Council for International Organizations of Medical Sciences (CIOMS)

Open Meeting on Patient Involvement in Development and Safe Use of Medicines
30 April 2019, Geneva, Switzerland

The meeting also marked the 70th Anniversary of CIOMS.

Download the CIOMS Anniversary Newsletter here.

Programme

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- Message from the President of CIOMS

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- 70 years of CIOMS: ethics and safety guidance to protect patients
- Patient centricity in medicines regulation: WHO viewpoint
- The role of patients in drug development and safe use
- Why working with patients is so important

SESSION 1

Chair: Annemiek van Rensen, Medicines Evaluation Board, the Netherlands

- Overview of the proposed CIOMS guidance
- Patient involvement initiatives around the world
- How can patients advance treatments for their disease?

SESSION 2

Co-chairs: Kerry Leeson-Beevers, Alström Syndrome U.K.; Nikos Dedes, European AIDS Treatment Group

- Guiding principles for engagement: avoiding conflict of interest, fair compensation …
- Patient involvement in designing medicines labeling
- Minimizing the risk of medicines: how patients can contribute

SESSION 3

Chair: Kaisa Immonen, European Patient's Forum (EPF)

- Using patient data to evaluate the benefits and risks of medicines
- If things go wrong: The role of patients in designing and distributing alerts
- Patient involvement in developing treatment guidelines

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INTRODUCTORY SESSION

Chair: Hervé Le Louët, CIOMS President

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Message from the President of CIOMS

Hervé Le Louët, President of CIOMS, welcomed all participants. CIOMS has a long history of bringing together world experts in specific fields to develop consensus-based guidance. Its current Working Groups are developing guidance on Clinical Research in Resource-Limited Settings, Drug-Induced Liver Injury, the use of MedDRA in standardized queries and product labelling, and Patient involvement in the Development and Safe Use of Medicines. Patient involvement is the topic of this meeting, which aims to obtain input from additional patient groups not represented in the CIOMS Working Group..

PRESENTATIONS

70 years of CIOMS: ethics and safety guidance to protect patients

CIOMS is an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949. Its mission is to advance public health through guidance on health research including ethics, medical product development and safety. CIOMS represents a substantial proportion of the global biomedical scientific community through its member organizations. CIOMS guidelines are translated into many different languages. The CIOMS guidance seeks to complement rather than duplicate existing work.

Transparency is important to CIOMS. The Council's work is described in its quarterly Newsletters and on the active Working Groups' webpages, which include the minutes of all face-to-face meetings.

Lembit Rägo, CIOMS Secretary General

Emer Cooke, World Health Organization

Patient centricity in medicines regulation: WHO viewpoint

WHO has several regulatory activities focusing on access to quality-assured medicines and outcomes for patients. Some examples were given of patient and consumer input to the work of WHO. CIOMS plays an important role as a trusted platform for building consensus on principles on patient involvement in regulatory work. There is a need for this guidance, and for supporting its implementation across economic settings globally.

The role of patients in drug development and safe use

Marc made the case for strategic collaboration and continued push towards more patient engagement. He outlined the tremendous progress made in the last 15 years in the U.S. to ensure that patients get the treatments and outcomes that are important to them.

Marc Boutin, U.S. National Health Council

Theresa Mullin, U.S. Food and Drug Administration (FDA)

Why working with patients is so important

Patients can contribute unique views on treatment options and unmet medical needs. Since 2013 the U.S. FDA has involved patients in its Patient-Focused Drug Development (PFDD) Meetings covering a wide range of conditions. The Agency has identified some of the questions to ask in order to understand the patient experience, and is seeking to integrate these perspectives into decision-making all along the medicines life cycle.

Introductory Session - Panel discussion

Additional panelists (from left):

- **Nicholas Brooke**, The Synergist
- **Poonam Bagai**, CanKids India/ Pallium India

Summary of discussion:

How can we make real change happen?

- Articulate the problem and propose a believable solution. However, change will only happen if many people see the problem as being important in their lives.
- The Patient Engagement for Medicines Development (PFMD) platform provides a map to existing tools and initiatives.
- In India patients do not have a say in medicines development and use. Support is needed from the global community to promote patient involvement.
- Awareness can be raised by "telling the story" – for example by showing what it means for a patient not to have access to effective pain control in palliative care.
- It was suggested that companies might be ranked on a "patient centricity scale". The U.S. National Health Council has proposed a Value Model Rubric as a guide for best practices of patient-centeredness.

What is "value" in health care?

- There is a perception that initiatives for patient involvement will drive up costs. However, information collected by the U.S. National Health Council indicates that people are often over-treated. There is growing recognition that delivery of patient-centered care may actually reduce costs in some cases.

What is the role of health care funders?

- In the U.S. there is growing trust by government and insurance companies that patient engagement can help to deliver needed care at less cost.

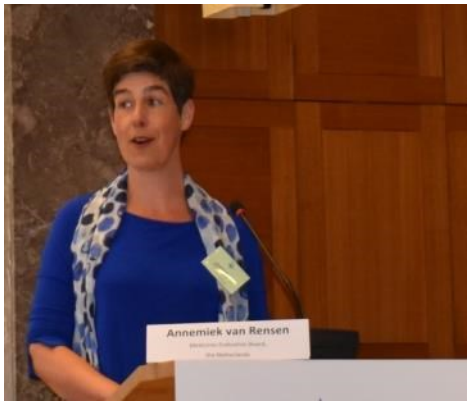
Patient data are subjective – can they be relied upon in research?

- Industry and regulators are coming to realize that they need to capture patient data – for example different types of pain – systematically to ensure that the information is valid and analysed appropriately.
- Appendix 1 to the U.S. FDA guidance deals with methods to collect patient experience data, and funding is being made available in the U.S. for development of tools for patient-centered outcomes research.

Who are the "patients"?

- All people should have a say in the development and safe use of medicines, including healthy young persons that may be patients in the future.
- Patients living with diseases, disorders and health conditions gain a unique experience and can provide valuable input into the development and the safe use of medications.
- Patients were defined broadly to not only include the individual patient, but also their care givers and families, and patient advocacy groups.

SESSION 1



Chair: Annemiek van Rensen,
Medicines Evaluation Board, the Netherlands

Presentations

Overview of the proposed CIOMS guidance

This presentation described the work of the CIOMS Working Group XI and outlined the topics that the proposed guidance is intended to cover. A comprehensive glossary will also be provided, compiling the terms and definitions used by different organizations.

Kerry Leeson-Beevers, Alström Syndrome UK

Elisabeth Oehrlein, U.S. National Health Council

Patient involvement initiatives around the world

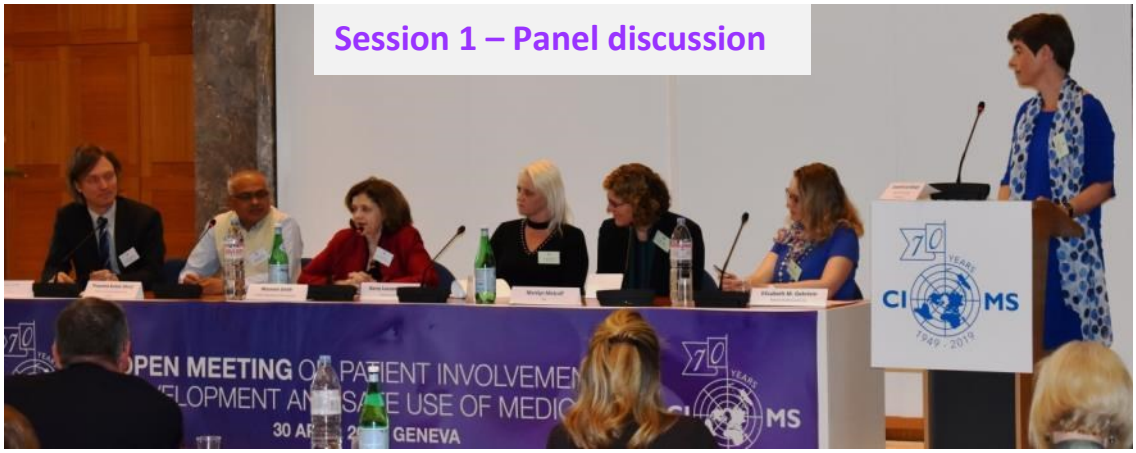
The CIOMS guidance will include a "landscape" of existing patient engagement / patient involvement initiatives around the world, and how these have developed over time. One aim of this section is to refer readers to relevant initiatives. The remainder of the guidance will focus on those areas where guidance is currently scarce, e.g. for patient involvement in low-resource settings and in the post-marketing phase of medicines.

How can patients advance treatments for their disease?

A chapter will address the different roles that Patients, healthcare providers, the pharmaceutical industry and regulators can play in advancing treatments to improve patients' wellbeing. It looks at each stage of the medicines life cycle, from when the need for a new medicine is first recognized through its development, and regulatory review, with special emphasis on communication and monitoring of medicines once they have been authorized for marketing.

Marilyn Metcalf, GSK

Session 1 – Panel discussion



Additional panellists (from left):

Kacper Rucinski, Fundacja SMA - Spinal Muscular Atrophy Europe
Prasanna Kumar Shirol, Organization for Rare Diseases India (ORDI)
Maureen Smith, Canadian Organization for Rare Disorders (CORD)

Summary of discussion:

Do you listen to individual patients, or to representatives of patient groups?

- When drug developers seek to hear the views of patients on meaningful endpoints in clinical studies, they typically invite expert patients or advocates representing patients with a specific condition.
- The FDA guidance on Collecting Comprehensive and Representative Input includes detailed provisions on representativeness.

Why should patients be consulted in drug development?

- Resources for drug development are limited and must be allocated strategically to maximize health benefits. Factors to consider include the public health impact of a given disease, existing products in the pipeline, urgency, and others.
- Patient involvement at the beginning of the drug development process is of vital importance, because quite often the clinical trial outcomes do not align with what matters to patients. This is reflected in a disconnect between the outcomes that patients report in their submissions to health technology assessment bodies and those measured in clinical trials.
- To identify unmet needs it is important to identify information gaps. For example, patients with diseases that cause few symptoms may be less vocal/organized than other groups.

What are the challenges in low- and middle income countries (LMIC)?

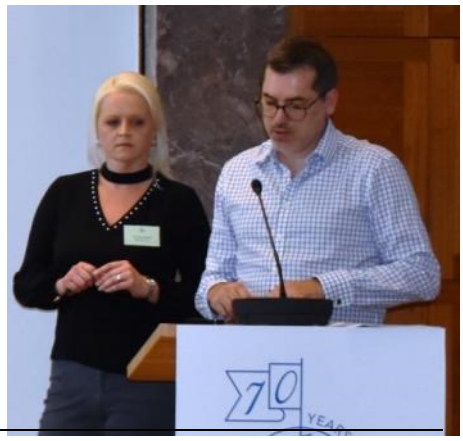
- Awareness is needed by patients and health professionals on how they can get involved in, for example, clinical trials.
- In Uganda, there are some patients sitting in research committees, but they are not participating in a meaningful way. It was recommended that the CIOMS guidance make a strong call for the patients' voices to be heard proactively, and the patients' experience to be translated into policy.
- In India patients don't have a strong voice. The CIOMS guidance should consider the special circumstances in resource limited settings. It was suggested that international documents like CIOMS guidance is respected in LMIC settings and could be taken up in national policies to support more patient involvement, including direct reporting of side effects.
- Pharmacists are patients' first (and sometimes only) point of contact in many countries, especially in LMIC. It was recommended that their roles should be considered in developing the CIOMS guidance.

Are there examples where patient involvement has led to better products?

- The U.S. NHC has documented some examples. One company was able to save unnecessary expense for a high tech dermatological product by finding about patient preferences at an early. Conversely, another company needlessly invested in an insulin delivery device that patients found cumbersome to use, and that was withdrawn after only six months on the market.

SESSION 2

Co-chairs: Kerry Leeson-Beevers, Alström Syndrome U.K.; Nikos Dedes, European AIDS Treatment Group



Presentations

Guiding principles for engagement: avoiding conflict of interest, fair compensation …

François Houÿez, EURORDIS

Many different stakeholders are involved in the development and safe use of medicines. Openness and transparency about their interests are the first step towards identifying and managing any conflicts. These should be seen and interpreted in context, and there will sometimes be a trade-off between competence and independence. The presentation gave real-life examples of the kinds of conflicts of interest that may arise, how they can be managed, what types of activities patient representatives can be safely involved in, and what constitutes fair compensation for their involvement.

Patient involvement in designing medicines labeling

Meredith Smith, Amgen

"Labelling" (called "product information" in the EU) are the documents providing officially approved information on a medicine for healthcare professionals and patients. There is increasing emphasis on labelling being understandable, actionable and relevant for patients. They CIOMS guidance aims to describe best practice principles for patient involvement in designing patient package inserts and patient information leaflets, pilot-testing materials, and evaluating their effectiveness once a product is on the market.

Isabelle Moulon, European Medicines Agency

Minimizing the risk of medicines: how patients can contribute

No medicine is without risk, and patients must be protected from these risks whenever they are taking a medicine. This is routinely done through the legal status of medicines, warnings on the patient leaflet, and appropriate packaging and pack sizes. For certain products there are also additional measures such as educational programmes, prescribing checklists or controlled-access programmes. The proposed CIOMS guidance will describe how patients can be involved in the design, implementation and evaluation of additional risk minimization measures. The presentation also showed how the European Medicines Agency currently engages with patients in risk minimization activities.

Session 2 – Panel discussion

Additional panellists:

- **Francesca Sofia**, International Bureau for Epilepsy (first from left)
- **Matthew May**, European Patients' Academy (EUPATI) (fourth from right)
- **Theobald Owusu-Ansah**, Hepatitis Foundation of Ghana (third from right)

Summary of discussion:

Conflict of interest: Are there any systematic rules?

- Simply speaking, conflict of interest can be defined as "circumstances posing risks that the primary interest is influenced by a secondary one".
- Conflict of interest and its implications should always be seen and managed in context.
- One should distinguish between individual and organizational conflict of interest. Organizations should have clear policies on what to do in which situation. Experience has shown that where there are such policies, there is less conflict of interest.

Who are the "patients"?

- The EUPATI Guidance for patient involvement in industry-led medicines R&D has a section defining the term "patient". A patient can be an individual, a carer, a patient advocate, a patient organization representative or a patient expert who has technical knowledge for example in research and development (R&D) or regulatory affairs.
- All patients have the same rights, but not all can champion their cause equally well. For example there are 65 million people worldwide living with epilepsy, but they have little visibility.

Taking the example of patients with epilepsy, what could affect their ability to get involved?

- About 30 percent of them have seizures despite taking medicines; they are motivated to get involved but it is difficult for them as they are not well, and in some cases have other health conditions too. And those who are controlled on their medicines may not see a need to get involved. Many epilepsy patients have "been taught to hide" due to the social stigma surrounding their condition.

How can medicines labelling be made more user-friendly?

- Complete information should be provided, but in a short and easy-to-read format.
- Digital technologies can be used to make information easier to navigate, possibly enabling specific groups to access the information that concerns them (e.g based on age, gender etc.).

Should a prescriber inform the patient when a product is used "off label"[1]?

- Yes, prescribers should give complete information if they want patients to trust them.

It would be ideal to involve patients and social scientists in testing risk minimization measures – but is it feasible?

- Medicines developers and regulators must carefully consider where to allocate limited resources. It was recommended that the CIOMS document should describe practical barriers to its recommendations in each chapter, and propose solutions on how to overcome them.

[1] Off label use: Use of a medicine for an unapproved indication or in an unapproved age group, dosage, or route of administration (from: European Medicines Agency Glossary).

SESSION 3

Chair: Kaisa Immonen, European Patient's Forum (EPF)

Presentations

Leo Russo, Pfizer , Inc.

Using patient data to evaluate the benefits and risks of medicines

Patient data are collected when people participate in clinical studies seek medical treatment, or report an adverse reaction to the health authority. These data are kept confidential and analyzed in an anonymous way. In the electronic age, the channels to collect patient data are multiplying, and people are not always aware that they volunteer their information. Patients should have a say in how their data are shared and used. They should also have access to their own data, and to the findings of studies that were based on their data.

If things go wrong: The role of patients in designing and distributing alerts

Patients are often the first to raise early warnings about medicines. They can also join groups that produce bulletins and contextual aids. A cohesive strategy is needed to harness additional patients, groups and information sources, and ensure that processes are in place before a crisis arises.

The drug development and oversight lifecycle is not the same as the patient lifecycle: experience symptoms, get a diagnosis, seek treatment, and possibly receive medication, which may need to be continued or changed over time. When a product is withdrawn or recalled patients should be informed of all their treatment options and supported in deciding what to do next.

Suzanne Schrandt, Arthritis Foundation, U.S.

Corinna Schaefer German Agency for Quality in Medicine.

Patient involvement in developing treatment guidelines

Having patients and members of the public at the table increases the credibility and legitimacy of guideline development. This has been recognized in the AGREE II international tool for the assessment of practice guidelines. And yet, not all guidelines are developed with patient involvement, because often there are not many active patients, and it is challenging to involve them due to their busy schedules. The G-I-N PUBLIC toolkit gives some best-practice examples of how patients and the public can participate in guideline development, and how information can be communicated to them.

Patient involvement cannot be tokenistic: people must “mean it”, and it should result in better outcomes for all stakeholders, including patients. Patient engagement activities must be planned carefully to fit the specific context, and it requires training and support not only for patients but for everyone involved.

Session 3 - Panel discussion

Additional panellists (from left):

- **Ariadne Guimarães Dias**, Casa Hunter, Brazil
- **Umesh Chawla**, India HIV/AIDS Alliance
- **Estelle Jobson**, EUPATI Switzerland; EUPATI fellow and patient advocate
- **Talia Lacroix**, Health Canada (CIOMS WGXI member)

Summary of discussion:

The focus of this discussion was about "real world data" that are generated about patients during routine health care.

"Big Data", "Real World Data":

- These often-used terms are potentially misleading, as they imply that these data are better than others. It was recommended that the proposed CIOMS guidance should define the meaning of these terms and discuss the use of such data.
- Not all real world evidence is used in regulatory decision-making. Factors such as data reliability and validity, scientific question of interest and study design are considered.
- Researchers should use caution when trying to answer research questions with data that were collected for other purposes.

Transparency, privacy

- Transparency in all interactions between stakeholders is crucial to create trust, as a basis for collaboration.
- On the other hand, overly stringent privacy and data protection laws can hamper the collection of data which would benefit patients. Most NGOs cannot afford lawyers to deal with these hurdles.
- Useful guidance on data privacy and transparency has been provided by the Patient-Centered Outcomes Research Institute (PCORI).

Do patient have access to their own data?

- The OpenNotes approach, where patients have online access to their primary care physician's visit notes from home, has been effective in the U.S and is emerging elsewhere.

What motivates patients to donate their own data?

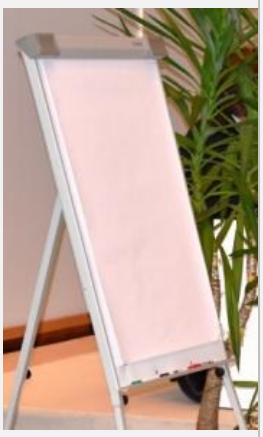
- In the U.S. a roundtable discussion has shown that many patients are unaware of the data that are being generated about them, but are happy to contribute if they see the benefits.
- Typically, patients will donate their data if they see that this might lead to improvements in their own medical care.
- In resource-limited settings, patients have to deal with many basic challenges in accessing health care, and most of them do not know what happens to their data.

Providing feedback to patients

- Patients must be given more feedback about how their data are used.
- Pharmaceutical companies are legally required to provide feedback to patients at the same time, which is challenging for example when a study closes prematurely and this is announced on general media channels, or when different time zones are involved.
- Researchers have an obligation to publish their findings, yet this does not always happen.

ADDITIONAL INPUT

(Collected on a flipchart in the meeting room)



- *Should the patient guidance be enhanced/modified for patient advocacy groups?*
- *In "safe use" we are not addressing medicines shortages, which often result in poor quality "generics" / substitutes / biosimilars on the market.*
- *Dosage of drugs under compassionate access programmes and while state reimbursement policy to be streamlined*
- *Guiding patients and teaching them about what clinical trials are, the role of regulatory bodies, what the processes are, etc? Expert patients already learn this through experience. What about individual patients? Whose role is it to educate them?*
- *Need for budget to support the action plan regardless of looking at source for funding (For future plans)*
- *What about very common conditions, where patients do not feel concerned, special, etc, and no patient organisations exist (ex. Cardiac conditions). From where should the patient engagement come?*

Input to the work of the CIOMS Working Group XI is welcome any time.
Contact us at info@cioms.ch.

Concluding session

The session chairs were invited to the podium to take extra questions. The following points were mentioned during the closing session:

The need for CIOMS guidance on patient involvement

Throughout the meeting, many participants confirmed that the proposed CIOMS guidance fills an important need. The following recommendations were made during the closing session:

- The guidance should call for patient involvement in clinical trials review and in health technology assessment (HTA). Even within Europe this is not yet happening everywhere.
- The guidance should speak for people in all economic settings, and be taken on board by regulators globally.
- All patients should have a voice – no patient groups are more important than others.

Dissemination and implementation

- It will be important to promote this guideline once it is published. A dissemination plan will be agreed in consultation with patient organizations.

Press conference

A press conference was held at the Geneva Press Club after the meeting.
See the video recording here.

Annex 1: Participant list

* = Member of the CIOMS Working Group XI on Patient Involvement

*	Leanne **Angst-Wu**	Roche
*	Ola **Apara**	Takeda
	Poonam **Bagai**	CanKids India / Pallium India
	Raffaella **Balocco**	World Health Organization (WHO)
	Janis **Bernat**	International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)
	Susan **Bhatti**	Merck KGaA
*	Stella **Blackburn**	IQVIA
*	Matthias **Boedding**	Merck KGaA
	Thomas **Bols**	Drug Information Association (DIA)
	Donato **Bonifazi**	Consorzio per Valutazioni Biologiche e Farmacologiche
*	Marc **Boutin**	National Health Council, U.S.
	Nicholas **Brooke**	The Synergist
	Nathalie **Cambon**	Roche
	Umesh **Chawla**	India HIV/AIDS Alliance
	Emer **Cooke**	World Health Organization (WHO)
*	Nikos **Dedes**	European AIDS Treatment Group (EATG)
	Guy **Demol**	MSD
	Bettina **Doepner**	CSL Behring GmbH
	Vanessa **Dos Reis Ferreira**	Santhera Pharmaceuticals Schweiz AG
*	Brian **Edwards**	International Society of Pharmacovigilance (ISOP)
	Brigitte **Franke-Bray**	International Federation of Associations of Pharmaceutical Physicians & Pharmaceutical Medicine (IFAPP)
	Ariadne **Guimarães**	Casa Hunter, Brazil
*	Linda **Härmark**	Netherlands Pharmacovigilance Centre Lareb
	Esteban **Herrero-Martinez**	Abbvie
	Pushpa **Hossain**	Metabolic Support U.K.
*	François **Houÿez**	EURORDIS
	Samia **Hurst**	Swiss Academy of Medical Sciences, CIOMS Vice-President
	Ghada **Ibrahim**	Patient Advocates for Cancer Research and Treatment (PACRT)
*	Kaisa **Immonen**	European Patient's Forum (EPF)
	Ulf **Janzon**	Sveriges Farmaceuter (Pharmacists' Association of Sweden)
	Shalini **Jayasekar Zurn**	Union for International Cancer Control (UICC)
	Estelle **Jobson**	European Patients' Academy (EUPATI) fellow and patient advocate
*	Regina **Kamoga**	Community Health and Information Network (CHAIN), Uganda
	Petra **Kirchner**	Roche
*	Talia **Lacroix**	Health Canada
	Sophie **Lasseur**	World Health Organization (WHO)
	Renata **Lazarova**	Roche
	Hervé **Le Louët**	CIOMS President
	Sue **Le Roux**	CIOMS
*	Kerry **Leeson-Beevers**	Alström Syndrome UK
	Agnès **Lillo-Le Louët**	Hôpital Européen Georges Pompidou
*	Marie **Lindquist**	Uppsala Monitoring Centre (UMC)
	Mariangela **Lupo**	Teddy European Network of Excellence for Paediatric Clinical Research
	Pia **Massatsch**	Clinical Trials Unit (CTU), University of Bern
*	Yusuke **Matsunaga**	Pharmaceuticals and Medical Devices Agency (PMDA), Japan

* = Member of the CIOMS Working Group XI on Patient Involvement

	Matthew **May**	European Patients' Academy (EUPATI)
	Olga **Menang**	PATH
	Adi **Mester**	World Health Organization (WHO)
*	Marilyn **Metcalf**	GSK
	Günther **Metz**	Santhera Pharmaceuticals Schweiz AG
*	Isabelle **Moulon**	European Medicines Agency (EMA)
	Bettina **Mueller**	Bayer AG
*	Theresa **Mullin**	U.S. Food and Drug Administration (FDA)
	Mai Lise **Nguyen**	Roche
*	Elisabeth M. **Oehrlein**	National Health Council, U.S.
	Theobald **Owusu-Ansah**	Hepatitis Foundation of Ghana
*	Shanthi **Pal**	World Health Organization (WHO)
	Giovana **Palma**	Roche
	Joan **Peppard**	European Association of Hospital Pharmacists
*	Peter **Pitts**	Center for Medicine in the Public Interest (CMPI)
	Lembit **Rägo**	CIOMS Secretary-General
*	Cheryl **Renz**	AbbVie
	Menico **Rizzi**	World Health Organization (WHO)
	Kacper **Rucinski**	Fundacja SMA - Spinal Muscular Atrophy Europe
*	Leo **Russo**	Pfizer
	Molly Kate **Rwankore**	National Forum of Networks for PLHIV in Uganda (NAFOPHANU)
*	Ken **Sakushima**	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
	Caroline **Samer**	International Union of Basic and Clinical Pharmacology (IUPHAR)
*	Corinna **Schaefer**	German Agency for Quality in Medicine /World Medical Association
	Suzanne **Schrandt**	Arthritis Foundation, U.S.
	Prasanna Kumar **Shirol**	Organization for Rare Diseases India (ORDI)
	Maureen **Smith**	Canadian Organization for Rare Disorders
*	Meredith **Smith**	Amgen Inc.
	Francesca **Sofia**	International Bureau for Epilepsy, Italy
*	Christine **Stürchler**	Novartis
*	Panos **Tsintis**	CIOMS Adviser
	Michel **Vallotton**	CIOMS Past President
*	Annemiek **van Rensen**	Medicines Evaluation Board, the Netherlands
	Roberto **Verna**	World Association of Societies of Pathology and Laboratory Medicine, CIOMS Executive Committee member
	Andreja **Vujičić Žagar**	Centre hospitalier universitaire vaudois (CHUV)
	Kathrin **Wawra-Hehenberger**	CSL Behring GmbH
*	Judy **Zander**	U.S. Food and Drug Administration (FDA)
	Elena **Zhuravleva**	Roche
	Monika **Zweygarth**	CIOMS