3rd meeting of the CIOMS Working Group WG XIV on Artificial Intelligence in Pharmacovigilance

19 January 2023

Virtual meeting

Meeting Minutes

Overview:

Summary

The CIOMS WG XIV on AI in PV held its 3rd meeting virtually on 19 January 2023.
The writing teams presented their chapter drafts and the WG agreed to meet again virtually in early April to review the updated drafts and discuss the scope of the future report in more detail.

Minutes of discussion

1. Opening and welcome

Hervé le Louët, CIOMS President, welcomed the WG members and chaired the meeting.
He urged WG members to consider the relevant information available but also to contribute their own ideas and remain forward-looking, as the goal is to create a report that can stand the test of time.

Lembit Rägo, CIOMS Secretary General, added his words of welcome and chaired the second half of the meeting. For a list of participants see **Annex 1.**

The meeting agenda was adopted.

2. Subgroups presentations of their drafts

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

Chapter 1-3 Introduction, landscape and scope

- Chapter 1-3 team will aim to present their draft at the next WG meeting.
- Walter participated in a meeting with safety leaders to discuss AI and its application to PV. He will investigate sharing the presentations with the CIOMS WG.
- Hervé questioned whether concentrating solely on signal detection is sufficient and invited the WG to share their thoughts.
- Walter believed that a greater emphasis on the practical implications would benefit a future document. He added that whenever new technology becomes available, it is not uncommon for people to lean towards the technology rather than the core problem it is meant to tackle.
- Beth proposed devoting some parts of the introduction to the general topic of AI in PV, as well as to the scope and the intended target audience of the report and how each chapter will address it, to ensure consistency across the document. While the goal is for the document to be relevant for longer than two years, we should determine how in-depth we wish to dive into certain themes.
- Walter noted that the most valuable CIOMS documents attempt to introduce an emerging issue to a wide audience, so having a substantial indirect impact on the field. We can create a framework for a way of thinking about AI in PV.
- As we consider AI, the countries with the most resources are the ones that are focusing the most attention on it. We should discuss the application of AI to PV in low- and middle-income nations.
- The WG agreed to add an introductory section on the nature of pharmacovigilance from the perspective of ML.

Chapter 4 Guiding principles

- Beth gave the Chapter 4 team presentation, and the following only represents the discussion points raised after the presentation.
- The WG discussed open-source and proprietary models and the possible ways of tackling the topic of models in the report. This is also relevant when considering AI in low- and middle-income countries, where there is benefit in open-source models.
- Both models could be included and discussed according to their nature. Should this be included in the introduction or Chapter 4?
- An open-source model is not necessarily thoroughly tested. Additional testing and transparency are relevant topics, and it would be essential to address this in one of the subsequent chapters concerning how the concepts are differently implemented.
- When we publish this report, the audience will expect the WG to suggest the best AI methods for different purposes. We may not be able to provide definitive answers or suggestions, but we must explain why.
- It was suggested that we discuss the advantages and disadvantages of each available method, depending on what is needed and the country and resources available. We should include a general statement or a recommendation to evaluate the situation or determine the suitable method.
- Denny noted that in the absence of open- source models for PV tasks, we could include topics such as qualification or certification, which would be included in Chapter 8 (Future vision). The main chapters of the report should address the process of models qualifying for acceptance.

Making the models available to all interested parties, including low-income countries, can be discussed in the Future vision chapter.

- Benny added that there is not always a specific tool for PV, but certain tools may work, e.g. data extraction tools that can also be used for literature reviews.
- The WG should consider that favouring proprietary models could lead to one or two companies gaining excessive leverage. We may choose to highlight this issue as one of the challenges we face in today's environment.
- As a WG, we are responsible for explaining the implications and guiding the audience in weighing the pros and cons of open-source solutions versus patented solutions. We should not avoid difficult topics or questions but explain why providing a simple answer is impossible.
- How can we ensure that we use the best method for specific requirements, regardless of whether we want to use a proprietary or an open-source algorithm? What are the different aspects to consider when choosing an open-source or proprietary method? Arvind proposed to address these issues in Chapter 5.

Chapter 5 Validation and qualification considerations

- Hans-Jörg gave the Chapter 5 team presentation, and the following only represents the discussion points raised after the presentation.
- Luisa proposed discussing the possible overlap between different chapters.
- Benny raised the following discussion points:
  - Do we wish to include the discussion on algorithmic impact assessment?
  - Once the tool is deployed, how do you assess the impact? Are there risks being highlighted and how do you mitigate those impacts?
- Hans-Jörg responded that the issues mentioned had not yet been discussed in detail, but that an initial risk assessment was needed and another once the model had been trained and used.
- Andrew cautioned the WG not to summarise existing guidelines as the target audience will expect recommendations from the future report. Could we try to challenge what is predicted to be the preferred method in four to five years?
- The Chapter 5 team will identify the status of the validation and qualification criteria developed and go beyond merely duplicating what others have done.

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

- Taxiarchis and Arvind gave the Chapter 6 and 7 team presentation, and the only following represents the discussion points.
- Arvind invited the WG members to send use cases to be included in the chapter.
- Robert suggested that WG go through all our sections and try to identify how the subgroups address different topics, e.g. the topics of data and validation. We need to decide whether or not these issues need to be addressed from a different angle in all sections of the future report.

Chapter 8 Future vision

- Denny gave the Chapter 8 team presentation, and the following only represents the discussion points raised after the presentation.
- The Chapter 8 team aims to bring their independent thoughts to the draft and review the content against the draft chapters. The unnecessary overlap will be removed and some topics that are only briefly mentioned will be further elaborated.

- Andrew urged the WG not to hesitate to discuss the more sensitive issues that need to be discussed as a WG to have an excellent report as a result.
- Future vision in a field like AI can be difficult to predict. We should remember that by the time the report is published, the technology may already be far advanced, so some aspects that were once considered a vision of the future may already be somewhat outdated.
- Walter suggested highlighting current or anticipated controversies in the report and outlining the advantages and disadvantages of these controversies to illustrate the challenges we face, e.g. the issue of open-source versus proprietary software.
- Robert noted that technology, including AI, must meet specific quality requirements from a regulatory perspective. Should WG focus on AI meeting the quality requirements rather than the technical details?
- CIOMS documents contain the best collective knowledge to advance the topic as meaningfully as possible. All CIOMS guidelines contain a vision for the future and all key stakeholders should benefit from this collective work.
- The future report allows the WG to tackle complex issues and identify alternatives where it is impossible to have only one consensus position.

Forming chapter editorial teams

- The WG agreed to form editorial teams within their writing teams, which will meet to discuss the content of each chapter and eliminate possible overlaps.
- Chapter leads are invited to send their drafts and any publications relevant to the WG agenda to the CIOMS Secretariat to be uploaded to the private members' area.
- At a later stage, groups may continue their work on a shared document, but not all parties may have access to specific environments, and we do not wish to exclude any WG members.

Glossary

- Should we have a set of acronyms and possibly a glossary at the beginning of the report?
- Lembit suggested that acronyms and glossary may add to the document's readability especially for those audiences that are not thoroughly familiar with the topic.
- As the field of AI and ML is rapidly evolving, it may be beneficial to record the concepts to a specific time frame and at some point, to review the terms and definitions.
- The CIOMS Cumulative Pharmacovigilance Glossary 2.0 is available on the CIOMS website and compiles terms and definitions from published CIOMS PV reports. The WG is welcome to consult it as a resource when considering its terms, definitions, and sources.
- The updated Glossary of ICH terms and definitions is available on the CIOMS website.
- Chapter leads will collect and suggest terms during the drafting process, which will then be discussed with the WG and added to the glossary.

3. Way of working

- All CIOMS reports contain references. Some working groups have chosen to add references after each chapter, for some reports all references are added at the end of the report.
- CIOMS reports are usually finalised by an editorial team consisting of five to six members from the WG. A near-final draft is presented to the whole WG during the final meeting.

- A public consultation will be held upon the decision of WG in the final stage of finalising the report. The consultation period will be approximately six weeks and provides an opportunity to gather additional feedback. The editorial committee will decide on the inclusion of comments received.

4. Next steps / Next meeting

- The next full WG meeting will be held virtually in the beginning of April 2023. The 2-hour meeting will be an occasion for the chapter teams to report on the progress made and discuss the scope of the future report.
- The WG agreed to 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.
- Post-meeting: The next WG two-day in-person meeting will be held on 6-7 June in Zürich.

5. Closing remarks

Hervé and Lembit thanked the WG members for joining and for the productive discussions.

Annex 1: List of participants

Participants

Justyna Amelio (AbbVie), Robert Ball (US FDA), Luisa Barrios (Merck Sharp & Dohme), Andrew Bate (GlaxoSmithKline), Arvind Bellur (Sanofi), Adrian Berridge (Takeda), Taxiarchis Botsis (Johns Hopkins University School of Medicine, US), Flávia Moreira Cruz (ANVISA, Brazil), Piero Francesco Franco (Pfizer), Stephen Heaton* (CIOMS), Thomas Henn* (Unither), Kirsten Egebjerg Juul* (Danish Medicines Agency), Vijay Kara* (GlaxoSmithKline), Dieter Kempf (Genentech, Roche), Jesper Kjær (Danish Medicines Agency), Benny Ling (Health Canada), Denny Lorenz (Bayer), Hervé Le Louët (CIOMS), Richard McAteer (Health Canada), Yusuke Matsunuga (Pharmaceuticals and Medical Devices Agency, Japan), Manuela Messelhäußer* (Paul-Ehrlich Institute), Niklas Norén (World Health Organization / Uppsala Monitoring Centre), Ravi Patel (Unither), John Reinhard Pietzsch* (Bayer), Beth MacEntee Pileggi (Johnson & Johnson), Kateriina Rannula (CIOMS), Lembit Rägo (CIOMS), Hans-Jörg Römming (Merck Group), Walter Straus (Moderna), Phil Tregunno (The Medicines and Healthcare Products Regulatory Agency, UK), and Panos Tsintis (CIOMS Senior Adviser).

*Alternate

Regrets

Russ Altman (Stanford University, US), Hua Carroll (Biogen), Jean-Michel Dogné (University of Namur), Kendal Harrison* (The Medicines and Healthcare Products Regulatory Agency, UK), Alexander Horst (Swissmedic), Yuki Kikuchi* (Pharmaceuticals and Medical Devices Agency, Japan), Roli Mathur (India Council Medical Research), Dirk Mentzer (Paul-Ehrlich Institute), Nicolas Perez * (Swissmedic), and Stephen Rosenfeld (North Star Review Board).

Annex 2: Writing teams

Chapter number(s)	Title	Team lead(s)	Members
1,2,3	1. Introduction 2. Landscape 3. Scope	Walter	Walter Straus, Stephen Rosenfeld, Flávia Cruz, Piero Francesco Franco, Justyna Amelio, Benny Ling, Hua Carroll, Niklas Norén
4	Guiding Principles	Elizabeth	Stephen Rosenfeld, Vijay Kara, Elizabeth Savage, Niklas Norén, Phil Tregunno, Justyna Amelio, Benny Ling, Manuela Messenhaeusser, Dirk Mentzer, Alexander Horst, Jesper Kjær, Kirsten Egebjerg Juul
5	Validation and qualification considerations	Hans-Jörg	Hans-Jörg Römming, Adrian Berridge, Hua Carroll, Manuela Messelhäußer, Dirk Mentzer, Dieter Kempf, Luisa Barrios
6,7	6. Consideration of AI 7. Implementation and maintenance lifecycle aspects	Taxiarchis and Arvind	Taxiarchis Botsis, Dieter Kempf, Arvind Bellur, Robert Ball, Elizabeth Savage, Phil Tregunno, Justyna Amelio, Thomas Henn, Hans-Jörg Römming, Luisa Barrios, Jesper Kjær, Kirsten Egebjerg Juul
8	Future vision	Ravi and Denny	Ravi Patel, Denny Lorenz, Piero Francesco Franco, Andrew Bates, Vijay Kara, Thomas Henn