Council for International Organizations of Medical Sciences

4th meeting of the CIOMS Working Group on Patient Involvement

16-17 October 2019, Basel, Switzerland

Minutes
26 November 2019

Participants
Leanne **Angst-Wu** (Roche), Stella **Blackburn** (IQVIA), Ton **de Boer** (MEB), Nikos **Dedes** (EATG), Brian **Edwards** (ISoP), Juan **Garcia** (EMA)*, Linda **Härmark** (Lareb), Stephen **Heaton** (Consultant, formerly Bayer), François **Houÿez** (EURORDIS-Rare Diseases Europe), Kaisa **Immonen** (EPF), Regina **Kamoga** (CHAIN), Talia **Lacroix** (Health Canada), Kerry **Leeson-Beevers** (Alström Syndrome), Marie **Lindquist** (UMC), Vanessa **Lyons** (HPRA)*, Marilyn **Metcalf (**GSK), Isabelle **Moulon** (EMA), Rebecca **Noel,** (Eli Lilly), Izumi **Oba** (PMDA)*, Elisabeth **Oehrlein** (US NHC), Sten **Olsson** (ISoP), Cheryl **Renz** (AbbVie), Ken **Sakushima** (PMDA), Sabine **Straus** (MEB), Christine **Stürchler** (Novartis), Annemiek **van Rensen** (MEB)**,** Judy **Zander** (US FDA), Lembit **Rägo,** Sanna **Hill***, Panos **Tsintis**, and Monika **Zweygarth** (CIOMS).

Participants via WebEx during some afternoon sessions
Charles **Garrigan** (Janssen), Beverly **Harrison** (Janssen), and Leo **Russo** (Pfizer).

Regrets
Fatima **Bhayat** (Takeda), Matthias **Boedding** (Merck), Marc **Boutin** (NHC), Wang **Dan** (CFDA), Mick **Foy** (MHRA), Shinji **Hirasawa** (PMDA), Theresa **Mullin** (US FDA), Shanthi **Pal** (WHO), Ravi **Patel** (United Therapeutics Industry), Peter **Pitts** (CMPI), Sonia **Potenze** (IAPO), Theo **Raynor** (retired from Leeds University, UK), Michael **Richardson** (BMS), Corinna **Schaefer** (WMA)*, Martina **Schäublin** (Swissmedic), Meredith **Smith** (Amgen), and Hervé **le Louët** (CIOMS).

* = new member

DAY 1 WEDNESDAY 16 OCTOBER 2019

Opening and introduction

- Birgitt Gellert, EU QPPV, Roche, welcomed everyone.
- Lembit thanked Roche for hosting the meeting and gave a short overview of CIOMS activities:
- There are some overlaps between the CIOMS WG XI working group (WG) and the CIOMS WG XII WG, both in terms of their subject matter and participants, and due to participants' overlap, we anticipate good coordination and avoidance of duplication.
- Currently there are five active CIOMS WGs, with the Drug Induced Liver Injury (DILI) guide expected to be published by the end of Q2 of 2020.
- New topics under consideration for CIOMS in 2020 include:
  - Real-World Data and Real-World Evidence in Regulatory Decision-Making;
  - Severe Cutaneous Adverse Reactions (SCAR);
  - CIOMS/IUPHAR joint project on herbal and traditional medicines organ toxicity;
  - Artificial Intelligence in pharmacovigilance (PV), on which there will be a workshop in Q1 2020.
- See www.cioms.ch for information on the CIOMS award for the best scientific article published.

- "Tour de table" for all to introduce themselves and welcome the new WG members.
- To optimise limited CIOMS resources, Monika is handing over the WG support to Sanna.
- The minutes of the 3rd WG meeting were approved with no comment.
- The minutes of the 4th WG meeting will be approved by the WG members and uploaded on the CIOMS website in the public domain if acceptable as they are appreciated by the public.
- The 4th WG meeting agenda was adopted with no changes requested.
- Kaisa and Talia co-chaired during the first day of the meeting after the coffee break.
- Rapporteurs for Day 1: Monika, and for Day 2: Vanessa and Kaisa for part of the day.
- Sanna to draft the minutes with the help of the rapporteurs.

Brief presentations on recent initiatives

DIA 2019 Global Annual Meeting, 23-27 June, San Diego, CA, USA, presented by Judy

Judy and other WG members achieved good visibility for the CIOMS work despite the many competing sessions. She received feedback from the patient engagement groups, who support CIOMS for lending a voice to their cause. The session had been set up to add to the European feedback received in Geneva in April 2019, thereby extending the conversation to the Americas. There were various presentations from the WG members and Judy led a community round table, where diverse stakeholders including patients, patient engagement groups, and experts in patient communication, had an opportunity for giving their input on four topics:

1) Special considerations for different patient groups e.g. rare diseases, paediatrics, and the disabled;
2) Patient involvement in benefit-risk (B-R) considerations and prescribing;
3) Patient engagement in risk minimisation;
4) Gaps for patient engagement that perhaps CIOMS should address.

Key takeaways:

- There need to be special considerations for different populations.
- Patients with multiple co-morbidities have multiple disease burdens and multiple medication requirements; they are a significant part of the population and should be included in clinical trials. Real-world evidence assessments are an opportunity to gain information about such patients.
- Paediatrics is not a single bucket, but rather includes everything from newborns to young adults, with each group having its unique considerations. It is handled differently in different countries.
- Many patient populations have disabilities. How can clinical trial participation be enabled?
- Identifying and targeting critical areas for patient engagement throughout the product lifecycle needs to be conducted as a systemic strategic process.
- To limit patients' efforts, we can share non-competitive resources e.g patient-friendly language guides; education and training materials; risk minimization tools; and survey methods.

Comments from discussion:

- This type of awareness raising preceding the CIOMS guide will help to achieve a better impact.
- The International Society of Pharmacovigilance (ISoP) will soon hold its Annual Meeting, which will include sessions on Latin American patient involvement.

Presentation of WGXI to the European Medicines Agency (EMA) Patients' and Consumers' Working Party (PCWP) by Isabelle, Juan and François

Isabelle, Juan and François explained the CIOMS XI guidance objectives and chapters' contents to the PCWP, which is composed of 22 European organisations representing patients. They commended the WG guidance for being the first such global initiative. It is timely, given the many elements that have emerged over the last years, which need to be brought together. The PCWP is willing to serve as a resource; and Isabelle, Juan and François requested references on the PCWP's patient

involvement initiatives. They received interesting documents on how PCWP involves patients in designing and discussing clinical trials e.g. in Thailand; Zambia; and Argentina. The PCWP will have its next meeting in March 2020, when healthcare professionals (HCP) will join to give their views. They mentioned the need to focus on patient involvement rather than patient recruitment, and to not "use" patients. This point is pertinent for ethics considerations.

Workshop on Opportunities and Challenges of Patient Involvement in Resource Limited Settings (RLS), 27 August 2019, Kampala, Uganda, presented by Regina, slides available

This was a consultative meeting hosted by the Ugandan national regulator, which generated much excitement, with it being the first of its kind on patient engagement. There was good participation from HCPs; regulators; social scientists; bio ethicists and research ethics committee members; Community Advisory Boards members, and professionals from supply chain organisations; academic medical institutions; media; and patients / patient organizations, representing patients suffering e.g. from cancer; epilepsy; sickle cell disease; hepatitis and HIV.

Comments from discussion specific to Uganda

- The young, the literate, and some HCPs, make use of social media platforms to communicate about patient issues but there may be further opportunities to expand this to optimize patient engagement, given the resources available.

Comments from discussion overall

- The current CIOMS guidance focuses on Europe and North America, and misses the LMIC perspective, and this is needed to make the guidance relevant globally.
- Many issues are common to different regions e.g. Regina's list of issues has common ground with issues in New York City too. Consider the common issues affecting patients globally.
- Perhaps we can reach out to regional patient organizations e.g. via ISoP, and other organizations around the table via their constituencies. This could be done for other regional stakeholders too.
- We should recognize that LMICs have some unique challenges.
- Drugs need to be developed with the needs of the patients who will be using them in mind.
- To obtain further patient input, suggest short interviews with patients. Rare Diseases International (RDI) will soon have a meeting and we could ask them some key questions.
- Need to decide the scope. If the guide covers the full medicine lifecycle and in real-world use globally, this can be done only at a high level, but we can go into more detail if it covers regulatory processes only in countries under the ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use).

Conclusion from Lembit

- It is challenging to make the guide relevant globally, and this is why we held the Open Meeting and the Uganda Workshop in 2019, and why we have identified other means to get input.
- In reality, patient associations are limited in some countries due to politics.
- CIOMS would like the guidance to be visionary.
- All countries are developing and we find RLS in high-income countries too.
- Large drug companies do not typically develop new medicines in low-income countries. E.g. in sub-Saharan Africa, it is mostly research about vaccines, neglected and tropical diseases, and some local academic trials and international community-sponsored trials, which are comparative trials on e.g. antimalarials.
- Some drug companies do not conduct clinical trials in countries where they do not intend to sell.
- But, those who today cannot afford the medicines may be able to do so in e.g. five years' time.
- In pragmatic terms, we are over half way through the guidance production process and therefore we should not choose a direction, which requires a completely new approach.
- The guidance would benefit from a chapter about patient involvement in RLS, which would point out the differences in countries along different development paths.

- We will try to get input from patient representatives outside the group, mostly via virtual satellite meetings and teleconferences.

Seeking additional input to the draft guidance

Survey on patient perspectives regarding working with various stakeholders along a drug's lifecycle: Request to European Patients' Academy (EUPATI), presented by Annemiek

The Chapter 4 team is in the process collecting all the rules, regulations, and go-to-practices available, and forming a broad overview, but it would like to capture patient views in order to formulate recommendations. The team proposes conducting a patient survey on the patient perspective on working with industry, regulators and other stakeholders. Other chapter teams may also benefit. EUPATI may be a suitable channel for conducting a survey as it is not a representative group, having members with varying backgrounds, consisting of about 150 EUPATI fellows, who have graduated with an affinity with the drug development field and experience on the topic, and who will not need a lot of contextualising before being able to participate in English. All of these reasons would make EUPATI feasible within the time available. A EUPATI survey could serve as a first step, with François' proposed initiative about conducting interviews as a second step to obtain more detail at a global level. EUPATI is waiting for a formal request by the end of 2019 and a draft survey has been circulated within the WG.

Comments from discussion:

- Patient Focused Medicines Development (PFMD) has conducted related surveys, and on Fair Market Value and principles of participation. Recommend consulting with Nicholas Brooke. The PFMD also has a repository where many organisations contribute their resources called Synapse.
- The US National Health Council (NHC) has organised several round tables and developed recommendations, as has been done by others, e.g. the NHC Rubrik was shared with Beverly.
- Regarding survey question 3, the NHC already developed resources to address these challenges.
- If we select individuals from organisations we know, the answers will reinforce what we already know. This is biased.
- We could phrase some of the questions such that they would reveal solutions.
- The European Patient's Forum (EPF) has observed some changes e.g. regarding openness of clinical trial results, data sharing, and end-product affordability. The survey could be re-focused.
- In the UK, there is survey-overload. It would need to be easy to complete.
- If we want patients to play a bigger role, we need to motivate them.
- To collect information from patients, would require an ethics committee review.
- Some may prefer a short informal phone call. This may help to sidestep the ethics committee review formality.
- If we finalise a set of generic questions, we could take it to EUPATI and other organisations.
- The NHC could circulate the survey to American patients.
- The Irish Platform for Patient Organisations, Science and Industry (IPPOSI) can also access patients who have an interest and an understanding.
- It would be interesting to get views from non-expert patients. The EPF could circulate it too.

Conclusion from Kaisa
We may need to continue discussion on this survey at another time.

Questionnaire on ethics issues, presented by Panos and Stephen

- The draft questions were circulated, comments addressed, and further questions added.
- Ethics on the subject of patient involvement in PV has not been addressed before.
- Lembit to consult the ethicists who contributed to the CIOMS guide published in 2016, *International ethical guidelines for health-related research involving humans*. The group of 22

ethicists was balanced in terms of gender, geography, and background. They will be asked firstly to review the questions and secondly to respond to them. We expect a consolidated answer.
- If the ethicists are not able to participate, we will invite a small number to give their views at a one- or two-day meeting. We have considered doing this online but expect it would take longer.
- We anticipate the ethicists will probably want to add questions, e.g. on patient groups financing.
- There are concerns that the ethicists may not understand PV.
- We should have results within one or two months, and at the latest, by the next WG meeting.
- Should we have a section in the guidance on ethical aspects?

Possible involvement of a digital specialist

We probably do not need to invite a digital specialist to join the WG.

This subject includes two different topics:

1. How to deliver a patient-friendly guide, accessible globally, via mobile devices?
    - CIOMS will explore options but the brief will need to be precise.
    - The guidance should be accessible to patients who are illiterate and those who have disabilities e.g. a visual impairment.

2. How to leverage technology solutions for patient involvement at various stages of the lifecycle?
    - Technical tools should be introduced in the relevant chapters.
    - The Chapter 3 team could include tools under development e.g. ePRO and eConsent.
    - The Chapter 6 team would appreciate a case study of a patient-facing, innovative, digital risk minimisation tool to include in the appendix, even only a generic case study.
    - The subject is moving so fast that the guidance could be outdated very soon.
    - This is a large subject, ranging from clinical trial recruitment, registries, data entry, to reporting of adverse drug reactions (ADR), and may require its own CIOMS guide.

Conclusion from Lembit
- Mention initiatives already under way, including some examples, but not have a full list.

Progress with draft chapters

Group 1 has had several teleconferences since the last meeting to coordinate between the chapters.

Chapter 1: Introduction, presented by Isabelle
- The chapter lead, Theresa Mullin, was absent from the meeting and the introduction is on hold at the moment.
- Originally, Theresa wrote an introduction, explaining the purpose of the guide, addressing concepts such as what is meant by patient involvement/engagement.
- Then, due to ongoing questioning within the WG over content, the introduction was put on hold.
- The less well-represented patients and/or special/minority groups e.g. children and pregnant women, need to be mentioned in the introduction, although we cannot start with exceptions.
- Under health literacy, we could explain PV concepts, risk minimisation, and drug development.

Chapter 2: Landscape of patient involvement in the development and safe use of medicines, presented by Elisabeth, slides available

The chapter format has changed and now it is the following:

- A brief history of patient involvement, which in time will align with the introduction chapter;
- Current and emerging landscape of patient involvement in medical product development;
- Current and emerging landscape of patient involvement in the safe use of medicines;

- Into the future: key outstanding needs or issues to enhance patient involvement.

The Chapter 2 team appreciates the documents received, and going forward, would like to ask for:
- Relevant global examples and insights, providing a summary / key takeaways, a reference within the document submitted, and show within the Chapter 2 outline where it applies;
- Examples of patient involvement in safe use / pharmacovigilance / pharmacoepidemiology.

Comments from discussion:
- Regarding translation and definitions, it would be helpful to explain the underlying elements e.g. what makes a patient "representative" or "advocate". Having a profile will help translation.
- As the guidance is becoming very long, it is important to keep Chapter 2 concise or place extra details in an addendum. Alternatively, we could put key initiatives in boxes or use a timeline.

Patient preference studies have led to decision making at the regulatory level, and in this context, Becky from Eli Lilly gave a brief summary about IMI-PREFER.

Chapter 3. Patient involvement in advancing treatments for their disease, presented by Marilyn

- There have been some questions about the chevrons diagram placement, i.e. in the introduction and use for navigation through the guide, both for the print and the electronic version i.e. with links? For the time being, it fits well at the start of Chapter 3.
- Public feedback suggested the first chevrons are distinct because patient groups work early on with registries and investments, before pharmaceutical companies get involved.
- The chevron heads and tails overlap, which reflects real life.
- Should the last chevrons apply to the whole lifecycle?
- Will continue to work with e.g. Chapter 2 to avoid duplication.

Comments from discussion:
- Will the frameworks developed be critically analysed or simply referenced?
  Answer: We have addressed the aspects that fit with the guidance and will give links to websites.
- Need to include information from non-Western countries.
- Need consistent use of terminology e.g. with reference to Chapter 6.

Chapter 4. Guiding principles and considerations for patient engagement, presented by Charles via WebEx, slides available, assisted by Annemiek in the room

- The Chapter 4 objective is to summarize and reference key sources for guiding principles for patient engagement, and to provide an overview of the key operational considerations.
- Request case studies and feedback on duplications, omissions, and content order.
- Drafts of all sections are complete except for sections B (survey results) and H (case studies).
- Charles walked through the sections A to H, giving extra details where helpful.

	Section
A	**Principles for Working with Patients and Patient Organizations** • Overview of various relevant principles and codes of practice types guidance documents
B	**Perspective of Patients & Advocates on Involvement with Drug Development & Safe Use** • Need for understanding the patient and patient organization perspectives for more effective engagement • Possible survey results on the patient perspective
C	**Positioning Patients as Partners and Mutual Benefit** • Importance of positioning as partnership, including goals/ outcomes important to all stakeholders
D	**Training & Education of Stakeholders** • Training / education of drug developers, regulators, others • Training / education of patients
E	**Contracts & Communication** • Consideration for what to include in contracts, making agreements reasonable (WECAN) • Need for effective and consistent communication, mechanisms to do so, patient friendly language
F	**Compensation & Fair Market Value** • Treating patients/ patient organizations as expert figures, and compensating accordingly • Concept of fair market value, factors for calculation. Reference to NHC calculator work
G	**Measuring Patient Engagement** • Why measure (e.g. show value, enable improvement) & considerations for measuring (e.g. fairness) • Current work on measuring patient engagement (Tufts CSDD/ DIA, IMI-PARADIGM, CTTI)
H	**Applicable Case Studies**

Comments from discussion:

- Regarding section A, should the list be as an addendum and should it be exhaustive? E.g. the list does not include the EMA and National Institutes of Health (NIH) principles of engagement with patients. Recommend finding all the places where research agencies, regulatory agencies, and industry have developed guidance, and draw out the principles.
- Could ethical principles e.g. on compensation, be included in Chapter 4?
- There are different modalities of engagement, such that sometimes we need to represent an expertise, sometimes a community of patients, or a specific disease.
- Maybe mention the issue of independence, even if this is also covered in another chapter.
- Regarding section D, a brief mention may not be enough. We need to address how to develop, apply, and structure training and education; who will deliver it; and how this will impact engagement with industry and regulators. Must not discriminate untrained patients.
- The less well-represented patients and/or special/minority groups e.g. children and pregnant women, need to be mentioned and their interests included.
- Regarding section E, could the contract content be explored in the qualitative patient interviews? Some patients say this is a difficult area. Maybe we can recommend documents?
- Regarding section F, patient participation can be more visible and recognised. Compensation can be about more than money, e.g. can compensate for lost working time. We could suggest some tools. Patients bring value into the process and their contribution should not be exploited.
- Conflict of interest could be mentioned and perhaps we could provide some evaluation criteria?
- We could recommend guiding principles for how to design a patient involvement process for a pharmaceutical company or a regulator, for them to customise. This could be in the form of Points to Consider, either in the main Chapter or attached as an Appendix.

Chapter 5. Patient involvement in patient product labelling, presented by Ton

- Brief walk through the chapter components:
  - Introduction;
  - Communicating drug B-R information to patients;
  - Sources of medicinal product B-R information for patients;
  - Initiatives to improve the quality of patient labelling;
  - What constitutes high quality, patient-centred labelling?
  - Principles for patient engagement in the development of patient labelling;
  - Evaluating the effectiveness of patient labelling;

    - Future directions for patient labelling.
- Brief walk through the tables in the chapter:
    - Table 1) Patient labelling requirements worldwide;
    - Table 2) Initiatives to improve patient labelling: 2003-2018;
    - Table 3) Best practice recommendations for patient labelling information.
- We could mention over-the-counter (OTC) versus prescription drugs, especially with regard to information on the outside of the packaging.
- We could highlight the approach of Bayer, which replicates the concept of the Company Core Data Sheet (CCDS) into something similar on the subject of "company core patient information".
- The Table 1 on "Patient labelling requirements worldwide," exists as a summary and as a detailed Excel table. Request the WG members to check if it is correct and feedback to Panos.
- The drug black box warning could be highlighted as an initiative and opportunity. Both the EMA and FDA are working on this.
- Looking at the subtitles, some of the content relates to communicating B-R information, which reaches beyond product labelling.
- Risk minimisation materials do not communicate benefit as they are strictly designed to communicate risk.
- Promotional materials are not related to labelling.
- The chapter oscillates between legal and communication aspects and these are not compatible.
- Many people cannot read and cannot understand medicines package leaflets. See e.g. *The European Health Literacy Survey*. Patients sometimes do not even look at them.
- Where do patients get the information if labelling is not required in their country? Sometimes information is unavailable in a local language or in a style that is understandable by laypeople.
- Need to steer away from local legislation, which varies by country. We should focus on principles, how to optimise patient understanding, and patient input to the labels.
- Must take care that we do not duplicate between Chapters 5 and 8.
- Maybe some of the background could go to e.g. the introduction because it relates to the safe use of medicines and specific patient populations.
- The requirements to go into an annex.

Chapter 6. Patient participation in design, implementation and evaluation of additional risk minimization measures, presented by Stephen and Cheryl

Brief walk through the chapter components:

- Define risk minimisation, including both "Routine" and "Additional" risk minimisation. A key part of "Routine" is the product labelling and will refer to Chapter 5.
- Section on regulatory aspects, covering the US, EU and Japan, with an example on how patient involvement has helped with additional risk minimisation decision-making.
- Patient involvement in risk minimisation, where there is need for additional efforts, what factors to consider, and how patients can participate.
- "Patient preference studies" and various risk minimisation meaures (design, development, implementation and effectiveness), pointing out where patients can be involved.
- Table 4 gives examples of questions to obtain patient perspectives.
- Could add a final section on patient organisation involvement.

Comments from discussion:

- Regarding the examples, Thalidomide and Butanoic Acid have been over-used. Try Valproate?
- Would like one example of patient involvement from each regulator: FDA, EMA and PMDA.
- Risk minimisation measures do not always work in practice, e.g. sharing medicines and illiteracy have led to Thalidomide-related birth defects. Mention this under effectiveness?
- There have been cases where foetuses have been deliberately exposed in order to receive compensation. It can be challenging to know what results from failure and what is deliberate.

- Would like to mention a digital risk minimisation tool, designed with patients for patients, focusing on a particular patient group, e.g. adolescents, even if it were only hypothetical.
- Consider recommending involving Patient Advisory Boards. This may apply more broadly than to risk minimisation. Stella and Judy mentioned companies that do this. May fit better in Chapter 4.
- The use of generic medicines poses major risks to patients as the appearance of packaging and pills can change frequently (size, colour, shape). This has implications for Chapter 5.
- Regarding health literacy, could create an infographic to explain PV concepts/meanings, risk minimisation, and drug development.

Chapter 7. Patient participation in the generation and utilization of safety and effectiveness data, presented by Leo via WebEx, with screen sharing, documents available

Leo wished to receive support from the WG on specific subjects in the chapter, feedback on whether his plan fits with the other drafts, whether all his sections are needed and possible omissions.

- Data needs to be meaningful and useful. Consider data in terms of informing decisions in drug development and post-marketing.
- All data sources and analyses have strengths and weaknesses, but other considerations contribute to determining "meaningfulness", e.g. circumstances, the seriousness of the risk, and the vulnerability of the patient population.
- Decisions made along the drug life cycle are informed by several types and sources of evidence, with patient perspectives being one of those sources.
- Should this chapter include generating patient preference methodology information?
- Consider what type of evidence provides the most scientific information. Descriptors would be useful so we can provide the best form of evidence.
- Do patients understand the connection between their data and public health?
- Does Chapter 7 only deal with post-market data? If yes, is pre-market data covered elsewhere?
- Regarding "Sources of patient data", could mention toll-free multi-lingual patient hotlines in India. Local ADR monitoring centre investigates further.
- Must ensure that engagement with patients, also in terms of data, is a two-way communication. Conclusions drawn must be made available to patients in an educational manner.
- Structured data alone may not be enough. What about unstructured data, such as obtained from public testimony, focus groups, open public hearings, and advisory committee meetings?
- Real World Data is mentioned under 'Challenges' but it could be moved earlier in the Chapter to under Data Sources.
- Define data, e.g. broad or narrow, or aggregated for certain uses, to remove ambiguity.
- Qualitative data is collected and handled in a different manner, with social context (values and attitudes), which can be important, especially for patients.
- Evidence-based policy tends to look at all types of data, resulting in holistic decision making. The reader's training and perspective will determine how they understand. Must define the terms.
- Instead of asking the patients for ever more information, how can we improve our own methodologies to use better what is already there?
- Regarding communication: patient data reaches us, we develop a product, and design the label, and thus communicate back to the patient; but we need to do more, be aspirational.
- In the context of rare diseases, there is often a lack of data, and sometimes we do not have enough data and medicines are not approved. There is a reliance on patient experience.
- Social media can also be a source of misinformation and do harm. How can we counteract this?
- We have not discussed liability.
- Create balance - anecdote on recruiting patients to unsafe trials.

Chapter 8. Patient input in developing safety issue communications regarding medicinal products, presented by Sabine

- The WG supports the broader understanding of urgent/risk communication, including Dear Healthcare Professional (DHCP) letters and drug recalls.
- Need perspectives from jurisdictions outside of Europe and the US, and from LMICs. In the WG, we have a WHO perspective but this has not been integrated into the chapter yet.
- How to reach patients? Have reached out and had some EMA public hearings, and received input, but there must be more to capture.
- How can we leverage patient groups for communication?
- Require good communication to be in place to implement the urgent communication.
- There exists virtually no information or evidence on urgent safety communication.
- The concept to date has been around the regulatory scene and we would need to decide whether this is going to be generic or relate to legislation.
- In a related case example from Uganda, where a drug was recalled using media with the message "hypertension drugs cause cancer", required long damage-control efforts.
- With better communication, we can prevent a knock-on risk scenario.
- Sten referred to a study in rural Uganda[1] where communication channels were rated differently by health providers and community members. Need to know what works in a local community.
- Need to think about what an urgency means on the ground level and what types of communications are needed and feasible.
- An example was provided when the risk of a commonly used OTC drug was identified and regulatory authorities engaged with patients who helped to develop patient-specific communications. When timelines are too tight to obtain direct patient input, it is still worthwhile to involve a plain language expert in the safety communications.
- Maybe we need to also consider what we do not want to happen and give guidance to prevent that, to avoid misinterpretation and harm. Maybe some examples with oral contraceptives.

Glossary, presented by Stephen

- The cumulative glossary contains definitions from all the CIOMS guides including over 250 terms.
- It will be a publication in its own right, scientifically referenced, reflecting evolution, and will be a living document and needs to be maintained.
- PV professionals especially should benefit from it.
- We would like to put the terms most relevant to patients into plain language. The NIH has good guidance on this. Due to high functional illiteracy levels, even in high-income countries, we should aim no higher than US 6th grade school level. Stephen has made available a guidance on how to write in plain language.
- The CIOMS WGXI guide will have a subset of terms relevant to the guide.
- All WG members should make sure their drafts are consistent with the current proposed glossary. All definitions within the guide must be aligned; we need to find consensus on definitions and be consistent.
- Once the guide content increases, the chapter leads should flag up to Stephen any key terms not covered by the Glossary.
- Some definitions will differ between jurisdictions, and this may need to be mentioned in a disclaimer.
- Sometimes we just need to find the commonalities in definitions.

[1] Figure 1, p13, Helen Byomire Ndagije, Leonard Manirakiza, Dan Kajungu, Edward Galiwango, Donna Kusemererwa, Sten Olsson, Anne Spinewine, Niko Speybroeck (May 9 2019), *The effect of community dialogues and sensitization on patient reporting of adverse events in rural Uganda: Uncontrolled before-after study*, Plos One. https://doi.org/10.1371/journal.pone.0203721

- We have tried to use the best resources available from an academic and scientific perspective and all glossaries will be referenced.
- EMA offered to share its definitions for the cumulative glossary.

Other topics:

Low and middle-income countries issues and contributions
A chapter on LMIC would be beneficial, which would deal with the specificity, with references throughout the other chapters too. All WG members are welcome to give their input.

Therapeutic decision-making contributions
- The World Medical Association (WMA) nominees have been unable to participate due to time constraints but Corinna will be able to contribute to the writing and leverage the WMA network.
- Read Corinna's concept before she invests too much time and consider where it could fit in.
- HCPs are critical in the safe use of medicines, they are the primary interface with patients, often their primary source of information, and are involved in clinical research.
- A healthcare provider is needed to review the content in the least. This will go a long way towards practicality, usefulness, making the guide relevant, and distinguishing it.

Some concerns raised about involving HCPs
- If we change the scope now to include clinical practice, we might require much longer to complete the guide. Could think about producing a 2nd follow-on publication with a wider scope?
- If excluded, HCPs will still be able to extrapolate the principles to other activities.
- There was some discussion about the role of health care providers in drug development. It was also recognized that population-based evidence does not always translate to individual outcomes.

DAY 2 THURSDAY 17 OCTOBER 2019

Lembit chaired the meeting during day 2.

Reflections on Day 1 and general discussion

Ensuring the guide's uptake
- CIOMS will consider distribution channels for the guidance, including approaching CIOMS members with a global presence, for assistance.
- Regarding distribution channels, pharmacists' also spend time at community level.
- From regulatory perspective, where there is ambiguity about when and how to integrate patients within the drug lifecycle in order to support decision-making, the guidance would provide this support. Patient involvement is a grey area, and so expect strong interest.
- The publication could be accompanied by e.g. a webinar. Could be a useful resource and serve towards capacity building.

Guide title considerations
- The subject matter applies differently geographically: drug development applies to high-income countries, and patient safety applies globally. There are different speeds and constituencies.
- These days, the medicine lifecycle does not end when the medicine arrives on the market. Due to conditional approvals, work continues after medicines enter the market. This was not the case 20 to 30 years ago. If the guide were to include patient involvement in this respect only, the guide scope would be more narrow.

- Select the opportunities for patient involvement where it can make the biggest difference.
- Several title options were considered:
  - *Patient involvement in development and safe use of medicines* (current title)
  - *Opportunities for patient involvement throughout the medicinal lifecycle*
  - *Patient support to the regulatory process to the development and use of medicines*
  - *Principles and opportunities for patient involvement throughout the lifecycle of medicines* (new title?)
- [Theo Raynor's comment after the meeting: I was very concerned that the issue of the title of the guide was being revisited - we are half way through the process and this issue had been settled. I am very content with the current title: "Patient involvement in development and safe use of medicines." I feel that it is precise enough - and titles need to be short for impact. The introduction of terms like 'throughout the medicinal lifecycle' does not add value. Firstly, patient and the public do not generally recognise that a medicine has a 'lifecyle' and this is not a lay-friendly word. The current title does not specify a specific timescale - and so it is implicit that it is throughout the 'lifecycle'.]

Writing style

- The language must be robust for experts and simultaneously accessible for a wide audience.
- We could produce a version for a different readership of experts at a later stage if needed.
- At this stage, we need mature content, not effort on sophisticated presentation.
- The guide will be a roadmap and readers will find parts to aspire to and will implement initiatives when they are ready. It is useful to lay down basic principles for reference.
- Well known concepts can be summarised and less known concepts can be expanded.
- Text can be moved and/or summarised but nothing is usually deleted.
- [Theo Raynor's comment after the meeting: I very much agree that 'the language must be robust for experts and simultaneously accessible for a wide audience'. However, I do not agree that we should 'produce a version for different readership of experts at a later stage if needed'. If we write well, in a clear and understandable manner (and with good navigation aids, so that different people can find the information relevant to them), there should be no need for different versions for different people.]

The WG then divided into its two sub-groups and smaller breakout groups to examine the chapter contents and the Glossary more specifically.

Report back from break-out sessions

Beverly and Charles joined via WebEx.

The below includes only new points not mentioned elsewhere in the minutes.

Group 1

- Chapters 3 (Recommendations) and 4 (Principles) were swapped over.
- Sten is invited to join the next Group 1 discussion to contribute examples.

Chapter 3

- Mention the CIOMS *International ethical guidelines for health-related research involving humans*. The *Declaration of Helsinki* is concrete and concise but the CIOMS guide has more explanatory notes and contextual content, and is more useful from an implementation perspective.
- Some patient organisations do not want to go through a process to become eligible, e.g. in order to protect their independence, and so are excluded from committees.

Chapter 5
- Written information is not the only option. Consider animation films.
- Early design and structuring of clinical trials to involve patients can impact what information is available to enhance labelling. Would be good to include examples.

Chapter 6
- Involve a patient advisory panel to help with the lifecycle approach and additional risk minimisation. Will share content to see if this can be useful for a Group 1 chapter.

Chapter 7
- Spontaneous v. solicited is artificial when discussing with patients as there may be a range.
- Need for protection of reporters. Related a case where doctors were sued for libel for reporting.
- Need to include General Data Protection Regulation (GDPR) and legal requirements.
- To achieve patient-centric data collection, patients need to be involved with the design of data collection forms, and related principles.

Ethics questionnaire
- Some questions were legal in nature, especially the ones in PV, and they will be removed.
- Consider issues of financing patients, patients' expectations, and those of patient organisations, public-private entities, and governments.
- Patient representatives will be invited to review and give their feedback.
- The ethicists may not fully understand the technical regulatory issues.
- Some of the ethicists in question have experience of working with pharmaceutical companies and/or patients. Need interaction to increase their understanding.
- Any additional questions for the ethics survey need to be submitted asap.
- Comment from Lembit that after the initial approach to ethicists, CIOMS may invite some of them to a future WG meeting to obtain their focussed input to the WG.

Glossary
- Reviewed the most pertinent terms from the stakeholder perspectives in the WG. These are relatively easy to modify into plain language.
- Some draft terms were removed, e.g. mainly on statistics, but can be put back at a later date if needed.
- The concepts of partnering and collaboration may impact both the writing style and definitions.

Discussion on the guide structure
- Could have an executive summary at the start.
- [Comment from Theo Raynor after the meeting: I feel it is essential that we have an Executive Summary.]
- Focused recommendations tend to be useful as they can support with concrete activities.
- If possible, separate out recommendations according to regulators, industry and patient groups.
- Consider listing challenges too at the end of a chapter, not only principles / recommendations.
- For Group 1, there is a natural flow: Chapter 1) Introduction; Chapter 2) Landscape; Chapter 3) Principles; and Chapter 4) Involvement. Chapter 4 would lend itself to giving a set of recommendations, based on the principles.
- For the benefit of those readers who will only dip in, there should be highlighting of principles.
- Some very high-level recommendations may be helpful too, perhaps at the start of the guide.
- Later, we may decide to have a recommendations summary at the end of the guide.
- We could add a future-orientation chapter at the end.

Implementation strategy

- There were considerations about a special guide launch event.
- Could also leverage major industry events e.g. the DIA events or patient organisation meetings.
- When have a clear publication date, CIOMS could organise a regional implementation meeting.
- Final meeting agenda to include the implementation strategy, i.e. steps and outreach.
- We can start planning for publication in mid-2021.

Next meeting

- Will send out Doodle for April-May 2020.
- Medicines Evaluation Board (MEB) is offering to host the first meeting in 2020 in Utrecht
- EMA is offering to host the second meeting in 2020, also in the Netherlands.

Thank you to Roche for hosting the meeting.