Council for International Organizations of Medical Sciences

6th meeting of the CIOMS Working Group on Patient Involvement

26th June 2020, virtual meeting

Minutes

Participants

Leanne Angst-Wu (Roche), Patrick Beeler (Swissmedic), Fatima Bhayat (Takeda), Stella Blackburn (IQVIA), Ton de Boer (MEB), Nikos Dedes (EATG), Juan Garcia (EMA), Charles Garrigan (Janssen), Linda Härmark (Lareb), Beverly Harrison (Janssen), Stephen Heaton (former Bayer), Sanna Hill (CIOMS), Shinji Hirasawa (PMDA), Javier Hourcade Bellocq (Civil Society Sustainability Network/International Civil Society Support/Independent Consultant, Argentina), François Houÿez (EURORDIS), Stefan Kaehler (Celgene), Regina Kamoga (CHAIN), Talia Lacroix (Health Canada), Kerry Leeson-Beevers (Alström Syndrome), Marilyn Metcalf (GSK), Theresa Mullin (US FDA), Izumi Oba (PMDA), Elisabeth Oehrlein (US NHC), Shanthi Pal (WHO), Ravi Patel (United Therapeutics Industry), Peter Pitts (CMPI), Lembit Rägo (CIOMS), Cheryl Renz (AbbVie), Leo Russo (Pfizer), Ken Sakushima (PMDA), Corinna Schaefer (WMA), Kawaldip Sehmi (IAPO), Meredith Smith (Alexion), Sabine Straus (MEB), Christine Stürchler (Novartis), Panos Tsintis (CIOMS), Pujita Vaidya (Amgen), Annemiek van Rensen (MEB), Manal Younus (ISOP), and Judy Zander (US FDA).

Absent members (including Alternates)

Nathalie Bere (EMA), Matthias Boedding (Merck), Marc Boutin (NHC), Wang Dan (CFDA), Ratna Devi (IAPG/IAPO), Mick Foy (MHRA), Kaisa Immonen (EPF), Veronique Kugener (Takeda), Hervé le Louët (CIOMS), Marie Lindquist (UMC), Isabelle Moulon (former EMA), Rebecca Noel (Eli Lilly), Sten Olsson (ISOP), Theo Raynor (former Leeds University), Daisaku Sato (PMDA), Martina Schäublin (Swissmedic), Oi Tsunehiro (MHLW), and Peggy Webster (Takeda).

Prior to the meeting

- The minutes of the 5th WG meeting held virtually on 1st of April 2020 were approved by absence of comments.

Welcome and opening remarks

- Lembit welcomed everyone and thanked them for their time.
- The agenda was adopted.

Issues that touch on all aspects of the working group

Editorial team

- The editorial team includes: Theo, Stella, Cheryl, Meredith, Panos, Stephen, François, Elisabeth, Annemiek, and a representative from EMA, provided the timings fit with the members' other responsibilities. Other patient representatives are welcome.
- This team will edit the final draft, e.g. bringing uniformity across the chapters, adding hyperlinks for the electronic format, and implementing changes following the public consultation.
- The final version of the manuscript will be circulated to the whole WG for comment before publication.
- Several approaches to the team were considered:
    - A core group and a back-up group to help in the event of unexpected workloads;

    - A summer team and an autumn team to share work according to availabilities;
    - One team to focus on content and a second to focus on language.

- The editorial team's work will begin in the autumn, once all chapters have reached the right level of content maturity, but offers of help during the summer are welcome.
- It was decided to make all subtitles a uniform short length, e.g. Chapter 3 subtitles are too long.
- Favour writing in plain, easy-to-understand English and aim for a simple and engaging style.
- There was a suggestion to structure chapters uniformly, including starting each chapter with bullets to identify key take-aways to ease reading and bring focus to patient engagement.
- Include prioritised recommendations in line with the WG vision. Prioritisation can be done in terms of maturity (if new to patient engagement, start at A, then follow this sequence B-C-D, and lastly cover E and F). Careful to not overwhelm the reader.
- Not all recommendations are of equal importance to all stakeholders, but it can be helpful to see all that is needed in one view, even if all cannot be implemented immediately.
- Recommendations could be formatted in the style of a check list so they can be used for an internal evaluation.
- Each chapter could move background information, i.e. what is not part of the main text, to a chapter appendix, to be reviewed at the end once we have all elements.
- Several reasons were recognised for including background information in an appendix:
    - There is a need for capacity building;
    - We have a diverse audience and some will require more background information;
    - To avoid interrupting the chapter flow;
    - Reduce the word count.
- In the electronic version, extra annexes would be easy to handle.
- Talia recommended an online layout and format as used here, although this does not have the key messages listed at the front of the chapters, which Talia would like to include.
- It was suggested we restrict the length of the chapters, so that each chapter is a comparable length.
- Regarding acronyms, several options were considered:
    - Including a list at the start of the report;
    - Including the acronyms in the Glossary;
    - Defining acronyms when they are initially introduced;
    - Including a list in footnotes on each page where they are used.

Ethicists' perspective

- Due to the pandemic, a number of ethicists are planning to confirm their participation at a later date.
- We may need to form a separate group of ethicists after the main guidance has been completed.
- Involving ethicists specialised in specific topics would require a large number of experts in order to arrive at a mature recommendation. We may need to request input from a smaller number.
- It was suggested that a preliminary, high level conversation take place with only a couple of ethicists in order to identify general ethical issues with regard to patient involvement in the development and safe use of medicines. This would allow the guidance to recognize and address any issues raised that we think are relevant to include in the global guidance. Then, we could have a broader group look at the guidance once it is closer to completion to see if anything was missed or if there are ethical challenges/problems associated with our recommendations that the guidance would need to recognize or address.

Implementation strategy team

- The implementation strategy team includes: Talia, Meredith, Elisabeth, Peter and Christine.
- The team produced an initial, broad-scoped draft plan, which is currently with the team members for feedback. The next version will be provided to the WG for review.

- The implementation strategy will cover the rolling out of the guidance, supports to help disseminate it, materials for capacity building, explanation of the roles and responsibilities of the WG members, and a strategy for reaching specific audiences to maximise the use of the report.

Chapters overview

Chapter 1: Introduction, presented by Theresa

- Having considered the other chapters, Theresa re-wrote the introduction with view to motivating the reader to engage with patients, trying to avoid duplication with the other chapters, focusing on why the patient perspective is uniquely valuable, and detailing what each chapter will provide.
- The introduction will be revised again once the next versions of the other chapters have become available.
- The chapter teams are requested to avoid repetition with their individual chapter openings going forward.
- There was wide appreciation for Theresa's draft.

Comments from discussion:

- Chapter 1 could provide a CIOMS definition for "patient involvement" or "patient engagement".
- It may be helpful to add that Chapter 6 includes an existing CIOMS framework on how to engage patients in risk minimisation.

Chapter 2: The landscape of patient engagement in the development and safe use of medicines, presented by Elisabeth

- The chapter has undergone many changes, such as including establishing opportunities for patients to engage with regulators.
- A few vignettes were received from Theo on the subject of safety.
- There are many elements to move in an appendix: tables, figures, and vignettes.
- Elisabeth would welcome examples for the section on the safe use of medicines.
- A few places focus heavily on the USA and would benefit from specifics from other jurisdictions.
- François submitted a table with rare, emerged-disease patient organisations globally, and there have been a number of examples from Japan for Table 2.
- Early examples added in 2018 on Australia, Korea and Taiwan require references and additional details. These date from before Elisabeth joined the WG. Please provide details if possible.

Comments from discussion:

- Regina recommends re-wording the section on patient involvement in LMICs as there is no equivalent section on high-income countries, and because there is now a chapter on RLS.
- Lembit elaborated that it is important to have a separate chapter on RLS because issues can be very different in these settings. In some cases, there is an opportunity to address needs at an earlier stage of development than was done in higher income countries.

Chapter 3. Guiding principles for patient engagement, presented by Charles

- Feedback was incorporated following the last meeting, and additional feedback from Talia, Meredith and Christine, e.g. an introductory paragraph was added on how the guiding principles were derived from various policy documents and codes of practice.
- The team would welcome:
    1. Real-world examples that demonstrate the principles implemented and their value. The current case example on conflict of interest is perhaps not the most appropriate.
    2. Examples of non-financial types of compensation and how they have been used effectively.

- A table was added on key principles and documents that contributed to the principles. The team would like to know if this should be included in the chapter or in an appendix.

Comments from discussion:

- Regarding the Table of key principles and documents:
    - Panos advised to keep it in the body text because it is highly relevant.
    - Elisabeth liked the sources being visible because they justify why we consider them as principles instead of simply recommendations that we wrote ourselves.
    - Theresa felt the table interrupts the flow of the text and would place it in an appendix.
    - Lembit mentioned that in an electronic document, we can add hyperlinks to the sources.
    - Meredith suggested we add a word about the fact that external source will get updated and that the links may stop working.
    - It would be helpful to see a short list of principles as the audience will vary in how much they wish to know. The team plans to use key words to make it easier for the reader.
- The key words could feature in the margins and refer back to the overarching principles. Using key words consistently throughout the report may add to the uniformity.

Chapter 4. Patient involvement in advancing treatments for their disease, presented by Marilyn

- Marilyn added the cyclical development diagram and would welcome feedback.
- She is grateful for the suggestions for reducing the chapter length.
- Marilyn will implement suggestions on the table, mostly relating to adding joint research priority partnership content, expanding the acronym JLA (James Lind Alliance), and incorporating risk minimisation measures.
- She will edit the recommendations into boxed-out bullet points.
- Marilyn received a suggestion that patient group representatives should be spoken of as "inclusive" because they cannot truly represent an entire population. We should be consistent on this point throughout the document.
- The descriptions of the phases of clinical development may be best placed in a shared appendix at the end of the report so that many chapters can refer to them.
- Marilyn will work with the Chapter 3 team on overlaps between the challenges and recommendations.
- The regulatory document section is dominated by EMA and FDA initiatives, and this section can be reduced a little, perhaps favouring summarising and focusing on the concepts.
- Becky will add the benefit-risk sections in a few weeks' time.

Comments from discussion:

- Lembit feels there is no need to refer to "CIOMS recommendations" as it is implied that they are all CIOMS WG XI recommendations.
- "User testing" should be addressed fully in one chapter and cross-referenced elsewhere if needed. Currently, it is mentioned in chapters 4, 5 and 6, and in maybe others too.
- Regina suggested referring to a guideline on ensuring an overall fair distribution of benefits[1] from the CIOMS guidance International ethical guidelines for health-related research involving humans.

[1] ***Fair distribution of research benefits.*** *Equity in the distribution of the benefits of research requires that research not disproportionately focus on the health needs of a limited class of people, but instead aims to address diverse health needs across different classes or groups. In the past, groups considered vulnerable were excluded from participation in research because it was considered the most expedient way of protecting those groups (for example, children, women of reproductive age, pregnant women). As a consequence of such exclusions, information about the diagnosis, prevention and treatment of diseases that afflict such groups is limited. This has resulted in a serious injustice. Since information about the management of diseases is considered a benefit to society, it is unjust to intentionally deprive specific groups of that benefit. The need to redress these injustices by encouraging the participation of previously excluded groups in basic and applied biomedical research is widely recognized. 2016 International ethical guidelines for health-related research involving humans Page 8*

- Regarding the challenges 1-10, some are challenges, and others which are not, may need re-wording or moving.
- There are a few mentions of "benefit-harm" in the report and it would be best to harmonise across the document to "benefit-risk".

Chapter 5. Guiding principles for patient involvement in patient product labelling, presented by Meredith

- Feedback from Theo has been incorporated.
- Meredith would welcome a patient representative to review section 5.3.
- The table 1 on patient labelling requirements worldwide has been completed.
- The team has added table 2 on comparison of content requirements: package leaflet, medication guide, patient package, and consumer medicines information.
- Meredith would like to know if there are other key initiatives to add to table 3 on initiatives to improve patient labelling: 2003-2018.

Comments from discussion:

- Kerry has reviewed the section and will send her comments.
- Kerry sees labelling as a way of providing information rather than changing or influencing behaviour or beliefs. We need to consider this in terms of the language throughout the report. We refer to e.g. shared decision making and partnership but we must not make it appear as if patients do not have the capacity to make decisions based on the information they receive.
- Kawaldip suggested we could reflect on guidelines on biosimilars labelling from FDA and EMA, and another one soon to be published by WHO. This subject is often not understood by patients and health professionals. Biosimilars are a new class of products and present challenges for health literacy, specifically on naming and pharmacovigilance information. Patients need to know where to report pharmacovigilance information relating to adverse events.
- Kawaldip referenced a recent paper on patient engagement as patient authors in journals and research dissemination on the Research Involvement and Engagement website.
- As this chapter is more descriptive by nature with fever recommendations, it may be because the package leaflet is so highly regulated that any recommendations would be only for policy makers.
- Some of the tables could be placed in an appendix as only some readers will require this level of granularity.
- It was suggested that table 4 should not "emphasise behaviours".
- Regarding the appendixes and references, there is much relevant health literacy available.
- Talia asked if this section was intended for:
    a) How patients are involved in the development of the label; or
    b) How the label is going to help the patients in their decision making.

  Meredith answered that the focus was on the development of the patient labelling, but not on all labelling, i.e. not in the post-market phase.
- It seems the table 4 recommendations are more about what should be in the label rather than the involvement of the patients.

Chapter 6. Opportunities for patient involvement in additional risk minimisation, presented by Cheryl

- Cheryl will re-frame the chapter to reach the core subject earlier, placing more background information in the appendix and directing readers to the CIOMS IX report where relevant.
- Cheryl will also bring out more of the patient involvement content under key points and recommendations.
- The chapter team will consider moving more sections, such as tables and regulatory examples, into an annex.
- Cheryl will condense the section on FMEA (Failure Mode and Effects Analysis) as a means to illicit patient involvement and make the decision about whether a product needs additional risk

minimisation. She suggests keeping FMEA in its place because it is a more futuristic opportunity for bringing patients into the decision making.
- Cheryl will expand the chevrons framework to read: Decision-Design-Development-Implementation-Effectiveness, and place the framework earlier in the chapter.

Comments from discussion:
- Meredith suggested mentioning FDA's most recent guidance on BRAHMS[2] assessment and design from 2019 in a focus on user-centred design, principles, and participatory research.
- It may be helpful to provide a summary for the reader on how during the CIOMS IX report development, a study was contracted with PatientsLikeMe (PLM), which included a survey with a variety of patient respondents. The survey concluded that patient groups did not want to be involved in defining a risk minimisation strategy but did want to be involved in implementation and user testing. The survey results were presented at the EURO DIA meeting and can be found in the CIOMS IX report appendix. This study could be mentioned in the CIOMS XI report as an example of using different platforms within the audience sectors to integrate patient engagement into broader initiatives. We could refer to this CIOMS experience as part of the audience includes the overarching regional organisations that were involved. The CIOMS XI report will be a follow-up to the initial considerations in the CIOMS IX report.

Chapter 7. Guiding principles for patient engagement in the development and use of safety and effectiveness data, presented by Leo
- The latest version has a new introduction which defines what is meant by data.
- The chapter is long but there is context missing under "gaps, opportunities, and recommendations". Leo welcomes feedback on which sections could be removed.
- Leo will add a summary of key messages up-front and will consider ways of condensing the background information.

Comments from discussion:
- There was agreement that Chapter 7 needs a clear direction especially on how to bring in patient involvement.
- Talia questioned whether the chapter considers patient involvement or patient view. At the moment, the chapter addresses how patients use data to facilitate their decision making in a clinical setting but there are also aspects on the use of patient data and the steps undertaken to integrate patients in an ethical way to obtain meaningful data for drug development. Acknowledging both ways of looking at the subject, and saying which view the chapter will focus on, might help with the scope and the framing of the chapter.
- Theresa recommended identifying the uniting theme within Chapter 7, and making Chapter 4 and 7 complementary as the content overlaps in places. Is Chapter 7 about real-world and observational data in the post-market setting? This has not been addressed in Chapter 4.
- Marilyn agreed and suggested Chapter 4 cover more the clinical trials side of drug development and up through the regulatory part and leave the real-world observational aspects to Chapter 7.
- Theresa suggested Chapter 7 could cover also patient-generated data - registry data. Some of the topics covered are not elsewhere and so need to be kept, such as data rights, data protection, sharing agreements, and data ownership.
- Judy suggested clarifying the nomenclature e.g. PASS (Post-authorisation safety studies), which is a European Union-centric term, whereas the intention was perhaps for a broader term.
- Judy asked whether the term RWE (real-world evidence) is limited to safety or does it apply to efficacy too? Patient input can be important and meaningful to both.

[2] Brodalumab assessment of hazards: a multinational safety (BRAHMS) study

- Does wearables data constitute patient involvement in the same way as patient-reported outcomes? At the moment the chapter is not so much about meaningful patient involvement but more about an array of different ways to collect data by patients in some places.
- Kawaldip felt that regarding wearables, switching them on is the basic patient involvement.
- Leo summarised that patients need to understand the value of their data and what it can do to advance medicine and safety. They need to be involved in the strategy and the potential going forward.

Chapter 8. Patient involvement in developing time-bound safety communications regarding medicinal products, presented by Stefan

- The chapter has been re-worked, including e.g. the safety communications scope. The team expanded Health Professions Committee (HPC) letters to include general time-bound, urgent communications to patients, with a mention about the different communication styles.
- The team incorporated a Covid-19 pandemic communication example, which can be applied to other pandemic situations too.
- There is a need for cross-referencing with the other chapters e.g. on additional risk minimisation measures and tools relating to communication and education, which can be time-bound in some countries.
- Stefan was grateful for Kerry's comments. These have been incorporated.

Chapter on guiding principles for patient participation in therapeutic decision-making: patient and public involvement in clinical practice guidelines by Corinna

- There has been little change since the previous chapter version as there were very few comments made.
- In light of today's discussion, Corinna will add a summary of the key messages and provide recommendations.
- The chapter sums up the different approaches to involving patients in clinical practice guidelines. The basis is more or less the work being done at the Guidelines International Network and so is based on international experience from different countries.
- Corinna re-worked the table on successful patient involvement to make it easier to understand.
- The chapter outline was composed in December 2019 and developed with the help of some WG members. The chapter is short partly to reflect how the main focus of the book is on patient involvement in the development and safe use of medicines, and less on clinical practice, this being more of an additional aspect. Corinna is open to feedback on desired changes.

Comments from discussion:

- François shared links on a project called Best Practices, which involved patients in developing and collecting rare disease guidelines: see here and here.
- Meredith found interesting the case study around the EnCoRe dynamic consent model, especially from the point of view of promoting active patient participation more broadly. Would this be a meta-message to bring out in the beginning and the conclusion of the document? How do we promote more active participation in medicinal product safety in general? It concerns changing the dynamics in the clinical encounter vis-à-vis the patients and pharmaceutical companies, and patients and regulators. Industry and regulators can become more patient-centred but we need patients to be more proactive.
- Elisabeth feels this is a matter of definitions and the patient voice guiding the work as appropriate.
- Lembit mentioned there are barriers and challenges for patient involvement. Some things are easier to change than others. Enablers and training can help patients to be more active and knowledgeable participants. Some patient organisations are better positioned.
- In the Netherlands, ongoing EUPATI training supports 16 patient representatives, providing them with knowledge and skills. Accompanying the trainees on visits to regulators, universities and pharmaceutical companies, helps them to gain confidence to speak up at meetings, write emails,

and pick up the phone, and feel they have an entrance. More work remains to be done to ensure patients that we want them to engage. The guiding principles chapter has already briefly addressed this. Lembit suggested adding some examples in the appendix.

- In the context of training and empowering patients, Corinna added that in the experience of the guideline panel, it is important to offer support and plan well when encouraging patients to be involved, taking into consideration specific requirements e.g. whether they can concentrate for five to six hours, and providing the means to help them attend. Achieving enablers is not only on the side of the patients but those who invite them. When evaluating processes, feedback shows patients rank this highly, as it helps them to feel appreciated and acknowledged.

Statement on patient involvement in pandemics (Covid-19) Statement and chapter by Stephen

- The subgroup has drafted a CIOMS WG XI Statement on the patient voice in the current pandemic and has circulated it for comments within the subgroup.
- The key message is we are in the middle of a pandemic; we are all patients (used the term "citizen patient"); the science and events are developing daily; there is variation in how mitigation is carried out in the various healthcare systems and countries, although we avoided speaking about governance.
- This is a unique situation where all healthcare providers, investigators, and people involved with clinical trials are also patient citizens. It is not "us" and "them" but "everyone together".
- There will be other pandemics and CIOMS has a chance to set guidance.
- The Statement will be proposed for publication in a journal.

Comments from discussion:

- Kerry asked if there will be an opportunity for learning through the pandemic e.g. with rare diseases. There is a lot of interest in accelerated access and collaborative approaches to drug development. Would this fit into the scope? Stephen answered no but that the ensuing principles will definitely impact rare diseases as there is an acceleration of informed consent.
- The conversations about the Statement have brought out the importance of "adhering to robust methodologies and responsible peer review in order to avoid decisions that could bring about dangerous public health consequences". Stephen quoted this from the Statement.
- Patients are keen to enroll in clinical trials, and patients have a voice, but the question is whether the system is protecting patient citizens in this accelerated drug/vaccine development.
- Lembit raised the question of whether during emergencies like Covid-19 patients could be more active partners and facilitate gathering certain data about the virus more quickly. We have not been able to benefit collectively from patient involvement to its potential.
- The draft chapter work will resume once we gain more knowledge on the pandemic. It will cover issues such as informed consent, ethics, public health processes, ongoing science, enrolling patients in broad clinical trials where most patients are eager to join e.g. a large phase IV trial.

Glossary presented by Stephen

- The glossary team requests for all chapter teams to provide their terms and definitions so that the whole WG can decide on their appropriateness for inclusion in the CIOMS WG XI Glossary.
- Marilyn provided the Chapter 4 terms and definitions already.
- Writers are requested to align with definitions e.g. in the EMA Glossary.
- The CIOMS WG XI Glossary will be expressed in plain English. The statistical terms will be translated into plain language where possible and Theo has accepted to help with some of these. If we cannot express all in plain language, we will simply keep the original definitions.
- There is a CIOMS Cumulative Pharmacovigilance Glossary (work in progress) to consult also if needed.

Comments from discussion:

- Talia offered to request assistance from her colleagues who review plain language documents, in the event that we are unable to express some statistical terms in plain language.

General discussion

Chapter on challenges and opportunities for patient involvement in resource-limited settings (RLS) by Lembit

- The chapter was not distributed as it is still work-in-progress but there is a draft, a small dedicated subgroup, and a Chapter Lead: Javier Hourcade Bellocq from Civil Society Sustainability Network/International Civil Society Support/Independent Consultant, Argentina.
- The next version is expected in mid-July.
- From CIOMS' perspective, it is clear that we need to have a chapter on RLS because circumstances can be very different.

Comments from discussion:

- Regina confirmed the chapter is progressing well. The team would welcome examples of initiatives on patient involvement in RLS from the WG.

Next meeting

- The WG was in favour of holding a virtual meeting in early September.
- Our next in-person meeting is provisionally scheduled for 20-21 October 2020, in Amsterdam, Netherlands, hosted by EMA. This will be confirmed at a later time, depending on the pandemic.