Council for International Organizations of Medical Sciences

5th meeting of the CIOMS Working Group on Patient Involvement

1st April 2020, virtual meeting

Minutes

Participants

Leanne Angst-Wu (Roche), Patrick Beeler (Swissmedic)*, Stella Blackburn (IQVIA), Ton de Boer (MEB), Ratna Devi (IAPG/IAPO)*, Charles Garrigan (Janssen), Linda Härmark (Lareb), Stephen Heaton (former Bayer), Shinji Hirasawa (PMDA), François Houÿez (EURORDIS), Stefan Kaehler (Celgene)*, Talia Lacroix (Health Canada), Marie Lindquist (UMC), Marilyn Metcalf (GSK), Theresa Mullin (US FDA), Izumi Oba (PMDA), Elisabeth Oehrlein (US NHC), Sten Olsson (ISOP), Ravi Patel (United Therapeutics Industry), Peter Pitts (CMPI), Theo Raynor (former Leeds University), Cheryl Renz (AbbVie), Ken Sakushima (PMDA), Kawaldip Sehmi (IAPO), Meredith Smith (Alexion), Sabine Straus (MEB), Christine Stürchler (Novartis), Pujita Vaidya (Amgen)*, Annemiek van Rensen (MEB), Manal Younus (ISOP)*, Judy Zander (US FDA), and Sanna Hill, Lembit Rägo, and Panos Tsintis (CIOMS).

Absent members (including alternates)

Fatima Bhayat (Takeda), Matthias Boedding (Merck), Marc Boutin (NHC), Wang Dan (CFDA), Nikos Dedes (EATG), Mick Foy (MHRA), Juan Garcia (EMA), Beverly Harrison (Janssen), Kaisa Immonen (EPF), Regina Kamoga (CHAIN), Veronique Kugener (Takeda), Kerry Leeson-Beevers (Alström Syndrome), Isabelle Moulon (former EMA), Rebecca Noel, (Eli Lilly), Shanthi Pal (WHO), Leo Russo (Pfizer), Daisaku Sato (PMDA), Corinna Schaefer (WMA), Martina Schäublin (Swissmedic), Naomi Siakpere (IAPO)*, Kristina Star (UMC), Oi Tsunehiro (MHLW), Peggy Webster (Takeda)*, and Hervé le Louët (CIOMS).

* = new member

NB: The Covid-19 pandemic put pressure on many WG members' time availabilities and some had to attend urgent meetings in parallel. In addition, there were some technical challenges, perhaps due to a vast number of virtual meetings taking place globally at the same time. Consequently, a number of comments were submitted after the meeting and have been added in the minutes in square brackets. Similarly, the order of subjects discussed in practice did not follow exactly as reported.

Prior to the meeting

- The minutes of the 4th WG meeting held in Basel, Switzerland during 16-17 October 2019 were approved by absence of comments.

Welcome and opening remarks

- Lembit welcomed everyone and thanked them for devoting their time during the difficult Covid-19 pandemic.
- Although in-person meetings can probably achieve more, it is helpful to be able to continue advancing using modern technologies, such as Zoom video conferencing, in the meantime.
- The combined chapters offer a good overview of where we stand including where the gaps are.
- All CIOMS working groups have been postponed and we hope to be able to schedule face-to-face meetings again around August – September 2020.

Meeting management
- Sanna mentioned some practical matters, such as using the video option and muting microphones, and recommended the Gallery view on the Zoom interface.
- She passed on apologies from working group (WG) members who were unable to attend.
- The agenda was adopted, and it was also agreed that participants would be able to leave to join outside meetings if needed and return when possible.
- Sanna to draft the minutes.

Issues that touch on all aspects of the working group

Brief presentation on recent initiatives
DIA Annual Canadian Meeting, 5-6 November 2019, Gatineau, Québec, Canada, presented by Talia
- This was the first plenary session on patient involvement, which is still largely a new topic in Canada.
- A three-person panel featured Health Canada, FDA, and a patient representative, and presented patient involvement from their perspectives, followed by a broader six-person panel discussion.
- The Health Canada panellist gave an overview, helping to define what is meant by 'patient involvement' in the context of drug development; discussed some of Health Canada's past patient involvement; and then spoke of the future direction of patient involvement, primarily of international collaborative initiatives. The Canadian post-election transition period limited the ability to speak about specific policy or future direction being considered.
- The US FDA panellist provided some real-world examples of how patient involvement can be integrated into regulation, various patient-centred legislations and programmes.
- The patient representative spoke of her work with the Canadian Arthritis Patient Alliance, the Clinical Trials Ontario organisation, as well as the global Patient Focused Medicines Development (PFMD) initiative. The PFMD in Brussels creates different tools including an online Patient Engagement Quality Guidance tool, which provides different streams for different stakeholders.
- In addition, the patient representative mentioned the Clinical Trials Transformation Initiative (CTTI) in the USA and an initiative to adapt it for the Canadian context, recognizing system differences between the two countries.
- Talia suggested that the CIOMS guidance implementation plan should consider expectations on WG members and how each is going to promote the guidance at their organisation internally, so that the ripple down effect will help to create a good patient engagement culture.
- Talia's article, published by DIA Canada, giving a high-level snapshot of the plenary session: *Patient Experience: What Is It, Where Is It Now, And Where Is It Going?*

PCWP/HCPWP joint meeting 3-4 March 2020, Amsterdam, Netherlands, by Lembit and François
- For many attendees, this was the first time they had seen a presentation about CIOMS' work overall and in particular about the CIOMS Patient Involvement initiative.
- Lembit made a presentation about the CIOMS WG XI guidance in progress. Kaisa and François gave the audience additional explanations and helped to answer the questions.
- It was well received and met with interest and requests to join the WG.
- Lembit explained that joining at this stage would be difficult as the WG is already very large, but that the online public consultation stage will be an opportunity for others to contribute. He encouraged interested parties to read the meeting minutes and voice suggestions and/or concerns at any time.
- The event attendees supported the public consultation opportunity, are favourable to participating in the guidance dissemination, and eager to put the new guidance into practice.

- Most patient organisations will be interested in advocating for more patient involvement or for enhancing the quality and dialogue of existing involvement.
- There was appreciation for gathering experiences from different regions of the world and the fact that the guidelines will be broad, addressing many different aspects of Patient Involvement.
- Some of François' main points from the meeting were:
  - It will be important to not accept complacency: sometimes companies have patient involvement methodologies that do not reflect what patients would like. Some governments or institutions impose the way they want to interact with patients, e.g. creating a position on an advisory board, but without an intention of making changes.
  - The ultimate goal needs to be to co-define the rules of engagement between a patient organisations and an interlocutor (agency or company), both regarding principles and eligibility criteria, or the methods for engagement, in accordance with principles of deliberative democracy and health democracy, in order to achieve a higher level of engagement, mutual respect and understanding.
- Lembit's presentation and François' presentation can be found on the event home page on the EMA website.

Ethicists' perspective
- Despite Lembit's best efforts to get ethicists involved, due to the cancellation of the face-to-face meeting, the logistical arrangements did not work out.
- He will next aim to organise a virtual meeting with a small group of ethicists.
- Given the advanced chapters at this stage, it seems challenging to integrate the ethicists' contribution. It may be best to plan to add a separate section in the guidance or an appendix.
- Some of the ethicists felt the subjects the WG is interested in are not really matters of ethics, and that joining may not be a good use of their time.
- Lembit will keep working on this and apologises for the delay.

Comments from discussion:
- [Comment added later: Christine: Do we have a clear understanding of what we expect from the ethicists? She suggested that each Chapter Lead works with his chapter team to define their needs e.g. a few bullet points.]

Practical steps in the report production process

Graphical representation
- The WG members are encouraged to specify what visuals are required and the CIOMS Secretariat will engage the services of a graphic designer to deliver these.

Editorial team
- Once the draft is more mature, a group of WG members will form an editorial team.
- At the moment, some chapters are still in note form i.e. the Resource-Limited Settings chapter.
- [Comment added later: Meredith brought attention to how the length of each chapter varies widely, from under 10 pages to over 30. Is there some value in setting a suggested page limit for each chapter, such as between 10-15 pages? That might improve the readability of the document.]
- [Comment added later: Talia mentioned that if something needs to be said, then there should be space to say it. However, some chapters are very long and were easy to get lost in. They will need to be streamlined and condensed. This will likely occur naturally, as the guidance develops, as working tends to get tighter the more chapters are worked on.]

Public consultation
- The expectation has been set externally for holding a public consultation.
- There will be a reasonable time frame for people to comment.

Chapters overview

Chapter 1: Introduction, presented by Theresa
- Previously, Theresa's approach was to wait and see how the other chapters mature but now seems a good stage to re-draft the copy.
- The introduction will reflect the motivation, the key audiences (patient groups, drug developers, regulators, and maybe others), and present the opportunities for engagement, improving and informing drug development, and post market safety etc.

Chapter 2: The landscape of patient engagement in the development and safe use of medicines, presented by Elisabeth
- The chapter format has changed and some parts are in note format.
- Special thanks to Talia, Annemiek and François for submitting content and reviewing.
- There are now several good international examples and Elisabeth has added a few vignettes that describe the emerging role of patient engagement across regulatory agencies, including some relating to safety issues.
- Here are the collected case examples: https://nhcprod.wpengine.com/patient-focused-medical-product-case-examples/
- Elisabeth requested the WG to send in patient engagement examples that relate specifically to safety and to patient involvement in low- and middle-income countries.
- She has sent questions to individual WG members regarding her chapter and requests for responses over the coming one or two months.
- Chapter 2 is very long and Elisabeth will be removing content that duplicates in Chapter 3.
- Any information added will be on the subject of safety, patient involvement in low- and middle-income countries, and references.

Comments from discussion:
- François suggested adding the below examples, which are interesting particularly because they allow comparisons of different methods:
    a) Sodium valproate in Europe, and maybe in other parts of the world. There were focus groups of patients and other experts, with written consultations and a public hearing at the EMA. The EMA is due to release a report within weeks on the various contributions via the different methods and what was learned. Annemiek added to this that from the PRAC discussion there was a follow-up to the national regulatory authorities. It went from patient involvement at a European level to implementation at a national level, and it involved patient organisations at both levels too, albeit in different capacities. [Comment added later: Panos recommended approaching Sabine for input in the context of the vignette on PRAC.]
    b) The European Multiple Sclerosis Platform (EMSP) contributed to the suspension of a drug due to reports of serious inflammatory brain disorders worldwide. EMSP was engaged with the regulators and the pharmaceutical company, and questioned the patients directly regarding how they weighed the new risks and whether the product should be reintroduced or not.
- François can offer further references if needed.
- [Comment added later: In response to Elisabeth's question on page 17 of the combined chapters ("is there a PRAC patient involvement vignette to include?"), Panos suggested including the EMA's formation of the Patient and Consumer Working Party.]

- [Comment added later: Panos also suggested adding a vignette perhaps regarding Bayer on the use of a patient safety communication group. Stephen would be able to provide more details.]

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

- Since the meeting in Basel, the Chapter 3 team re-focused the chapter on the key overarching principles for patient engagement and reduced the operational considerations originally intended for inclusion. The team found it difficult to include all the operational considerations and make them applicable to the CIOMS stakeholder members / target audiences.
- The chapter team, and especially Annemiek, scanned the 15+ available codes of practice and policy documents from various stakeholder groups (patient advocacy organisations, regulators, industry organisations, public-private partnerships, etc) that contain principles for patient engagement. They identified overlapping and similar principles for inclusion, having found a large degree of overlap and consensus, despite differing focuses and terminologies.
- The new chapter outline was reviewed by Elisabeth, François, Theresa and Isabelle.
- The chapter team would like to confirm with the WG XI whether they are in agreement on the choice of principles.
- The team also asks WG members (specialists in the field) to volunteer to write/work on specific principles.

Comments from discussion:
- The careful work of reviewing, collating and synthesising the existing principles needs to be described as this is an important step and adds weight to the guidance. Readers will want to know where the principles came from and how the team distilled these particular ones.
- This work could springboard to the public consultation.
- Talia mentioned the copy is a little fragmented. It would be helpful to group the principles under common headings e.g. the principles of transparency, then provide the sub-sections underneath, and lastly, the specific recommendations or ways in which the principle is instituted in this context. She provided for consideration some links in her comments within the compiled chapters document on how the Canadian regulators have done similar things. She feels headings would help to focus on the broader picture and the intellectual flow. Talia identified the following headings: Clarity and transparency, Meaningfulness, Equality, and Independence of participation, based on the principles identified in the draft guidance. Charles said it may be easier to discuss this directly. He said the team has tried five to six different reiterations of groupings like Talia describes.
- Talia also said that capacity building is perhaps not a principle but more to do with transparency / issuing information, and other chapters have mentioned it.
- Theresa suggested the principles section would benefit from specific examples of good practice, or practices that are not in alignment with the principle. Charles agrees and invites the WG to email him related examples. Annemiek added that they are also interested in examples that would help to make the guidance applicable to all the audiences.
- François recommended a Delphi-like process to help reach consensus on the principles. Charles and Annemiek agreed that this method would allow for everyone's voice to be heard but are concerned over timelines. Annemiek would prefer to not have too many principles. There are five at the moment. She would rather like to hear from the WG whether these are the right topics, and whether they are worded in an acceptable way.
- Annemiek elaborated on the subject of wording that some of the principles focus on specific stakeholders and the chapter team would like to ensure the principles apply to all audiences equally.
- Panos felt the chapter is a little word-heavy and it may be easier to give a list of concepts that have to be part of the principles. This may help it to be more memorable for different audiences.

Chapter 4. Patient involvement in advancing treatments for their disease, presented by Marilyn
- The earlier version of Chapter 1 had a lot of information about drug development, and now that the chapter will be re-drafted, Marilyn would like to bring this back to Chapter 4.
- Thank you to Christine, Kerry, Theresa and Isabelle for contributing a good amount of writing.
- Marilyn recommends keeping the table with chevrons in Chapter 4, and that it be left intact. There had been some attempts to divide it up into sub-tables but the feedback suggests this is more confusing. Using the table intact will allow readers to find what they need and navigate through the document easier.
- There had been some discussion about whether the table should be made general or specific, and it seems there is a preference for it to be specific, in order to bring forth the examples and links.
- There is also a circular chevrons infographic, which communicates the iterative process, where some of the sections, e.g. communication, happen throughout the life cycle. Marilyn will draw this and it will be placed towards the start of the chapter. The circular infographic will effectively then be "rolled out" as the chapter progresses.
- Regarding the editorial smoothing and comments from WG members, there have been some suggestions to remove some of the examples and that is fine.
- Marilyn is happy to work on the comments from the WG members, but suggested that from this stage onwards, members provide text edits rather than comments.
- Marilyn would like to get all sections of the chapter to their correct places, and she is pleased to include content on e.g. paediatrics, and then she would like to work on the text more, remove redundancies, help the paragraphs fit together better, and improve the flow.
- She would like to make sure we have permission to use illustrations, tables and graphics from other sources. Please confirm this in the text.
- At times, Marilyn was not sure whether illustrations were included simply to demonstrate to her what was meant or whether they were intended for printing in the final report. Please clarify.

Comments from discussion:
- Theresa supports the use of the circular diagram and unrolling it and continue on with the table. The table presentation will be very effective for the handbook approach for the readers.
- Annemiek questioned whether some of the content elsewhere in the guidance should be moved to Chapter 4, e.g. some of the content in Chapter 7 is not only about the post-marketing time. There is content on specific methodologies for involving patients, and a sub-section on agenda setting and prioritisation, and these would fit better in Chapter 4 because it concerns the beginning of the life cycle. Marilyn will cross-reference and make sure that Chapter 7 can also still refer to it if needed, if we want to move some of that guidance.
- Annemiek wondered whether we have a toolkit section on methodologies. This could guide the reader on when to ask what and from which kind of patient / patient representative / patient organisation, with regard to specific roles and settings. It could refer to selecting the right patient, methodology, and the right moment within the life cycle. Marilyn is aware of other guidances being developed on this kind of approach and she will reference these.
- Annemiek also mentioned that in general when you look through the first part of the WG XI guidance, the first part focuses on the collective input of patients, whereas the second part focuses on the risk communication and risk minimisation, and is much more about the individual patient input, i.e. about generating data about individual patients. It seems sometimes this comparison between the collective and the individual gets lost and we may need to address it.
- [Comment added later: After reflecting on the guidance chapters, Talia emailed Marilyn after the meeting, asking to consider if it might be best to include discussion of the whole lifecycle (including broad post-market aspects) into Chapter 4. This would enable the guidance document to provide an overview of what the post-market stage involves and enable Chapter 5 to solely

address labelling. Right now there seems to be a bit of a gap in providing an overview of the post-market stage.]

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

- The Chapter 5 is close to a final version.
- Thanks to Panos and Ravi for the table on global patient labelling information.
- The chapter sets forth some principles for how to involve patients in the patient labelling process, and Meredith would welcome feedback particularly from those working in industry and aware of the challenges of doing something different.
- Meredith would welcome feedback on table 3 on best practice recommendations for the creation of patient labelling information.
- There is a summary of major initiatives over the past approximately 20 years of initiatives to improve patient labelling in an effort to capture the international landscape. Please let the chapter team know if this is missing anything.
- Regarding the section on future directions, the team thought it was important to develop and establish metrics to enable internal and external benchmarking for the degree that sponsors are meeting standards of excellence in patient labelling. Meredith is not sure if this is considered provocative and is flagging it to the WG's attention.

Comments from discussion:
- Ton acknowledged that the chapter team still needs to action comments from the last meeting minutes.
- Peter found the labelling chart incredibly useful and that metrics are worthwhile to include, as being able to measure success is key.
- Meredith confirmed that the guiding principle behind each section of this chapter was how to involve patients, what would be the methods, and the pragmatic steps needed to enable this to happen, providing the checklist of elements to follow when developing plain language labelling for patients, the principles to adhere to when approaching a plain language labelling project, rather than focus on the current-day patient labelling.
- Stella wondered how much scope there is for making changes because e.g. in Europe there are prescriptive templates for everything.
- Meredith agrees. She explained that she worked with Theo on the Quality Review Document (QRD) template for the patient information leaflet and feels it is not so much about changing the template as about changing the approach to populating it, i.e. the choice of language, use of headers and white spaces etc., while still keeping within the scope of the templates and regulatory guidance.
- Meredith and Theo tested filling out the templates, making use of the recommendations and suggestions, and submitted options (within the current regulations and the template) to the EMA, and the results were encouraging.
- Meredith added that they started to get some positive traction too from Health Canada and potentially also from TGIA.
- Theo confirmed the templates allow for creativity, and although he is not sure how you would measure it, it would be good to try. Stella added that with the use of a metric, it might encourage people to be even more creative.

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

- The chapter team has made good progress since the last face-to-face meeting.
- Some of the new ideas raised by the chapter team have been incorporated and further examples have been added.
- Cheryl talked through the structure of the chapter:
  - ➢ Introduction to risk minimisation - optimising the benefit-risk profile of a product

- Description of risk minimisation
  - Routine vs. additional risk minimisation measures - definitions and value
- Regulatory aspects of additional risk minimisation - history and examples
  - In EU
  - In US
  - In Japan
- Determining the need for additional risk minimisation - with examples
- Patient involvement in the design, development, implementation and effectiveness of additional risk minimisation measures - link to patient care pathway, importance of user testing of tools, how to reduce burden in the healthcare setting, options for digitalising tools, patient involvement in the effectiveness evaluation of the measures.
- The chapter team and Theo have reviewed the chapter and given comments, which have been incorporated.

Comments from discussion:
- Nomenclature has been handled well as this is an acronym-rich subject where different authorities have different approaches.
- Cheryl finds the meeting discussion has helped with how to introduce and end the chapter i.e. the right language and how to highlight the key takeaways.
- [Comment added later: The concept of "principles for patient engagement" is not always evident from chapter to chapter. In particular, Chapter 6 covers much of the same territory as was presented in the CIOMS IX Report. It is only in the final section, and a little of the next-to-last section, that there is discussion of methods to use in engaging patients.]

Chapter 7. Guiding principles for patient participation in the generation and utilization of safety and effectiveness data, presented by Peter
- Leo was unable to join the meeting and Peter kindly improvised a summary.
- The content is now in place and the chapter team has been working on improving flow between the sections.
- The next version is expected to be only roughly 5% different from the current version.

Comments from discussion:
- Peter mentioned that as the guidance is distributed broadly to various audiences, this technical chapter will require education on the part of patient groups.
- We may need to think about putting resources at the disposal of patient groups.
- Sten mentioned that Manal, based in Iraq, has contributed at least three major paragraphs very recently, and in his opinion, this now meets the need for contributions from low- and middle-income countries.
- Regarding the section dealing with reporting adverse reactions, a part of the story seems to be missing, and it makes it look like Europe was lagging behind other territories, and this was maybe not accurate.
- We need to communicate that initially in most jurisdictions, reporting of adverse reactions was by healthcare professionals or industry, and in recent years, there has been a shift to integrate patients so they can directly report adverse reactions to regulators. In terms of data, this gives regulators an extra piece of the puzzle.
- In the last 5-10 years, Western countries have changed their systems, forms, and ways in which adverse reaction reports are submitted to be patient-friendly. This shift in industry-regulator-patient adverse reaction reporting has not been included in the chapters. This is as much true for physicians as it is for patients. Linda, who wrote the section in question, will look to amend the text.
- Linda went on to say that although changes have been made in Europe, they are still not as widely implemented and promoted as they could be.

- The shift has gone from just physicians reporting to other healthcare professionals reporting, such as nurses. In Canada, there are also now requirements (in some instances) for hospitals and clinics to report where traditionally they have not had to and patients can also directly report adverse reactions directly to the regulatory authority.
- Talia suggested that the text could perhaps include a short blurb explaining the impact on the type of data available to the regulator that can be aggregated and inform policy decisions.
- Linda said that with the current set up, we cannot make optimal use of patient data, e.g. they write very rich narratives, but at the moment, narratives are not very much used for signal detection purposes in spontaneous reporting. At the moment, we cannot make best use of the richness.
- Stella agreed that when you are doing signal detection, rich narratives do not play a part, but when you have a signal and you start to look at the raw data, i.e the individual reports, then the narratives are incredibly important for getting a much better idea.
- If you depend on statistical signal detection, the narratives will not help to highlight anything, but when you do case-by-case signal detection, as you will do in low- to middle-income countries, then you can much more make use of this as a trigger for signals.
- Judy commented that this is a complex topic, and I think sticking to the principles and telling the story are important. This is a subject that has evolved over time. In the USA, there have always been patient reports, both to regulators and to industry, at a time when this kind of patient reporting to regulators was not happening in Europe. When you talk about the difference between statistical signals and narrative quality, for example in the USA, in the case of patient reporting to industry, patient reporting was always a very large proportion of the reports. And 5-10% of the FDA reports are direct reports. So, patient reporting does play a role in the statistical signals, and when the signal is being reviewed, as far as the quality is concerned, the detail is in the narrative. It is important to stick to the larger story and the potential contribution.
- Linda agrees but feels that the patent contribution could be even larger with a different technique. She will elaborate in the text.

Chapter 8. Patient involvement in developing safety issue/crisis/time-bound communications regarding medicinal products, presented by Sabine

- Michael Richardson recently had to step away from the WG due to time restrictions and named his successor as Stefan Kaehler from Celgene, who works very closely with Michael. Stefan is in the process of reading all the documents he has received from Michael.
- Sabine welcomed Stefan. She went on the say that the Chapter 8 team has had a bit of a rough path but will be getting there now with the new lead.
- Linda, Ravi and Stefan have been working on the chapter, and now with new leadership, they anticipate being able to advance further.
- Linda agrees the team has made progress, and now needs to seek alignment and combine their texts. They have a clear vision for the chapter.
- Ravi also welcomed Stefan and agreed that there is a good structure in place. Following Michael's advice, the team has been adding details to the various sections. Now with Stefan, they expect to be able to tie the loose ends. He expects better progress by the next meeting.

Chapter 9. Challenges and opportunities for patient involvement in Resource-Limited Settings (RLS) by Lembit

- The CIOMS Secretariat is looking at options for helping with the chapter drafting.
- At the end of 2019, the patient organisation members recommended a number of contacts for our informal satellite RLS subgroup, and the subgroup now includes representation from Argentina, Brazil, Cameroon, Ghana, India, Iraq and Malawi. We had a meeting, created a skeleton draft, received the satellite RLS subgroup's input on that, and then Regina was meant to develop a more mature draft, but has not been able to due to her daughter's health concerns. We will probably encourage one of these members to take the lead.

Comments from discussion:
- Peter recommended that Manal would be a valuable resource.

Chapter 10. Guiding principles for patient participation in therapeutic decision-making: patient and public involvement in clinical practice guidelines by Lembit
- Corinna was unable to join the meeting.
- She requested feedback from the group and is willing to amend the chapter as needed.

Comments from discussion:
- Annemiek values the chapter as it gives a clear overview of the topic.
- The HCP element must be included in the life cycle visuals earlier in the guidance. It fits at the start of the life cycle as HCPs carry out research and provide input into modifications to a drug and drug innovation, but also at the end, when a drug has arrived on the market and has to be implemented into daily medical care.
- The chapter refers well to available literature.
- There may be some overlap with other chapters regarding methodologies to consult patients and different roles of patients and patient representatives.
- Overall, Talia shares Annemiek's opinion that the chapter is well written, gives a good overview, has good flow and good sections, and it captures all the components. She will be able to provide more comments on this chapter, after consulting colleagues. She noted that due to divisions of roles and responsibilities in Canada, it might be useful to invite the royal colleges or standards associations to provide feedback on this Chapter.

Glossary presented by Stephen
Stephen presented three glossaries:
1. CIOMS Cumulative Pharmacovigilance Glossary
   Each CIOMS WG has developed terms and definitions over the years, and the definitions have evolved. This glossary brings together the terms and shows their evolution. This will be a working document that will be updated as we go forward, but professionals, the public, patients, regulators etc. will be able to use it. The document will be on the CIOMS website, which is what other organisation e.g. Cochrane do, but it will also be printed.
2. CIOMS WG XI Patient Involvement Glossary – patient-friendly version
   We worked with the WG patient representatives on a glossary of terms that would be relevant for patients. The idea was to use as simple language as possible, and invite Theo's help with this.
3. CIOMS WG XI Patient Involvement Glossary – statistical version
   It has been very challenging to provide simple definitions for statistical terms, into patient-friendly terms, and we were hoping Theo would be able to help.

- Whenever the chapter teams define a term in their chapters, it needs to be related to and linked to the glossary. Please send it to the Glossary team: Stephen, Panos, Stella and Sanna. We need to make sure terms are consistent.

Comments from discussion:
- Theo commented that he is not sure if he understands all the statistical terms and therefore whether he will be able to help.
- He feels the translation of the definitions into patient-friendly terms will probably take a lot of time and effort.

- The patient representatives have already helped to select the terms that will be relevant to the WG XI report. The next step will be to select from this list the terms for translation into lay language.
- Panos agrees the statistical terms are difficult to translate into plain language and questions whether it would be necessary.
- Lembit suggested choosing as pilots three terms that would be both necessary and do-able, while avoiding the technical terms, to see if we can add some value, and then see how we can take it forward.
- The term "patient engagement" will need to be defined by the WG. Some definitions exist but they vary according to whose they are, i.e. the definition used by regulators is different from the one used by industry. We would need to find a definition agreed by all the stakeholders. We need to make suggestions and get input from everyone.
- At the moment, we use terms like patient involvement, patient engagement, and patient voice, and it is not always clear that they are synonymous.
- Once a definition has been agreed, we need to go through the text and make sure the term is used consistently throughout.
- Alternatively, we could use the different terms interchangeably – patient involvement, engagement, voice – and state this upfront, as it would allow for more variety. Lembit agreed it may be easier to use terms interchangeably to avoid larger editorial issues.
- Stephen confirmed the task of going through all the terms in the glossary was assigned to him, and he agrees that if there are two to three different versions, they have to be aligned.
- It may make the text cleaner if we use the term "patient" to include caregivers and advocacy organisations etc, but this would require the introduction to say that there are differences in these groups and that perspectives can be different.
- Annemiek would like to be involved in the terminology discussion when it comes to "who represents the patient" as this needs clarifying for Chapter 3 too.
- It was confirmed that CIOMS writes in British English. Currently there are inconsistencies in the chapters and it will be the job of the Glossary team to make the language consistent.
- In the context of terminology discussion, Peter recommended for all to look at how Chapter 6 begins:

> **Introduction to Risk Minimisation**
> *Medicinal products are developed with the intent of providing benefits (desired or favorable effects), such as curing a medical condition, slowing disease progression or alleviating its signs and/or symptoms, restoring some function of the body, or in the case of vaccines, preventing disease. Generally, these products may also have risks (unfavorable or harmful effects), which can vary in severity or likelihood of occurrence (e.g. ranging from mild events such as occasional drowsiness to a potentially life-threatening arrhythmia) and in opportunities for minimisation ….*

Any other business (AOB)

Implementation strategy
- A small team will start work on an implementation strategy which will be finalised at a later date.
- The implementation strategy should be carried out collectively by all the stakeholders: regulators, industry partners, and patient representative organisations.
- As we would like the patient groups to use the report aggressively, and as a lot of it is technical, we could put some of the WG XI contact details in the report and make ourselves available for consultation.

- It may be helpful to hold webinars for each of the chapters targeted at the patient groups, making available the full chapters and key graphics. Many patient group staff, who are new to the topic, would maybe not access the guidance in the form of a printed report.
- Peter suggested that we could offer workshops that co-locate with various conferences, and some WG members could assist with this type of outreach.
- Lembit suggested we could produce recorded webinars that could be repeated. He has participated recently to implementation webinars with large numbers of participants from different parts of the world. They allowed those who were involved with drafting the document to provide explanations on the context and why certain things were reflected in a particular way. Once the guidance is ready, CIOMS can host such webinars and provide links to other resources.
- Kawaldip shared his experiences with Envision Pharmagroup and lessons learned:
  - To interact with pharma groups at the top level, it is best to contact the patient representative who has been appointed by the pharma group;
  - It is helpful to convert peer-reviewed papers into simple fact sheets, briefings and even Tweets for use by patient groups;
  - The documents authored by patients were widely circulated;
  - Such documents need to be sliced into several parts, although in the end, it should look like it is one whole;
  - Secondary training webinars and workshops are very important.
  Without this effort, the guidance gets left on a shelf.

Guidance target audience
- Theresa mentioned she has found helpful in the past having a scoping document to reference, e.g. reminding who is the primary audience and helping to drive the messaging.
- Lembit encouraged checking the past minutes. The guidance should address all the stakeholders around the table – regulators, patient groups and industry.
- All the audiences should be reflected in each of the sections and the principles should be applied to all.
- Alternatively, we could consider the audience as the health-interested population, and therefore address a wide audience and talk about the roles that each group may play, but not specifically write to those groups, but rather more about the way they are all working with each other.
- The writing needs to be persuasive and explain why the investment in resources and attention is worthwhile. Change requires extra effort. We who are close to the subject, may feel it is obvious and that the case does not have to be made, but many companies will not want this, and it will be harder for patient groups who turn to pharma for funding.
- More effort can bring added value to the industry, to patient groups, and to regulators to have better thought through and structured engagement with patients.
- Patient groups would be able to understand a document targeted towards industry, with maybe some messages tailored to patient groups. Even if the guidance were not targeted towards patient groups, having an infographic targeted to patient groups, would maybe be enough.

Guidance structure
- Include a two-page foreword with comment from each of the main stakeholder groups in each jurisdiction encouraging their colleagues to read it.
- Theresa added the guidance could be like a handbook: if you are audience x, you will find helpful section y.
- It will be important to clarify that this is a handbook and not intended to be read cover-to-cover.
- At the end of each chapter, there could be a short summary and key takeaways for each audience.
- Kawaldip related how in the past when IAPO has collaborated with the WHO, they always produce lay summaries for specific groups, and these are targeted for specific conferences. It

provides a sense of co-creation and co-engagement, and the enthusiasm for patient groups to use this document, to refer to it, to create summaries in their own languages and mind sets. Eg rare diseases group will do something differently from eg non-communicable diseases or infectious diseases groups. These could go in the appendixes and groups could write their own summaries.
- Consider the placement of the RLS, HCP, and Covid-19 chapters.

Translation to other languages
- CIOMS does not systematically translate all its reports. The *International ethical guidelines for health-related research involving humans* report was translated into the UN languages (English, French, Spanish, Arabic, Chinese, and Russian), as had been the commitment at the time. For the WG XI Patient Involvement report, we will need to decide which UN languages will be prioritised. Spanish will probably feature high on the list and we can ask The Pan American Health Organization (PAHO) / WHO office if they are able to support this. Similarly, for the other regional WHO offices for other UN languages, if translations are seen as an added value. We cannot promise to deliver translations into all six of the UN languages. Translating individual elements or summaries alone may be helpful too.

FDA's four patient-focused drug development guidance documents
Theresa gave a summary about FDA's series of four patient-focused drug development (PFDD) guidance documents, which the FDA has been formally directed to provide by congress:
- o Guidance 1: Collecting Comprehensive and Representative Input
  (about patients)
- o Guidance 2: Methods to Identify What is Important to Patients
  (impact of disease and burden of treatment)
- o Guidance 3: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments
  (measures that can be used, clinical outcome assessments, developing and resurrecting available tools to capture this)
- o Guidance 4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making
  (measurement and what constitutes meaningful change, technology)

The content in the four guidances becomes progressively more technical, and consequently, the FDA probably will need to develop a series of training materials, or a webinar, or a version for different audiences. E.g. writing for patient groups can get in the way of communicating effectively to the technical people who need to use them. Similarly the CIOMS WG XI report could be written for one audience and then we could create training materials / webinars in support. The FDA will probably need to develop training materials for the more technical audiences too in order to go into more detail on the technology and the methodological aspects in technology for those audiences as well. We cannot produce one document that will address every audience's needs.

Comments from discussion:
- We can probably take the general-towards-technical approach to a lot of our writing. Marilyn related how she often hears suggested that in health-related documents, it is good to have a solid introduction that is understandable, not without good information but in non-technical language. Obviously, the more technical chapters would have to have technical language, but then we talked about having this digitally available, with links where you can go to dig in further in some of the key areas, either for more detail historically or for more technical details. These are some additional ways to support this technical approach.

Covid-19 Chapter

- We are living through a pandemic that has never occurred before our time, and this guidance is being written during this historic moment.
- The WG agreed that Covid-19 needs to touch on some part of the book, be it a foreword, a pre-introduction, a paragraph in the introduction, a section within a chapter, or a full chapter.
- We will start planning a new chapter.
- In the current climate, there is talk of super-fast tracking patient involvement, super-fast tracking vaccine development, with safety probably going to be a major issue.
- This will impact vulnerable patient groups, the elderly, HIV patients, and other patients with many other diseases.
- As no one has immunity to Covid-19, everyone in the world can potentially become infected and become a patient.
- Benefit-risk has had to be considered in an unprecedented way, and balanced on a global scale, and addressing this for vulnerable populations and their specific needs.
- Government, industry and academia are cooperating, and it is time to add the patient voice to this team / ecosystem.
- It is important to capture the agility of the drug development system in this time of need
- The guidance has a section about urgent communications in Chapter 8 that could be referenced.
- Regulatory authorities are reviewing drugs, devices, vaccines, clinical trials, and hand sanitisers – everything to address products that support pandemic activities and treatments. The challenge in a pandemic is time urgency, volume of activities, and agility of the organization to mobilize its internal resources to support core functions while potentially working from remote locations. : How do you engage patients in those processes when the processes are being expedited so significantly?
- The Covid-19 subject may be too sensitive if things go the way they look like they are going to go. Other examples can be chosen.
- Elisabeth related that The Health eHeart Alliance, a patient registry formed for research purposes, has started a Covid-19 registry. Through their existing patient data networks, they are able to go directly to the patients and help them with their daily symptom tracking and complete a survey. This is a good example of how existing patient involvement methods can be leveraged for other purposes, especially in this type of environment where things are changing every single day. This is a way to get straight to the larger public.
- [Comment added later: Elisabeth also shared information about a new initiative by the UC San Francisco physician–scientists, dubbed the COVID-19 Citizen Science (CSS), will allow anyone in the world age 18 or over to become a citizen scientist advancing understanding of the disease. The spread of coronavirus that causes COVID-19 has varied across individuals and regions, and the factors that determine how it affects individuals and populations are not well understood. A critical mass of CSS participants uploading information though the app, launched on March 26, 2020, could help data-crunching researchers gain insight into how the virus is spreading and identify ways to predict and reduce the number of new infections, according to Gregory Marcus, MD, MAS, professor in the Department of Medicine at UCSF and a co-leader of CSS. Based around a smartphone app, information on the study can be accessed via https://eureka.app.link/covid19 (if prompted, enter the study key: covid) or by texting "COVID" to 4141.]
- Stephen made the point that in the context of safety/efficacy/effectiveness, there is an ethical aspect that will come to light: if there is an 80-year-old on a ventilator, and a fast-tracking clinical trial is under way, does the 80-year-old get the experimental drug, or is it the 20-year old, who has no underlying disease and very little risk of dying from the infection, will they be the ones going into the trial? This whole discussion will be needed.

- Panos mentioned advice from the FDA saying that a benefit-risk discussion needs to include whether additional minimal risk minimisation measures, e.g. getting a laboratory / imaging test, are necessary when you take into consideration the risk of contracting Covid-19 at a test centre.
- Lembit commented that the Covid-19 patients are often otherwise healthy people.
- There is an opportunity with the current emergency population, including educated and computer-literate people, as well as doctors, who could inform us about how we could do things better, more efficiently and more quickly.
- With every day there will be experiences and information emerging, also through our own collective thinking, on what could be done better when given the next opportunity. How can we be better prepared to have more active contribution from patients in this type of situation to address their needs.
- Peter mentioned that writing a Covid-19 chapter may be presumptuous and premature at this stage. It may be best more of a discussion on how it affects this guideline.
- The Covid-19 chapter and the RLS chapter have in common how currently many places in the world are learning about resources constraints in a whole new way.

Next meeting
- Lembit suggested holding another three-hour virtual meeting later in June, similar format to this meeting, in order to continue progressing work while in-person meetings are difficult to plan in the near- / medium-term future.
- Many WG members supported this way forward.
- Our next confirmed in-person meeting will be in Amsterdam, Netherlands, 20-21 October 2020, hosted by the European Medicines Agency (EMA).

Closing remarks
- Lembit thanked all for their time, their loyalty and continuing to contribute at difficult times.
- The group has made good progress, and there still remain some objectives to meet.
- We look forward to a good, valuable guidance document in 2021.