



Seventh 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

1 April 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), Stella Blackburn (IQVIA), Mariette Boerstoel (Alexion), 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), Juhaeri Juhaeri (Sanofi), Laurie Lambert (CADTH), Jie Li (US FDA), Mareike Millner** (Maastricht University), Andrea Machlitt (Bayer), Takahiro Nonaka (Pharmaceuticals and Medical Devices Agency, Japan), Kateriina Rannula (CIOMS), Daniela Rojas** (Maastricht University), Lembit Rägo (CIOMS), Anja Schiel (Norwegian Medicines Agency), and Kristina Zint (Boehringer Ingelheim).

Regrets

Elodie Baumfeld Andre (Roche), Thomas Brookland (Roche), Wim Goettsch (Utrecht Centre for Pharmaceutical Policy), Britta Haenisch (Bundesinstitut für Arzneimittel und Medizinprodukte), Steffen Heß (Bundesinstitut für Arzneimittel und Medizinprodukte), Solomon Iyasu (Merck, Merck Sharp & Dohme Corp), Michele Jonsson Funk (University of North Carolina), Lu Hong (National Medical Products Administration, China), Miguel-Angel Mayer (Universitat Pompeu Fabra Barcelona), Andreas Rudkjoebing (World Medical Association), Julia Stingl* (University of Aachen, Germany), David Townend (Maastricht University), Julia Wicherski (Bundesinstitut für Arzneimittel und Medizinprodukte), and David Wormser (Novartis).

Alternate not attending

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

* New members since last meeting.

** Observers

Introduction

- Lembit welcomed the members and chaired the meeting.
- The [CIOMS Cumulative Pharmacovigilance Glossary](#) has just been published. This will be a living document and the terms from the CIOMS WG XIII report glossary will be added in time.
- CIOMS has issued its [quarterly newsletter](#).



- Two new CIOMS WGs will be launched soon on the following topics:
 - Recommended standards for education and training for health professionals participating in medicines development - the initiative came from a CIOMS member organization, [The International Federation of Associations for Pharmaceutical Physicians](#);
 - Ethical assessment of clinical trials.
- Lembit also made the following announcements:
 - Julia Stingl, Prof. of Clinical Pharmacology at the University of Aachen, Germany, and former BfArM Vice-President, has joined the WG and the Chapter 5 team;
 - Mareike Millner and Daniela Rojas, master's students from Maastricht University working with David Townsend, joined the WG meeting as observers.
- A CIOMS editorial guidance document has been shared with the WG and a sample chapter from the CIOMS WG XI on Patient Involvement will be circulated too.
- The meeting agenda was adopted.
- Kateriina was rapporteur.

Chapter teams' presentations

Chapter 1. Introduction

Sean gave an update on Chapter 1 and added that the introduction will be finalized when the rest of the chapters are ready.

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

- Elodie A gave an overview of the most recent additions to chapter 2 and invited the WG members to provide feedback, particularly on sections regarding different regions.
- Mariette confirmed the section on the US needs additional information and she suggested re-considering the balance on health technology assessment and regulatory decision making.
- Juhaeri observed that the chapter's focus is mainly on the benefits of RWE/RWD and he offered to give comments on safety aspects. A brief example or quote would suffice.
- Andrea said that the report is trying to extend into benefit-risk assessments and create the groundwork for regulatory acceptance for new indications and conditional approvals. She added that the document should elaborate on how to confirm efficacy or effectiveness and describe their natures in terms of regulatory acceptance. She suggested stating what could be considered acceptable by regulators and identifying the ambiguities in the field. The CIOMS report could make recommendations on what should be achieved in the following years to increase the regulatory acceptance of RWE.
- Enrica commented that from the regulatory viewpoint of benefit-risk, it is difficult to provide recommendations for using RWD, because if a particular medicine is not on the market, collecting RWE is impossible. RWD can complement information that is collected in other ways for demonstrating benefits.
- Lembit added that conditional approvals can be issued in the case of rare diseases/emergencies, providing faster patient access to new drugs, and thus accelerating RWD collection. He suggested including the topic.
- John commented that sometimes RWD is used in an observational study research design. FDA has accepted RWD for decades and the evidentiary standards will not change. There is a need



for adequate well-controlled studies, not trials. The focus should not be on describing randomized controlled trials versus observational studies or RWE versus its historical counterpart.

- Juhaeri agreed and added that the focus should not be on the effectiveness or efficacy but on benefit-risk; risks and safety need to be addressed.
- John commented that the sponsors and stakeholders' interest seems to be on effectiveness, not necessarily on new molecular entities. There is a consensus on the main concepts in theory, and the wording needs careful consideration.
- Stella added that we need to consider the questions to be answered and then decide on the most appropriate way to obtain the data and the evidence required to answer the questions.
- Gracy commented that the totality of evidence is always considered. Chapter 2 includes the topic of integrated evidence, which, as much as possible, feeds both into regulators and payers. The report is attempting to describe the continuous use of RWD along the medicine lifecycle.
- Stella added that [The NEW Drug Development ParadIGMs \(NEWDIGS\) initiative](#) has investigated integrated evidence generation and she suggested drafting a section on this.
- Monica has included examples on drug approval using RWD in the regulatory process in both the pre-and post-approval stages and comments on external control in the chapter.
- Akihiro offered to create a descriptive section on the PMDA activities for the subsection 2.4 for the next WG meeting.

Chapter 3: Real world data and data sources

Juhaeri gave a brief overview of Chapter 3, saying that all suggestions from the previous meetings will be implemented by the next meeting.

Chapter 4: Key scientific considerations in regulatory RWE generation

- Laurent addressed the challenge of choosing the most appropriate issues and resources for his section in Chapter 4. Chapter 4 will probably be one of the most extensive sections in the report.
- Andrea urged the WG members to provide their perspectives on the best practice for creating transparency of protocol posting or results posting.
- Laurie suggested consulting the [Duke Margolis STaRT-RWE tool](#).
- Chapter 4 team agreed to edit the text to remove possible overlaps and to shorten the chapters for the sake of the report's proportionality.
- Lembit suggested Chapter 4 team to hold a meeting before the next WG meeting if necessary.

Chapter 5: Ethics, governance and related issues

- David sent his apologies for not being able to attend the meeting.
- He will be holding a meeting for the ethics chapter in the second week of April.

References in CIOMS reports

- Sanna recommended referring to the Editorial guideline and its advice on references.
- The CIOMS Secretariat will assist with references at the editing phase, if needed.



- Hyperlinks are welcome as the report will also be published in an electronic format and will incorporate cross-referencing as much as possible.

Future meetings and closing remarks

- CIOMS will help to set up chapter team meetings.
- There is a Doodle poll open to help to schedule the next meeting in May.
- Lembit thanked all the WG members for joining and for their efforts in drafting the chapters.

Actions

Who?	What?
All members	- Provide feedback on Chapter 2. - Provide input towards Chapter 4.
Team leads	Send the latest versions of the chapters to Sanna.
Stella	Provide references and draft a section for Chapter 2 on the NEWDIGS initiative.
Akihiro	Provide input on PMDA's activities for subsection 2.4.
<u>Gracy</u>	Provide assistance to the Chapter 4 team.
Juhaeri	Send comments on Chapter 2 regarding the safety aspects of using RWD. [done]
Sanna	Set up a Zoom call for Chapter 4 team. [done]
Sanna	Circulate the draft meeting minutes. [done]
Sanna	Circulate the Editorial guideline and example chapter from CIOMS WG XI. [done]