Council for International Organizations of Medical Sciences

8th meeting of the CIOMS Working Group on Patient Involvement

20-21 October 2020, virtual meeting

Minutes

Participants
Alison Bateman-House (Grossman School of Medicine, NYU Langone Health)*, Nathalie Bere (EMA), Stella Blackburn (IQVIA), Ton de Boer (MEB), Nikos Dedes (EATG), Juan Garcia (EMA), Charles Garrigan (Janssen), Linda Härmark (Lareb), Stephen Heaton (former Bayer), Sanna Hill (CIOMS), Shinji Hirasawa (PMDA), François Houÿez (EURORDIS), Stefan Kaehler (Celgene), Regina Kamoga (CHAIN), (Takeda), Talia Lacroix (Health Canada), Kerry Leeson-Beevers (Alström Syndrome), Marie Lindquist (UMC), Dinesh Mehta (EMA), Marilyn Metcalf (GSK), Theresa Mullin (US FDA), Rebecca Noel (Eli Lilly), Elisabeth Oehrlein (US NHC), Sten Olsson (ISOP), Shanthi Pal (WHO), Ravi Patel (United Therapeutics Industry), Peter Pitts (CMPI), Lembit Rägo (CIOMS), Theo Raynor (former Leeds University), Cheryl Renz (AbbVie), Leo Russo (Pfizer), Ken Sakushima (PMDA), Kawaldip Sehmi (IAPO), Meredith Smith (Alexion), Sabine Straus (MEB), Christine Stürchler (Novartis), Panos Tsintis (CIOMS), Jun Urushidani (PMDA), Pujita Vaidya (Amgen), Annemiek van Rensen (MEB), Jamie Wilkins (Pfizer), Manal Younus (ISOP), and Judy Zander (US FDA).

Absent members (including Alternates)
Leanne Angst-Wu (Roche), Patrick Beeler (Swissmedic), Fatima Bhayat (Takeda), Matthias Boedding (Merck), Marc Boutin (NHC), Wang Dan (CFDA), Ratna Devi (IAPG/IAPO), Mick Foy (MHRA), Yan Gao (NMPA), Beverly Harrison (Janssen), Javier Hourcade Bellocq (Civil Society Sustainability Network/International Civil Society Support/Independent Consultant, Argentina), Kaisa Immonen (EPF), Veronique Kugener, Hervé le Louët (CIOMS), Daisaku Sato (PMDA), Corinna Schaefer (WMA), Oi Tsunehiro (MHLW), and Peggy Webster (Takeda).

* New member since 7th meeting on 11 September 2020

NB: The Covid-19 pandemic put pressure on many WG members' time availabilities and some had to attend urgent meetings in parallel. Consequently, some presentations were delivered when convenient but have been reported here in a sequential order.

DAY 1: 20 October 2020

Welcome and opening remarks

- Lembit welcomed everyone and thanked them for their time.
- He mentioned Christine's comments on the previous meeting minutes regarding the WG's Covid-19 Statement and ongoing work on the Chapter 4 appendix.
- The meeting agenda was adopted.
- The latest version of the combined chapters document will be distributed after the meeting as further edits have been provided for Chapters 4 and 8.
- The deadline for submitting applications for the CIOMS 2020 annual student award for the best peer-reviewed scientific article published in the areas of pharmacovigilance and research ethics will be 30 November 2020.

Chapters overview

Chapter 1: Introduction, presented by Theresa

- Theresa has received suggestions for the introduction, and she will act on these once the other chapters have matured more, in order to accurately introduce the report.
- She is open to someone else taking over if the WG wishes, if more frequent updates would be helpful, but Lembit reassured that her approach is good.
- Theresa will be waiting for a word on when she needs to do her part.

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

- Elisabeth requested for help with vignettes on Australia, Korea, Taiwan, and a few other countries. These will need to be removed if there is no information or references available.
- She is satisfied overall about the good number of vignettes in the chapter.
- Elisabeth would welcome input on the safety landscape aspects as patient involvement in the safe use of medicines is not her area of expertise. Any additional insights, case examples, and/or important initiatives for inclusion would be appreciated.
- Regarding the part on future developments, she would appreciate receiving facts towards the key outstanding needs/issues to be addressed in terms of safety.

Comments

- Judith suggested referring to a vignette in Chapter 6 on Risk Evaluation and Mitigation Strategy (REMS). This is an example about how patients can impact on the safe use of medicines.
- Cheryl will also mention this cross reference in Chapter 6.
- At the editing stage, the two passages will need to be hyperlinked.
- Peter will make available extra information to Elisabeth.

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

- The actions from the last meeting have been addressed.
- The team considered options for adding key take-aways and recommendations, e.g. using the six higher-level principles as the key take-aways. However, not wanting to re-use the six higher-level principles as recommendations too, the team is open to suggestions on how to approach this.
- Otherwise Chapter 3 is ready for handover to the editorial team.

Comments

- Panos felt it would be helpful to list the six higher-level principles early in the report e.g. in Chapter 1 and perhaps at the start of Chapter 3, and then repeat them in more detail in the middle of Chapter 3. The list of principles will be a valuable element in the report.
- Annemiek proposed making use of the Chapter 3 key words across the other chapters too, thereby referring back to the Chapter 3 principles. It may be challenging to do this in a way that brings value to the reader. This may be for the editorial team to consider. It would be helpful if the Chapter Leads could make a note when the principles and key words feature in their chapters.

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

- Marilyn requested help with explaining the stages of clinical research and treatment development. The team has a number of suggestions, e.g. using EUPATI's approach, but has not reached a consensus. Marilyn assumes others may wish to reference this also and that it would be helpful to have a graphic in an appendix.
- [Post meeting comment: Marilyn shared the graphic from EUPATI on *Patient-friendly summaries of the drug development process* and the following links:

Drug development: the journey of a medicine from lab to shelf published in *The Pharmaceutical Journal*

The Drug Development Process by US FDA

Clinical Trial Phases by PennState Eberly College of Science]

- Alternatively, the different phases could be included as separate items in the glossary.
- The Chapter 4 team will be adding a section on the use of preferences.
- The chapter has also seen minor edits on definitions and to help to break up the text.

Comments

- Talia shared a link on Classification of Clinical Trials by the Canadian government.
- [Post meeting comment: Nathalie shared a graphic entitled "From Laboratory to Patient" from EMA.]
- François added that to help understand these phases, we refer to "proof of concept" (POC) studies (phase I and phase II), then "confirmatory" studies (phase III and IV), indicating a POC study can evolve to a confirmatory one. This is a useful classification, as important decisions are made at the end of the POC step; and even more important ones at the end of the confirmatory step. It also includes the fact that confirmatory studies take place after authorisation.
- Annemiek commented that Chapter 10 has good figures on the different phases of guideline development and explains the roles that patients could have at each phase. See Figures 1 and 2 of Chapter 10. This approach may apply to Chapters 4, 5, and 6.
- Ken suggested discussing simplifying the Chapter 4 diagram at 4.7.2. with Marilyn and she agreed. Christine supports this too.

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

- Meredith provided a short overview presentation of the chapter.
- Since September, the chapter team has added:
    - The description of requirements in Japan as per the input from PMDA;
    - A reference to *Health Canada's Expert Panel* in the Effectiveness of Health Product Risk Communication (2015) in the section describing sources initiatives to improve patient labelling;
    - A passage on the impact of Covid-19;
    - Table 1 – one final citation was added by Panos.

Comments

- Theresa - Regarding Chapters 5 and 6, as we enter the post-marketing phase, there is a focus on traditional communication, such as labelling/paper communication to the patient. While this may still be the regulatory basis for communication, we know that patients also use social media and see advertisements, as companies use other ways to communicate. To ensure that the document is up-to-date, it would be helpful have a short discussion about these other means of communicating information to patients, while preserving what was so carefully looked at in the labelling, to ensure that communication is still truthful and accurate, and not misleading, in these other media. Meredith said there is an extensive discussion of this in Chapter 5 under 5.3.4. Theresa suggested making it more visible. There is no need for a compendium of sources of information and ratings in terms of reliability and accuracy.
- As an example, Theresa appreciated in Chapter 7 the way there was a description of an opportunity with a source and some ideas of what could be done. It also gives some caveats and possible limitations. We do not need to say we are proponents of the others sources but we can just say what we know are being used. Chapter 5 gives a good historical context on how we got to where we are, and the regulatory parameters driving that. It is written in a more of a narrative form maybe and spends a fair amount of time on traditional approaches.

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

- The chapter is in its near-final version.
- The next step will be finalising the key take-aways, recommendations and conclusions.

Comments

- Please see Theresa's comments under Chapter 5 comments.

Chapter 7. Guiding principles for patient engagement in the development and use of safety and effectiveness data, presented by Peter

- The chapter has made good progress. Peter has consolidated the text, connected the various topics, improved the flow, and helped to walk the reader through the chapter; and Kaisa wrote some new sections.
- The team is currently drafting the conclusions.
- Linda is not sure if the team should write an executive summary at the beginning and recommendations/guidance at the end.

Comments

- Judith liked how Chapter 7 has evolved and how the role of the patient is introduced via the disparate sources. This chapter is somewhat unique given the many different methods and data sources. An overall introductory paragraph to link the concepts together would be welcome.
- Annemiek said this is an interesting chapter, as it refers to the various kinds of sources of data and how we can make use of them in patient involvement, but in some paragraphs, we need to take care that we do not reduce patient involvement to data handling. E.g. the key message does not fit well with sentences such as: "The 21st century patient voice can and must evolve into a tool used to impact regulatory decision making from both the heart and the head." Perhaps this is a matter of choosing the right phrases? In the context of patient preference, on the one hand, this is about using data that has come out of patient preference studies, but on the other hand, we need to involve patients in an active way on how to conduct the patient preference studies. This balance is missing in this chapter.
- Theresa said there is still a lot of content. It is improving, getting tighter; although some of the sections may still not be to do with patient engagement per se and could be considered for paring down further. E.g. using artificial intelligence and machine learning to comb through advert events reports is important to do but it may not be needed here.
- It may be useful to add some text on discussing rare disease populations because they are an important source of patient-generated information. These populations are some of the most active and motivated groups of patients. Increasingly, they are engaging in forming patient registries, which are important sources of data for characterising a disease. They are patient-owned and patient-managed data sources. There is a need to design these registries with the end in mind in terms of making them as usable as possible for the purposes of drug development, which the populations really care about and want from development. We need data sharing agreements for consenting patients, so that subsequently, their data are as readily usable as possible for research, modelling and simulation, trial designs and all the other activities we want to do to help advance rare disease drug development. There is information on data sharing agreements and related issues on e.g. the websites of the Center for Policy Analysis on Trade and Health (CPATH) and National Institutes of Health (NIH).

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

- The most recent updates result from addressing recently received comments.
- The next step will be to add the key take-aways and recommendations.

Comments

- Sanna proposed the Chapter 4 team's format for key take-aways and recommendations as a model for others to follow.

Chapter 9. Challenges and opportunities for patient involvement in resource-limited settings (RLS) by Lembit and Regina

- Javier had to stop drafting due to health reasons and Regina has accepted to write the chapter.
- She has just started incorporating comments received from the informal subgroup, which involves expanding the content and categorising and prioritising recommendations.
- Obtaining specific examples from different settings remains a challenge.
- Regina intends to share an updated chapter in two weeks. [Post meeting comment: Regina confirmed to deliver her draft on 6 November.]
- It may be necessary to arrange another meeting of the RLS informal subgroup.

Comments

- Sten expressed disappointment that this chapter is late. He feels Chapter 7 needs to link to Chapter 9 and hopes that the progress will follow.

Chapter 10. Guiding principles for patient participation in therapeutic decision-making: patient and public involvement in clinical practice guidelines by Lembit and Sanna

- The chapter is near completion and Corinna welcomes any feedback from the WG.

Comments

- Annemiek likes the chapter including its structure, finding it provides a good overview of the ways patients can be actively involved. She agrees the chapter is quite mature.

Chapter 11 and the Covid-19 Statement by François, Peter and Lembit

Chapter 11 on Covid-19

- The table of contents has been updated, such that it only contains elements on how patient involvement can impact on research, evaluation, and pharmacovigilance in relation to Covid-19.
- François can share the new table of contents if requested.
- The Chapter Leads were invited to highlight in their chapters passages which would have changed due to Covid-19 and particularly to reflect on three overarching questions:
    - What has changed in our practices due to Covid-19?
    - What have we learned? (to help us in this pandemic or in the next one)
    - Where is patient engagement going to help?

  The questions would ideally be answered from the following perspectives, when applicable:
    - Research aspects;
    - Evaluation aspects;
    - Pharmacovigilance aspects;
    - Real-time dissemination of reliable information and awareness;
    - Trust (vis-à-vis regulators, industry, learned societies), situations where it could have been harmed, and how it can be restored. (Or how Trust was reinforced, there are also some positive elements in this crisis).
- François will explore the potential for expanding the "patient" to "concerned citizen" element, or alternative phrasing.
- He is collecting representative examples of patient engagement during Covid-19.

Comments

- Annemiek suggested going over the principles in Chapter 3 and considering how they would apply to medicine research and development under Covid-19 conditions. The principles will guide thinking to identifying who e.g.:
    - Who is the patient we wish to involve;

- Which group does he/she represent;
- What is the agenda;
- What are the topics?

Using the principles would lend a good structure for covering all the elements.

The CIOMS WG XI Covid-19 Statement

- *Therapeutic Innovation & Regulatory Science* (TIRS), the official scientific journal of DIA (https://www.springer.com/journal/43441), has formally accepted to publish the CIOMS WG XI Covid-19 Statement in the form of a Letter to the Editor, with minor adjustments e.g. TIRS uses American English.
- The Statement was presented as authored by Peter and François.
- CIOMS is willing to pay to achieve open access status for the Statement.
- The next step will be for TIRS to provide the final proof to Peter for approval. Peter will share this with Lembit, and it will be distributed to the group. The date of publication online and in print remain to be confirmed. [Post meeting comment: the Statement was published on 27 October 2020 here.]
- CIOMS will consult with TIRS about any possible conditions pertaining to CIOMS publishing the original version of the Statement on its own website and in the CIOMS Newsletter.

Ethical considerations

- The WG welcomed the new member, Alison Bateman-House, who is an Assistant Professor, Division of Medical Ethics, Department of Population Health, Grossman School of Medicine, NYU Langone Health.
- Her speciality is research ethics and particularly access to investigational medicines, e.g. trial design; questions about what can be done in clinical research settings; and access to investigational medicines outside clinical trials, such as expanded access.
- Alison read two versions of the combined chapters document, dated 11 September and 19 October, and found them to be sound overall but with room for improvement by adding moral justifications.
- She presented her slides, of which the main points are here below:
    - Pragmatic rationales have moral components:
        - Utilitarian rationale – "do that which leads to the best outcome"
        - "Patient as partner" – equality (different from sameness)
    - Additional moral rationales to consider:
        - Beneficence – obligation to secure the well-being of persons (Belmont Report, 1979)
        - 2 general rules: (1) do not harm, and (2) maximize possible benefits and minimize possible harms
    - Respect for persons "incorporates at least two ethical convictions: (1) that individuals should be treated as autonomous agents, and (2) that persons with diminished autonomy are entitled to protection"
        - Propose another ethical conviction? – respect for persons means involving them as partners in drug development and research
    - Justice - who ought to receive the benefits of research and bear its burdens?
- Comments/feedback on the draft CIOMS WG XI combined chapters document from Alison:

  1) Shifts between speaking of the patient as participant/source of data and patient as consultant/guide
        - Example: compassionate use/preapproval access
        - Ethical principle of reciprocity plays out differently if you are reciprocating for participating in a clinical trial versus reviewing a document [post-trial

access + compensation + information about outcome of trial versus compensation]

2) Did not see much about patient role in funding/vetting of drug development effort/as sponsor

- Patient/family/patient advocacy funding of research (traditional, crowdfunding)
- Patient advocacy as shareholder in biopharmaceutical company
- Department of Defense's Congressionally Directed Medical Research Programs

3) Acknowledgement of ethical considerations of Chapter 7 (going to be covered in 7.8 "The patient's perspective")

- Consent
- Ramifications of data use (for example, stigmatizing patients as non-compliant)
- Ownership

Comments

On the subject of approaches to ethics in the biopharmaceutical sector

- Kawaldip highlighted two other approaches:
  - Oviedo Convention;
  - Mexico City Pharma Business Ethics Principles.

On the subject of consistency

- Marie proposed ensuring consistency in tone throughout the report regarding how we consider patients or explaining why we consider them differently in different chapters. Are they active subjects in charge, partners, or helpless victims of circumstances (passive, reactive, dependent), but useful providers of something we need?
- Marilyn proposed ensuring consistency/clarity also about the way patients are involved. Some are participants in clinical trials, some are asked about their experiences in clinical trials, and other are asked about trial design ahead of time. We need clear distinctions.

On the subject of grey areas

- Marilyn asked if in a spectrum of ethical discussions on patient involvement the exists some grey areas e.g. patient organisations that invest in the development of medicines. Are there differences in how patient involvement is perceived in medicines development? How should we frame such discussions? Are there key points and places to reference?
- Alison answered this is not an area that US ethics has debated but it may have been covered on the European side. She is aware of a concern that pharmaceutical companies may control patient organisations by funding them and perhaps thereby controlling them.

On the subject of the term "research participant"

- Alison said for the last 10-12 years in the US, in the ethics and Institutional Review Boards (IRB), i.e. the research and ethics community, there has been a battle over terminology. Many companies and patient groups use the term "research participant." It is felt that patients are integral to research and co-creators of data, and it is dehumanising and rude to call them "research subjects." However, the term "research participant" is suggestive of a happy situation, which is not always the case, because many patients involved in research are being used as a passive means of obtaining data rather than as a participant in any meaningful way and they really are a subject. Alison suggests reserving "participant" for e.g. community-sponsored / community-engaged research where there is a meaningful relationship with the patient community in designing the endpoints, planning the trial, as well as where and for how long it is to last, etc.

- Leo asked how we accommodate the notion that not all patients like to be active. Some patients are comfortable with just being subjects, and you have to respect that even though we like to aspire to the active patient.
- Alison answered that not all patients choose to participate in the same activity. At a Patient Advisory Board, the more active/outspoken patients will probably volunteer to help to design research trials, whereas the more passive patients, e.g. those who may prefer for their doctor/spouse to decide for them, will probably rather enrol in a clinical trial. There will be a process of self-assortment into active/ passive positions.
- In the WG report, there were a few comments along the lines that we should encourage patients or patient representatives to work with more than one pharmaceutical company to ensure they have multiple perspectives. Alison agrees with this but feels that the self-selected patients who are reviewing guidances and looking at website language, will end up differentiating from the more passive patients, such that they are not necessarily the best proxy any more. There are patient representatives who are unsuitable for certain tasks – e.g. a newly diagnosed patient who has never participated in a clinical trial before may not be best suited to commenting on a new patient leaflet in the way that a patient advocate who has participated in lots of roundtable discussions would be. It is possible to have a patient representative who is not suitable for participating for all purposes.
- Lembit said this is why we use the term “patient expert.”
- Alison said when she works with patients, she tries specifically to find a patient expert, who can advise on sources of power and connectedness in the patient community, and a naïve user, who can give feedback with fresh eyes. We always need to find both.
- Leo said the term “professional patient” is found pejorative by some patients, but not by all.
- Theo said some use the term “real patient” in contrast to “expert patient.”
- François mentioned how in the report, we have a 360˚ observation of patient roles, from the patient as the recipient of care, as a source of data, a consultant, a funder of research, and developers of medicines. Perhaps we focused more on the frequent roles (recipient of care, source of data, consultants) and we may have overlooked some of the roles? There are cases of patients creating their own pharmaceutical company and successfully marketing the product; or others who funded research and then partnered with industry for the same positive outcomes. There are not many such examples in the report maybe mainly because the objective is to draft a universal guidance and it is inappropriate to focus on limited experiences. However, recently the EMA changed rules on conflicts of interest for patients to recognise the role of patients as medicine developers.

On the subject of “benefits and harms” versus “benefits and risks”

- Theo asked about the difference between “benefits and harms” versus “benefits and risks”. He felt “risk” is a less direct and forceful term. Should we be using “risk” in the report?
- Alison answered that for her, “risk” is more biomedical/physical or clinical e.g there may be a risk of increased heartbeat or anaphylactic reaction. “Harms” are broader and can include e.g. the opportunity cost incurred in participating in research; having to go to hospital for monitoring every two weeks and missing life events and/or work opportunities; and if following research, people think of a patient community as non-compliant. There are many harms that are not biomedical/physical in nature.
- Marilyn added that with “harms” we tend to think of things that do happen whereas “risks” are more probabilistic.
- Alison said she typically speaks of the possible risk of harm and the possibility of benefit(s)– it is not guaranteed in either case.
- Marilyn mentioned that under "acceptable risk" in Chapter 4, there will also be a reference to benefit-risk and preferences from the patient's perspective.

On the subject of data ownership and legal matters

- François said that ethical aspects, e.g. on data ownership, may need to be complemented with legal aspects because, e.g. in Europe, the concept of data ownership does not exist legally; nobody owns data. It is part of the extrapatrimonial law. When you die, no one inherits your data. There are people who can control access, but the concept of data ownership does not exist.
- He went on to talk about the moral aspect of patient involvement, e.g. soft justice, and the importance of consulting with and involving all stakeholders in decision making, which is even more important when evidence is weak. This was developed and published by Noman Daniels and other authors in the US. This is another important reason why patients should be involved in the development and evaluation of medicines.
- Lembit commented that in some jurisdictions health data is owned by the patient. In some countries, you can limit/withdraw data access from anyone and access who has approached your data. In some countries, there is legal regulation on patient ownership and rights on their health-related data.
- François agreed that data rights, access and control are regulated, and more and more patients can control this access, but this does not mean that the patient owns his/her data.
- Lembit added that good governance of data is an important element that some patient groups advocate for. However, many patients do not feel the need to be involved in discussion about how their data may be used provided that there is good governance. There can be unnecessary blocks to research which can be harmful for the patients in the long term. It is a matter of balance and setting the controls right.
- Alison agreed it is enormously complicated to get this right. It is one thing to say we have data from a national health service (huge and anonymised) but quite another to say we have an ultra-rare patient organisation and we want our own registry and we have 10 people. Even if the data is anonymised, we can tell which data goes with which patient.

On the subject of how to include ethical considerations

- Many different options were considered and some of the points raised included:
    - The passages relating to ethics need to be written by an ethicist to prevent each contributor from putting in their own belief into the text;
    - It will be important to present some of the ethics principles and how they may apply, such that readers will be able to apply them as new situations / future directions / interpretations arise;
    - The ethical considerations are their own concept. We do not want the ethics questions to conflate with the key take-aways from the chapters;
    - The ethical principles will apply more weightily to some chapters e.g. pharmacovigilance;
    - It would be helpful to have a stand-along piece on ethics early in the report so that it can be applied in a consistent manner throughout the other chapters;
    - Writing the ethics chapter first would allow each Chapter Lead to efficiently review how it can apply to their subject;
    - Formatting-wise, we could have a bubble at the top of each chapter for ethical considerations – an ethical snapshot for the chapter.
- Alison's advice was to have a short chapter, which lays out the principles, and a paragraph in each of the other chapters providing the relevant points for the topic in question. This was welcomed widely.
- Alison accepted to try to draft a short chapter for the second week of November.
- Christine suggested adding some ethics vignettes to the chapters where possible.
- Dinesh suggested placing the ethics chapter as Chapter 3 or 4.
- Talia suggested that once we see the proposed chapter, we can still reconsider whether it would fit best as a part of the introduction.

DAY 2: 21 October 2020

Glossary team

The CIOMS Cumulative Pharmacovigilance Glossary by Stephen

- The task was to gather the terms and definitions from the CIOMS pharmacovigilance reports through time and prioritise the most recent and viable definitions. We wanted to provide a historical perspective on how CIOMS has progressed and how the science behind CIOMS has evolved. The document will go on the CIOMS website as a living document, which will get periodically updated as more CIOMS reports are published. The most recent CIOMS report terms, on Drug-Induced Liver Injury (DILI), will be integrated into the glossary too.
- Stephen invited the WG members to go through the document and feedback.

Comments

- Stella feels some of the definitions are incorrect, and given that we are trying to make it publically readable, she has re-defined some of them and would like to put them in as the CIOMS WG XI report glossary is added.
- Stephen is not sure about this as some of the terms in question do not fit into the patient involvement subject area. He proposes including the revisions in the cumulative glossary as comments.
- Talia agrees that any terms we add must be in our scope as a WG.
- Lembit sees no problem with updating the cumulative glossary definitions as we have said it will be a living document. When there is new information and/or science to support change, we need to update the definitions.
- Dinesh made two points:
    1. Perspective: every dictionary, glossary etc has a perspective. CIOMS may approach its work in different ways in its different documents, and the perspective will change. We need to be careful that when we cast one particular description that we do not undermine what any particular group might have been thinking.
    2. Description: the term “description” is looser than “definition” and it allows us to just make sure that it fits the case that we are talking about. If we try to define things, then we have to think about every little case that needs to be included.
- Marie added that there are ISO rules for definitions and many of the definitions we see are not created according to those rules. She agrees that “description” would be a more loose and accommodating term to use.
- Peter said once the glossary goes online, we could offer a place where visitors can propose their opinions and possible edits.
- Lembit agreed this would be quick and easy to do. We would also need to add some disclaimers as this work will be continuing and there is value in making the group’s work available as a resource.
- Judy suggested reflecting on the governance aspects of how the glossary is going to be maintained and updated. What if two WGs are working on the same concept and disagree? Will there be a glossary board?
- Lembit agrees we will need to form a team for this purpose, which may also include members from other CIOMS WGs.

The CIOMS WG XI Glossary by Stephen

- This glossary is patient-centric and for the current guidance document.

- The terms and definitions we use in the report must match throughout the report. We need to achieve alignment as inconsistencies will reduce the value of the work. Stephen asked the Chapter Leads to take care over this.
- Stephen thanked the Chapter Leads who have submitted terms and definitions from their chapters.
- Stella made the point that the CIOMS Cumulative Pharmacovigilance Glossary is up to date with the latest definitions but the WG XI glossary is lagging behind and needs updating.
- Regarding the discussion over the definitions on "patient," "family caregiver," "patient organisation," and "patient engagement," - there is bias and this needs further discussion.

Comments

- Regarding the discussion over the definitions on "patient" - this is probably one of the most important definitions in the glossary.
- There were many viewpoints raised before and during the meeting on the definitions on "patient," and these will be collated in a separate document, but some of the salient comments raised at the meeting were:
    - There are a lot of definitions possible, depending on the perspective and what we want to achieve;
    - The definition has to fit to our purposes;
    - A lot of the arguments for why patients bring a particular expertise are because they have experience with a disease/disorder/condition - that is contextually the background for this document;
    - There are legitimate reasons to involve people who are at risk of a disease/condition or might get a vaccine, but they are not able to report as an expert who is living with the disease;
    - A too broad definition will not be helpful, e.g. anyone who has, has had, or will have a medical condition;
    - The patients' relation to the healthcare provider and the healthcare system are not key;
    - We need to be careful to not undercut some of the assertions in the report text;
    - This discussion has an ethical dimension too and we may need to link to Alison's chapter and tie in with the discussion about "experienced patient or not" and "patient representative or not."

The Patient Community Matrix by Stella and Elisabeth

- The matrix diagram was developed following conversations among the glossary team members and was based on the NHC patient engagement rubric. Using a visual helps to make it clear.
- The NHC used its own version for discussing the patient community, e.g. to refer to which parties from the patient community would engage in which activity.
- Some of the definitions for "patient" in the field can include entities such as "family caregiver" and "patient organisation," and it was felt we needed to split the term in order to distinguish between the person who has/had the disease and the other people i.e. the "family caregiver" and the "patient organisation."
- Other people, e.g. the "family caregivers," may have a different perspective than the "patients."
- We could use the term "patient community" when we want to include everybody.

Comments

- Regarding the term "family caregiver," there were several alternative suggestions: "caregiver," "informal caregiver," "non-professional caregiver," and "non-HCP care giver."
- Kerry mentioned we also need the term "patient representative."
- Elisabeth's only concern with the matrix is that, because it is a circle, it looks like the "patient" is a subset of the "family caregiver" community, which is a subset of the "patient organisation."

We would need to think of a way to present the information so that it does not look like a Venn diagram that is on top of itself.

- Marilyn suggested having a pyramid-like visual. Ideally, the patient would be making choices themselves, but if for whatever reason that is not appropriate, then it would come to the next level/ hierarchy with closeness to the patient.
- François suggested using overlapping shapes with intersections as people can be both a member of a patient organisation and a patient; or a patient representative and a patient; or not a patient representative but still a member of a patient organisation and a caregiver.
  At EUPATI, we have:
  - "the patient" - someone who has a disease;
  - "the patient advocate" - someone who advocates to represent that person;
  - "the patient expert" - someone who has expertise of the disease but also the knowhow to interact with different interested parties e.g. regulators, industry players, and project managers.

  Maybe we can have different matrix/graphs to illustrate the complexity of the topic. There is not a single definition or approach to presenting, or even a perspective.
- Stella felt it would be best to try to keep it as simple as we can, although she agrees people can be in lots of different categories. The aim is simply to represent the different elements.
- Annemiek will share a diagram with overlapping parts that is used at MEB training.

On the subject of patient organisation legal statutes

- Talia questioned whether a patient organisation must be not-for-profit.
- Elisabeth said this is a hugely important distinction. In the US, there are groups based in lobbying offices that are 100% industry-funded with a particular mission, and as such, they are not considered to be patient groups. At least in the US, there is a need to differentiate between real patient groups that have a mission to improve the lives of patients versus groups that are often not not-for-profit and have some sort of other agenda.
- François added that there are also different legal statutes, e.g.:
  - In the UK, there are for-profit organisations that are charities (the organisation can make profit and re-invest their profits as they wish, but the trustees or the board members cannot enrich themselves. It is a for-profit organisation but different from a usual business);
  - In the Netherlands, there are foundation with no elections, no General Assembly, no members, and they can be for-profit (can be authorised to receive payments for running the foundation).

  In different jurisdictions, there are different definitions and statutes used by different types of patient organisations: some are not-for-profit and some are for-profit. In the for-profit sector, we can also distinguish between those where people can receive funds and those where it is not possible.
- Dinesh pointed out that there are also patient groups that are not-for-profit but which are heavily funded, and potentially influenced, by pharmaceutical companies.
- Nathalie said being fully funded by industry does not mean that patient organisations do not have patients' interests at heart. They need to be transparent and funding needs to be spread among several companies. Many patient organizations receive support from industry but are not rooted in a company. Statutes should state that individuals cannot make a "profit" personally.
- Marilyn added that there are also patient organizations that are for-profit-based according to the services they provide but that are not funded by any one organization. There are also funding structures through unrestricted grants that are designed to maintain independence.
- Elisabeth shared a source of good operating practices.
- François said a work-able definition of a patient organisation is:
  - Criteria 1: an association of individuals who elect their governing bodies, the majority of whom should be patients or carers. The election aspect is important because there are

some foundations which do not hold elections - there is a board of funders but no elections.
    - Criteria 2: the governing body members (board of trustees and board of directors) do not receive revenue for serving the organisation. The organisations can have paid staff.
- Stephen questioned whether this subject has been covered sufficiently in the report. It is always coming up with industries and agencies and touches on ethics. It needs to be more than a glossary item.
- Annemiek confirmed that there is a guiding principle on this in Chapter 3 but Stephen was not sure if this would be enough.
- Talia questioned whether the terms could be changed to "patient advocacy organisation," such that it focuses only on the patient and the disease rather than the industry element.
- Elisabeth answered that it depends how complicated we want to get. The NHC has 38 different good operating practices for patient organisations, mostly about transparency of funding and programmatic efforts. This is an important discussion that Chapter 3 already addresses, citing principles and good governance practices. As part of a definition, it is important that there are some distinctions between a "patient advocacy group" or a "patient organisation," and at least in the US, it should be a not-for-profit organisation. There are certainly a lot of other great groups that do a lot of work on behalf of patients and that are not not-for-profit organisations.
- Lembit concluded that regarding the definition, the not-for-profit principle is an important distinction in most jurisdictions and we need to consider how to better reflect it, in addition to the guiding principle and mention in the glossary. The patient organisations need to follow good governance principles and there are some legal nuances related to non-profits.

Editorial team

- Lembit confirmed that the editorial team currently includes: Annemiek, Cheryl, Dinesh, Elisabeth, François, Meredith, Panos, Stella, Stephen, and Theo.
- The WG discussed switching the bulk of the work from the full WG to the editorial team. This approach will hopefully be more constructive at this stage and not take up too much time from all the WG members. The full WG will continue to be involved nevertheless as the editorial team will still most likely consult with the chapter teams. The full WG will be kept updated about all major decisions.
- The following approach was tentatively agreed:
    - The editorial team will meet and agree on guidance for the chapter teams, including a checklist and possibly even a loose template;
    - In parallel, the chapter teams will finalise their content, including the key take aways and recommendations;
    - The chapter teams will be given a deadline, e.g two weeks, for finalising their content, using the checklist and maybe a loose template;
    - The editorial team will focus on the organisation of the full report, aligning the structure and formatting;
    - The resulting full report will be shared with the full WG for review;
    - The full WG will reconvene virtually to discuss;
    - The full report will be updated (maybe around March 2021?);
    - Public consultation.
- Stella felt this would perhaps be too ambitious.
- In terms of the report structure, there was support for starting the "pre-autorization" phase after Chapter 3.

Implementation team

- Talia said the team developed a draft document and discussed the scope of the task.
- The team's comments are currently being integrated and the draft will be shared with the full WG for feedback, finalised, and handed to Lembit.
- There was a short delay due to Talia's unexpected leave.

Concluding remarks

Lembit thanked all for their time and warmly commended everyone for their contributions.

Working group structure

In the table below, the Chapter Leads are in bold.

Group 1 **Chair: Juan, co-chair: Kerry**					**Group 2** **Chair: Meredith, co-chair Stefan**						
Ch. 1	**Ch. 2**	**Ch. on Ethics***	**Ch. 3**	**Ch. 4**	**Ch. 5**	**Ch. 6**	**Ch. 7**	**Ch. 8**	**Ch. 9**	**Ch. 10**	**Ch. 11**
Theresa	**Elizabeth**	**Alison**	**Beverly**	**Marilyn**	**Meredith**	**Cheryl**	**Leo**	**Stefan**	**Regina**	**Corinna**	**Stephen**
	Talia		Charles	Becky	Ton	Stephen	Linda	Linda	**Shanthi**		**François**
	Theresa		Matthias	Christine	Panos	Leanne	Kaisa	Marie	Lembit		Fatima
	Shanthi		Annemiek	Theresa	Patient rep. to review	Peter	Peter	Sabine	Ratna		Lembit
	Kerry		Regina	Kerry		Judy	Elizabeth	Ravi	Manal		Meredith
	Ken			François		Stella	Ravi	Elizabeth			Nathalie
				Pujita		Nikos	Manal	Fatima			Panos
				Kaisa to review		Jun	Patrick	Kerry to review			Peter
						Shinji					Ton
						Jamie					
Glossary team **Stephen** Elisabeth, Panos, Sanna, Stella, and Pujita											
Implementation strategy team Christine, Elisabeth, Meredith, Peter and Talia											
Editorial team Annemiek, Cheryl, Dinesh, Elisabeth, François, Meredith, Panos, Stella, Stephen, and Theo.											

* The placement of the Chapter on Ethics was not discussed. It has been added after Chapter 2 as a starting point and this can be confirmed/changed at a later date. For the time being, the chapters numbering has not been changed.