Council for International Organizations of Medical Sciences

Minutes (web)

Fourteenth meeting of the CIOMS Implementation Working Group on Standardised MedDRA Queries (SMQs)

11-12 September 2018

CIOMS offices, Ecumenical Centre, 150 Route de Ferney, 1218 Geneva, Switzerland

Report from the CIOMS Secretariat

Dr Lembit Rägo gave an overview of CIOMS, including its history, current setup and working procedures, recently established Working Groups, and potential ideas for future groups. Comprehensive and up-to-date information about CIOMS is available (https://cioms.ch/).

To increase transparency and stimulate comments, CIOMS has started to publish high-level web versions of Working Group (WG) meeting minutes on the web. An example from the CIOMS WG on Drug-Induced Liver Injury (DILI) was handed out. In principle, the participants supported the idea of high-level summarized versions of the SMQ Implementation WG meetings being posted on the CIOMS website.

L Rägo updated the group on progress with setting up a potential new WG on MedDRA Labelling Groupings (MLGs). The concept paper and slides were circulated to the ICH MedDRA Management Committee ahead of its meeting held in Kobe, Japan, in June 2018. The Committee requested that a one-pager be prepared. This was provided in August and will be discussed by the Committee during the ICH meeting to be held in Charlotte, U.S., in the week of 10 November 2018. [1]

MedDRA Labelling Groupings (MLGs)

I Große-Michaelis presented the one-pager that had been prepared for the MedDRA Management Committee by a subgroup as named in the agenda. The one-pager starts by providing some background about product labelling, including regulatory guidance, and about MedDRA. It explains

[1] *Post-meeting note: at the ICH Meeting held in Charlotte, U.S., in November 2018 the MoU was renewed for another year for the purpose of developing SMQs. In addition, it is envisaged that a new CIOMS Working Group (WG) will be convened to develop principles and points to consider type guidance for making MLGs. The new CIOMS Working Group on MLGs will emerge using expertise from the existing CIOMS SMQ IWG, and several new members may also join. As a first step, the group aims to reach consensus on an international approach to MLGs for voluntary consideration by companies.*

how MLGs can supplement the use of published MedDRA term groupings to convey simple, clear, and complete information about a product's adverse effects – including their frequencies – to health professionals and patients as required by regulation and guidance, and states the benefits of MLGs and some of the key points to consider in their design and maintenance.

The group agreed that the development of consensus principles for MLGs would be timely, given that different approaches to term groupings are currently emerging. An FDA analysis showed that groupings of MedDRA Preferred Terms (PTs) were used in 14% of U.S. product labels from 2008-2014. Several industry representatives participating in the meeting confirmed that their companies create and use their own ad hoc MLGs when needed.

The participants felt that concrete examples of MLGs would be helpful to explain the concept to stakeholders. The example of the MLG that had been created by one pharmaceutical company to describe the concept of headache was presented.

Some challenges of implementing MLGs were mentioned. Thus, differences in labelling requirements between jurisdictions can lead to different labelling even for one given product to be marketed in different countries. Also, as not all clinical trials have results on all PTs, fair comparisons between products would require that certain PTs are excluded from an MLG for certain products.

All participants agreed that the labelling should include full detail of the content of an MLG. The labelling should clearly state all PTs that are included, as well as relevant PTs that are excluded. Such traceability is critical for regulators and applicants. For example, in Japan the adverse events listed in the labelling are categorized by severity, and data for each PT are needed, as not all PTs included in an MLG would necessarily have the same severity rating.

It was postulated that MLGs could be part of MedDRA, although it was hypothesized that this could be challenging. Participants from MSSO felt that it would be challenging to standardize MLGs. An in-depth discussion cannot occur until MLG principles are under development. The group agreed that, at this stage, a potential new WG should first develop consensus principles on how to define, apply, and maintain MLGs. Thereafter, some specific MLGs might be developed, if this is considered practical and useful. Eventual use might be non-binding and voluntary (another topic for future discussion).

It was further suggested that MLGs could be tested before implementation (especially for complex and critical MLGs), that insights might be gained from comparing the definitions of MLGs across organizations, and that it might be useful to calculate proportions of patients matching specific PTs within a grouping.

Participants were asked to state any objections to setting up a CIOMS Working Group on MLGs. There were no objections. D Ronan said that ICH will state its position after discussion of the issue at the ICH meeting in Charlotte, U.S., in November. [2]

Participants agreed to the following next steps, in order of priority:

(1) Further develop the one-pager with input from stakeholders;
(2) Present the concept at the ISoP annual meeting on 11-14 November 2018 (a presentation outline was discussed on Day 2 of the WG meeting)
(3) Prepare an article for submission to the DIA journal (Therapeutic Innovation & Regulatory Science), based on the concept paper.

[2] *See footnote 1.*

Review of Standardised MedDRA Queries (SMQs) in development and in production

The status of SMQs listed in the agenda were reviewed. The outcomes and next steps were recorded separately as part of the operational records of the Working Group, whose activities are overseen by the MedDRA Management Committee.

Date of next meeting

The date of the next meeting was tentatively scheduled for 2-3 April 2019.[3]

Participants

CIOMS	Lembit **Rägo**	Secretary-General
	Susanne **Le Roux**	Administrative assistant
	Monika **Zweygarth**	Technical writer *(morning of Day 1)*
MedDRA organizations	Tomás **Moraleda**	Maintenance and Support Services Organization (MSSO)
	Eva **Rump**	Maintenance and Support Services Organization (MSSO)
	Yutaka **Nagao**	Japanese Maintenance Organization (JMO)
ICH	Dawn **Ronan**	
Regulators	Sonja **Brajovic**	U.S. FDA *(by phone)*
	Mari **Kobayashi**	PMDA, Japan
	Lynn **Macdonald**	Health Canada
	Miki **Ohta**	PMDA, Japan
	Norbert **Paeschke**	BfArM, Germany
	Aniello **Santoro**	European Medicines Agency (EMA)
Product R&D	Silvia **Bader-Weder**	Roche
	Brian S **Dillman**	Eli Lilly
	Bill **Gregory**	Pfizer
	Ilona **Große-Michaelis**	Bayer
	Judith **Jones**	PharmaLex
	Christiane **Michel**	Novartis
	Hitomi **Takeshita**	Chugai Pharmaceutical
	Yu **Tanaka**	Chugai Pharmaceutical

Apologies:

Judy **Harrison**, MSSO; Constantin **Mirea**, Boehringer Ingelheim

[3] *Post-meeting note: Due to the numerous topics proposed for the agenda, the meeting will be held over three days.*