



Ninth virtual meeting of the CIOMS Working Group XIII Defining Intent, and Guiding Harmonization and Ethics Standards for Real-World Data and Real-World Evidence in Regulatory Decision-Making

22 June 2021, Virtual Meeting

Meeting Minutes

Participants

Enrica Alteri (former EMA), Yoshiko Atsuta (Japan Data Center for Hematopoietic Cell Transplantation), Elodie Aubrun (Novartis), Laurent Azoulay (McGill University), Elodie Baumfeld Andre (Roche), John Concato (US FDA), Gracy Crane (Roche), Monica da Luz Carvalho Soares (Agência Nacional de Vigilância Sanitária, Brazil), Sean Hennessy (University of Pennsylvania), Sanna Hill (CIOMS), Alar Irs (State Agency of Medicines, Estonia), Akihiro Ishiguro (Pharmaceuticals and Medical Devices Agency, Japan), Jie Li (US FDA), Andrea Machlitt (Bayer), Takahiro Nonaka (Pharmaceuticals and Medical Devices Agency, Japan), Kateriina Rannula (CIOMS), Anja Schiel (Norwegian Medicines Agency), Julia Stingl (University of Aachen, Germany), David Townend (Maastricht University), Julia Wicherski (Bundesinstitut für Arzneimittel und Medizinprodukte), David Wormser (Novartis), and Kristina Zint (Boehringer Ingelheim).

Regrets

Stella Blackburn (IQVIA), Mariette Boerstoeel (Alexion), Thomas Brookland (Roche), Ulka Campbell (Pfizer), Wim Goettsch (Utrecht Centre for Pharmaceutical Policy), Britta Haenisch (Bundesinstitut für Arzneimittel und Medizinprodukte), Steffen Heß (Bundesinstitut für Arzneimittel und Medizinprodukte), Lu Hong (National Medical Products Administration, China), Solomon Iyasu (Merck, Merck Sharp & Dohme Corp), Michele Jonsson Funk (University of North Carolina), Juhaeri Juhaeri (Sanofi), Laurie Lambert (CADTH), Miguel-Angel Mayer (Universitat Pompeu Fabra Barcelona), Andreas Rudkjoebing (World Medical Association), and Lembit Rägo (CIOMS).

Alternate not attending

Daisaku Sato (Pharmaceuticals and Medical Devices Agency, Japan).

Introduction

- Lembit sent his apologies for being absent on this occasion.
- Sanna welcomed the WG members and made the following announcements:
 - Version 1.1 of the [CIOMS Cumulative Pharmacovigilance Glossary](#) was published on 10 June 2021 and is available on the CIOMS website. This version includes some newly added terms and definitions, including for vaccines too.
 - The CIOMS WG on [Clinical Research in Resource-Limited Settings](#) has published its consensus report;



- The CIOMS WG on [Recommended Standards for Education and Training for Health Professionals Participating in Medicines Development](#) has been launched;
- New CIOMS WG on Principles of Good Governance for Research Institutions will be launched in July;
- A spokesperson from the Association of the European Self-Care Industry ([AESGP](#)) is invited to join the next WG XIII meeting to present its findings on work carried out on RWD and RWE.
- Elodie Aubrun kindly chaired the meeting.
- The meeting agenda was adopted.
- Kateriina was rapporteur.

Progress updates and discussions on chapters

Chapter 1. Introduction

- The introduction will be finalized when the rest of the chapters have been finished.

Chapter 2. Uses of RWE in the regulatory process during the product life cycle

- The chapter 2 team reviewed the draft to improve its flow and address any remaining questions.
- The team requested suggestions for a use case for the post-marketing setting, ideally outside the topic of safety studies.
- Expertise from the WG on drafting a regulatory section on China would be appreciated.
- The section on pre-registration of protocols is included in chapter 4 and will not be discussed in chapter 2.
- Should the STROBE checklist be included in chapter 2 or is there a more suitable location? The team agreed to discuss it in conjunction with the other chapters.

Chapter 3: Real world data and data sources

- The draft focuses too heavily on the US space, and although the [Big Data Steering Group](#) is mentioned in chapter 2, Anja suggested checking through the report and adding the following:
 - European Health Data Space ([EHDS](#)), which is a rapidly developing area;
 - [DARWIN EU](#) project;
 - Towards the European Health Data Space ([TEHDAS](#));
 - Plus other similar initiatives that will be in place by the time our report is finished.
- Alar added that if any WG members are involved in any European projects, it would be beneficial to include this perspective. Alar will contact Peter Arlett, Head of Pharmacovigilance and Epidemiology Department, EMA, and seek information or a suggestion regarding a person interested in drafting a section on European Health Data Space.

Chapter 4: Key scientific considerations in regulatory RWE generation

- Yoshiko informed that there have not been recent updates to the chapter.
- Laurent added that the chapter team is working towards removing overlaps with other sections and improving flow.



Chapter 5: Ethics, governance, and related issues

- David shared key progress milestones on chapter 5:
 - An understanding of the technical law that was outlined in previous presentations has been reached;
 - David will add content in line with research on equity, diversity, inclusion, and investigating how people in traditionally excluded communities around LGBT+ issues consider the idea of data sharing. This research is being conducted in cooperation with David's master's student, Daniela Rojas, Maastricht University.
 - Daniela will contact Sanna to set up meetings with the chapter 5 team to discuss the chapter outline and start drafting.
- David will circulate the chapter draft among the WG members for feedback in advance of the next meeting.

General discussion

Combined chapters

- The WG made a plan to merge the chapters into a single document by the 16th of August, ahead of the next full WG meeting anticipated for September, allowing everyone time to read and reflect on the document.
- This will be an occasion to remove potential duplications and balance the text - some areas seem to be US-heavy and others HTA-heavy.

Possibilities for simultaneous text editing

- Sharing documents via email and the password-protected CIOMS web pages were felt to be time-consuming and prone to errors as chapter leads need to maintain chapter version control and compile comments received from many directions, sometimes simultaneously. Some WG members reported not always feeling confident about having the latest version and disliked having to wait to see the combined chapters document.
- Some requested placing the full draft report on an online, collaborative, text editing platform for easy access to the combined chapters in real time. Solutions such as Dropbox, Microsoft Teams, Google Docs, SharePoint etc. were mentioned, with a preference for Dropbox.
- A platform that would be accessible to all WG members does not seem to exist, mostly due to security reasons, and CIOMS does not wish to exclude any WG members. Some felt that finding a solution that would suit the majority would suffice and that we could find a way to support the few who cannot access the document in this way.
- The chapter 2 team has temporarily tested using the Google Docs environment, and although this was found to be satisfactory for many team members, there is no appetite to continue hosting in this way. Some members created personal Google email addresses in order to access the draft but not all were able to access it from their work environment, e.g. PMDA.
- Elodie enquired whether CIOMS would be able to provide technical support to the WG members using such technical solutions.
- Sanna will research options, starting with Dropbox, and will update the WG in time for hosting the combined chapters document after the 16th of August.



Covid-19 statement

- In 2020, some of the CIOMS WGs issued statements to provide tailored guidance in their specialist areas on the unfolding medicines development and pharmacovigilance activity during the pandemic. See the [WG XII's statement](#) on the benefit-risk balance for medicinal products; and the [WG XI's statement](#) on patient involvement in the development and safe use of medicines.
- A similar opportunity is open to CIOMS WG XIII and a potential statement could be published ahead of the report publication.
- In more detail, potential subject areas to explore would be guidance on generating RWD and RWE on treatments (re-purposing drugs, developing new drugs) and vaccines (given the emergency use authorisations, limited data, uncertainties) for regulatory decision making in the unprecedented pandemic context.
- Interested WG members will contact CIOMS.

Case studies

- The main aim of including case studies is to provide clarity and insight into the topics included in the document.
- We should discuss which case studies to use and how to include them. A standardised format would be helpful. Should the case studies be embedded into the main body of the text or added as an annex?
- We could review the case studies as a team to ensure that they cover the report's scope and represent both pre-marketing and post-marketing periods.
- Would WG members be able to present use cases in a month, as it is easier to coordinate the use of case studies across the chapters before the chapters and the use cases are nearly finished?
- Sanna described the different approaches that the CIOMS WG XI on Patient Involvement and WG XII on Benefit-Risk Balance have taken towards handling case studies.
- Anja added that there is a benefit-risk involved for each product that is approved or not approved. For RWE, there might not be many use cases. It is challenging to use examples as the interpretation often depends on the reader, and she cautioned the WG about including possibly confidential information.
- Sanna commented that examples could be used without specific names, only to demonstrate a principle.
- Elo felt that chapter 4 would possibly have different views than chapter 2 regarding describing good practice. Chapter 2 presents examples of already active discussions with regulators or RWE leading to a decision by regulators. In chapter 4, the intention is different.
- Anja agreed that chapter 4 is about methodology, and there is less controversy around the topic. If examples are to be found for chapter 4 that are relatively neutral, perhaps they can be referred to in chapter 2 as well?
- Kristina suggested reflecting on the use cases in September, once there is a consolidated version of the chapters.
- Enrica added that we could reconsider in future discussions whether to include examples like in chapter 2 or full case studies. Each chapter has used examples, and if the WG considers them valuable, two or three examples could be used as proper case studies. The WG should first review the examples in each chapter and decide how to incorporate them.
- The WG agreed that case studies should be chosen from the public domain.



Glossary

- The chapter teams will forward their suggested glossary terms and definitions to Sanna together with the latest version of their chapters by 16 August. Sanna will distribute the combined chapters and glossary.
- It would be helpful to add references to the definitions where possible.

Future meetings and closing remarks

- Sanna will send a Doodle poll to help schedule the next meeting for September.
- Elodie thanked all WG members for joining and for their time and effort in progressing the WG's agenda.