Progress is crucial as several health authorities, including the European Medicines Agency, are working on similar initiatives. The goal is to avoid creating a document that is repetitive of others.
- Niklas noted that organisations are occasionally the end users of AI solutions, while at other times, they may be the solution providers. It is important to consider these dynamics as well.
- We should not be overly prescriptive or create a rigid structure to the document but instead ensure a comprehensive coverage from different areas focusing on developers, users, and compliance aspects.
- While there are a limited number of vendors currently providing safety platform solutions, the growing interest in AI could attract a wider variety of vendors, even those lacking prior expertise in pharmacovigilance.
- Walter noted that there is value in incorporating case studies in the future document to make the material more tangible and relatable. Case studies could provide beneficial insights into real-world situations and potentially illuminate areas of difficulty within these contexts.

Chapter 5. Validation and qualification considerations

- Manuela gave the Chapter 5 team presentation, and the following only represents the discussion points raised after the presentation.
- There is a significant overlap in content concerning training and validation data.

- Chapter 5 team called for collaboration and invites members from regulatory agencies to join their writing team to enhance the chapter's alignment with regulatory perspectives.
- The drafting process for Chapter 5 has brought up specific, technically complex questions that would benefit from vendor interaction. Feedback from vendors is believed to add value to the chapter.
- It was agreed to wait until the full WG meeting in June before engaging with external vendors, as it would provide all the opportunity to contribute to the decision-making process.
- Niklas commented on the discrepancy that exists between the expectations of what regulators might contribute, particularly in relation to the technical aspects of the project. This discrepancy in expectations is a critical point that needs to be addressed in the scoping of the document and the presentation of the information.
- The main question from the regulator's perspective would be how the systems will be inspected, rather than focusing on technical details.
- The FDA has recently released two guidances on AI and ML in medical devices, outlining evaluation principles and expectations for algorithm retraining. These guidances are general in nature and focus on topics like explainability and approaches, rather than specific performance metrics.
- The EMA is working on a draft Reflection paper on the on the use of AI in the medicinal product lifecycle. It was decided that collaboration between the EMA and CIOMS WG would be valuable.
- Lembit suggested engaging with regulators, as this will help in gaining a better understanding of the regulatory landscape and exploring potential collaborations or alignment with ongoing efforts.

Chapter 6 and 7. Consideration of AI; Implementation and maintenance lifecycle aspects

- Kendal gave the Chapter 6 and 7 team presentation, and the following only represents the discussion points.
- Chapters are progressing well. There is a need to clarify the scope and intent of the chapters in relation to the rest of the chapters to avoid duplication.

Chapter 8 Future vision

- Denny gave the Chapter 8 team presentation, and the following only represents the discussion points raised after the presentation.
- The group has been working on a draft working document and reviewing it internally. Input from other chapters is needed to shape the future vision and identify technical challenges.
- Exploring themes that are futuristic and not yet fully developed is a priority, while the emergence of new technologies like ChatGPT has influenced the teams' thinking and challenged existing ideas.
- The availability of data and data bias are significant issues for future technical solutions or tools.
- Ravi encouraged team members to think outside the box and explore AI in PV without limitations.
- Robert noted that a case study highlighting the application and potential future developments of large language models could be beneficial for focusing on key future issues. Future WG report

should ensure it adequately addresses the unique characteristics and challenges associated with large language models.

- Should the topic of large language models be addressed in the main body or as a separate section?
- We should highlight the challenges related to the availability and lack of transparency surrounding new large language models and explore various aspects beyond technical considerations, including governance, data sharing, model size, and energy usage.
- Future vision topics will be revisited multiple times before finalising the report due to the evolving nature of the field and emerging technologies like ChatGPT.

Glossary

- The WG agreed that the future document will include a glossary, which contains definitions for terms used throughout the document.
- Walter suggested using glossary as a tool for the team to reach consensus on definitions that are subject to debate.
- CIOMS Cumulative Glossary, with a focus on Pharmacovigilance (Version 2.1) is available and can be used as a reference to check existing terms and definitions, but flexibility is allowed to update or modify terms based on the context of the current work product.
- Glossary of ICH terms and definitions (Version 3, 20 April 2023) is also available on CIOMS website and is recommended for reference.
- Chapter leads will start collecting terms for the glossary.
- New terms introduced by the working group will be added to the cumulative glossary, ensuring a comprehensive resource for future editions.
- The glossary is not limited to pharmacovigilance terms alone but encompasses a wider range of terms relevant to the field, reflecting its evolving nature.

3. Next steps / Next meeting

- The next full WG meeting will be held in June 2023 in Zurich and is hosted by Takeda.
- The WG will continue working on the chapter drafts. Once the drafts are more matured, the chapter editorial teams will meet to discuss possible overlaps, the content and location of each section and the general structure of the document.

4. Closing remarks

Hervé and Lembit thanked the WG members for joining and for the productive discussions and are looking forward to welcoming all in Zurich.

Annex 1: List of participants

Participants

Justyna Amelio (AbbVie), Robert Ball (US Food and Drug Administration), Luisa Barrios (Merck Sharp & Dohme), Adrian Berridge (Takeda), Flávia Moreira Cruz (ANVISA, Brazil), Piero Francesco Franco (Pfizer), Kendal Harrison* (The Medicines and Healthcare Products Regulatory Agency, UK), Kirsten Egebjerg Juul* (Danish Medicines Agency), Vijay Kara* (GlaxoSmithKline), Dieter Kempf (Genentech, Roche), Benny Ling (Health Canada), Denny Lorenz (Bayer), Hervé Le Louët (CIOMS), Yusuke Matsunuga (Pharmaceuticals and Medical Devices Agency, Japan), Manuela Messelhäußer* (Paul-Ehrlich Institute), Niklas Norén (World Health Organization / Uppsala Monitoring Centre), Ravi Patel (Unither), Beth MacEntee Pileggi (Johnson & Johnson), Kateriina Rannula (CIOMS), Stephen Rosenfeld (North Star Review Board), Lembit Rägo (CIOMS), Irene Scholz (Swissmedic) Walter Straus (Moderna), and Phil Tregunno (The Medicines and Healthcare Products Regulatory Agency, UK).

*Alternate

Regrets

Russ Altman (Stanford University, US), Andrew Bate (GlaxoSmithKline), Arvind Bellur (Sanofi), Taxiarchis Botsis (Johns Hopkins University School of Medicine, US), Hua Carroll (Biogen), Jean-Michel Dogné (University of Namur), Stephen Heaton* (CIOMS), Thomas Henn* (Unither), Yuki Kikuchi* (Pharmaceuticals and Medical Devices Agency, Japan), Jesper Kjær (Danish Medicines Agency), Richard McAteer (Health Canada), Roli Mathur (India Council Medical Research), Dirk Mentzer (Paul-Ehrlich Institute), Nicolas Perez * (Swissmedic), John Reinhard Pietzsch* (Bayer), Hans-Jörg Römming (Merck Group), and Panos Tsintis (CIOMS Senior Adviser).