Council for International Organizations of Medical Sciences

# Eighth meeting of the CIOMS Working Group on Severe Cutaneous Adverse Reactions of Drugs (SCAR)

**12 December 2022**

Meeting Minutes

## Participants

Priya Bahri (EMA), David Brott (Takeda), Siew Eng Choon (Monash University), Chia-Yu Chu (National Taiwan University Hospital), Roni P. Dodiuk-Gad (Emek Medical Center), Alexandre Kiazand (AstraZeneca), Gerd Kullak-Ublick (Novartis), Haur Yueh Lee (Singapore General Hospital), Sylvia Lesperance (Novartis), Hevé le Louet (CIOMS), Filippa Nyberg (Karolinska University Hospital), Ariel Porcalla (AbbVie), Violeta Regnier Galvao (Eli Lilly), Melissa Reyes (FDA), Sarah Schlief (Bayer), Takahiro Ueda (PMDA)

**Secretariat**: Lembit Rago, Catherine Bates

**Regrets**: Leslie Dondey-Nouvel (Sanofi), Matt Doogue (IUPHAR/Univ of Otago/Christchurch), Koji Hashimoto (Ehime University), Neil Shear (University of Toronto), Sabine Straus (MEB)

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### Introduction

Lembit welcomed the group and updated members on the two glossaries CIOMS has produced, one is the Cumulative Glossary of all CIOMS reports, version 2.0 and the other, a glossary of ICH terms. CIOMS will meet with ICH to coordinate future glossary updates.

### Discussion highlights and key changes

Chia-Yu and Melissa reviewed their respective chapters and raised points for chapter leads to consider.

**Introduction, Chapters 1, 2, 3**

### References

The group discussed how references should be listed e.g. at the end of each chapter or at the end of the report. While the former is more reader-friendly, the latter would help to avoid duplicate references and reduce the length of the report. The group is free to choose how they wish to proceed.

### Adding lay language text boxes at the beginning/end of each chapter

The group suggested inserting a box at the beginning or end of each chapter with the key characteristics of SCAR, which would help to communicate with patients. Another view was that this should not be pursued and is not consistent with the intent of the report. The executive summary could serve this purpose, but ultimately, the group needs to decide which is the best way forward. A question was raised as to who might be able to write these lay language inserts. Catherine volunteered to help in this regard. Another suggestion was to include lay language in Chapter 2 In the sections that describe communication with patients and carers.

- The group decided to discuss this in the editorial committee.
- A survey will be sent around to gage members' preference.

There were no further comments on the first four sections.

## Discussion of Chapters 4, 5, 6, 7, 8

### Chapter 4

- The group agreed to include a recommendation in the report that biomarker information be provided in the label when appropriate.
- Another point was raised regarding the biomarkers that are described in this chapter and whether they are genetic in nature. This will be mentioned in the introduction instead of making the title more specific as this could change in the future.
- The editorial committee will review the definition of biomarker and decide if the FDA version should be used or that of EMA.

### Chapter 5

Regarding terminology, the WG discussed the difference in meaning between timeline (prior to the onset of SCR) and time point. Please see changes Section 5.1 lines 451-453. The eight week review period applies to SJS and TEN, but for DRESS, sometimes 12 weeks is required. Also, it was suggested that the report should explain why the review is over eight weeks, i.e. the latency or the period between taking the culprit drug and the onset of a reaction for a SCAR lies within this time frame.

- These comments will be addressed in the editorial committee

Should the report refer to pre-marketing or pre-authorization? According to the CIOMS Glossary 2.0, the preferred term is “pre-authorization”

There was a proposal to reorder Chapters 5, 6 and 7 as follows:

7 should replace 5
5 should replace 6
6 should replace 7

The group was asked if it would be acceptable to move from clinical to causality and then talk about the specifics of surveillance and pre and post authorization.

- The editorial committee should look at causality assessment at individual level vs population level to ensure the language is clear. The report should mention that causality can occur in both.

- Maybe the report should keep the original version of Chapter 5, i.e. the individual level, but mention in the introduction that based on the review and assessment of individual cases, there will be a summary risk assessment on the causality and whether the drug has the potential to cause these reactions. If so, it will be labelled as such. Then the report can refer to the other chapter on post-authorization surveillance and risk management. So one sentence could “do the trick”, and then it's clear that the chapter focuses on the individual level.

- As an alternative, there was a suggestion to refer to “assessment” instead of causality assessment as the former includes causality assessment and then one could mention signal which applies to the totality of the information.

- The editorial committee should also discuss whether to include a reference to "authorization" in the title. Where should this line of authorization be introduced? In Chapter 5 or in the introduction to Chapter 6?

- Chapter 5 point 1.3: Should the reporting of genetic information be covered in this section for the sake of completeness?

Chapter 5 point 2.2.1 The group discussed the tools and how many are really needed. The group did not want readers to think that all of them are required every time one was developing a SCAR programme. Rather, the tools should serve as a reference.

- A sentence could be added to this section to explain a method for how these tools have been used in the past.

- An alternative could be to add an introductory sentence about how to use these tools potentially.

- Then, there could be a section on target follow-up forms

A question was raised about vaccines and whether they were in scope? No signals were found to this effect in the study conducted by the Uppsala Monitoring Centre.

- The editorial committee could add a sentence in the introduction to Chapter 5 that based on current evidence, there is an 8 to twelve (DRESS) week time frame in which exposure or events should be reviewed and this applies regardless of the half-life.

Is there anything with a long half-life that could trigger a SCAR, e.g. infectious diseases? 8 weeks is sufficient and an infectious disease would not need to be considered as an alternative course.

**Chapter 6**

The editorial committee will be asked to review the following:

1. Decide if the information in table 1 is accurate. Is all the information that should be collected by an investigator for a suspected scar event included?
2. Duplicate language in Chapters 5 and 6 and decide where it belongs.
3. The meaning of the term "adjudication". Add more detailed explanation.
4. Should "adjudication" also be mentioned in the chapter on causality assessment?

**Chapter 7**

Change the title for consistency with Chapter 6, i.e. Pre/post-authorization.

- The group agreed that "pharmacovigilance" should at least be mentioned e.g. in Chapter 1 and then referred to in either Chapters 6 and 7.
- The editorial committee should look at the introduction in Chapter 7 and determine how much clinical information should be repeated e.g. incidence. The WG agreed to repeat the information in Chapter 7.1, but insert a cross-reference to Chapter 1 and for the next instance on SCAR, a cross-reference to Chapter 2 could be added.
- The paragraph on pre-authorization was moved up so it is the 1st paragraph. The editorial committee could look at this.

**Chapter 8**

The group discussed the title of the chapter and which term, risk minimization or mitigation, is the preferred one. This was checked in the CIOMS Glossary 2.0 and the group agreed that "risk minimization" is the preferred term.

- The editorial committee is tasked with checking the references throughout the chapter and ensuring consistency (see definition of risk management provided by Melissa)
- Also, a decision should be made regarding the use of "product labelling" or "product information". The group felt that "labelling" was more appropriate. Product labelling is fine, provided it includes the patient information leaflet.
- The editorial committee will need to go through the CIOMS glossary again.
- A table could be inserted to list the regulatory terms.
- Clinicians in the group were asked if they knew of any examples of product labels related to SCAR that they found useful. A doodle will be sent around to receive member input.

**Other agenda items**

Regarding the internal member review, the WG could hold one editorial committee meeting and then send it back to the whole WG prior to sharing the report internally.

**Next steps and timeline**

- The WG agreed that chapter members should review their respective drafts and share changes with the chapter lead (January 16th)
- Chapter leads to circulate drafts to the WG (January 30th)
- 1st editorial committee (February 6th)
- Editorial committee shares new drafts with the WG (March 1st)
- 9th WG (March 14th)
- Internal consultations (3rd week of March – beginning April)
- 2nd editorial committee (Mid-April)
- Review by WG (Beginning May)
- Public consultation (May 2023)