Patient Involvement in the Development, Regulation and Safe Use of Medicines

A **consensus report by CIOMS WG XI**
Geneva, Switzerland, 2022

Presented by François Houÿez, EMA meeting with all Eligible Patient Organisations, 15 November 2022

CIOMS – Introduction https://cioms.ch/

Council for
International
Organizations of
Medical
Sciences

- Founded in 1949 by WHO and UNESCO
- In official relations with WHO
- UNESCO associated partner
- ICH Observer since 2016

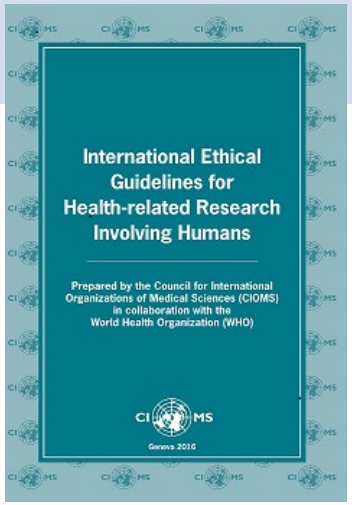
Mission Statement

CIOMS mission is to advance public health through guidance on health research including ethics, medical product development and safety

CIOMS Main Areas of Work

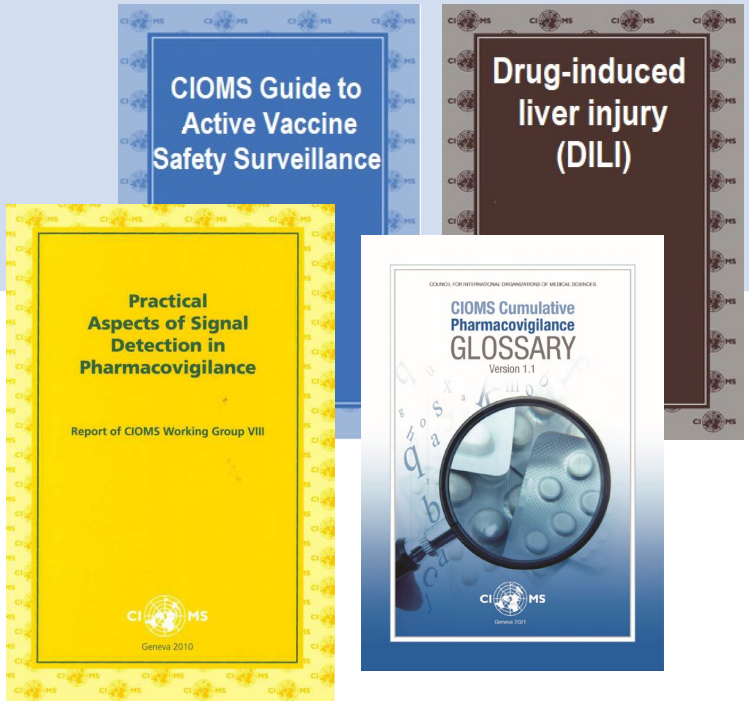
Bioethics

- Since 1967; 1st CIOMS Round Table Conference 'Biomedical Science and the dilemma of Human Experimentation'
- Issued significant guidelines
  - Latest revision 2016
  - Focus on 'low -and middle-income countries'
  - Available in 10 languages, e.g. Chinese, Spanish, Japanese, Russian



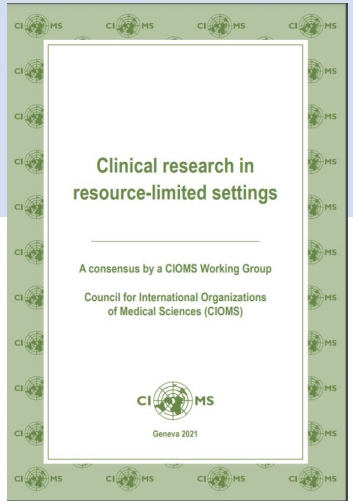
Pharmacovigilance

- 1986: first PV Working Group
- 13 more working group reports to date
- Several ICH Guidelines are based on results of CIOMS Working Groups
- Cumulative Glossary 2021



Product development

- Since 1977
  CIOMS Round Table Conference, 'Trends and Prospects in Drug Research and Development'
- 2021: Clinical Research in Resource-Limited Settings, CIOMS Working Group report



CIOMS Working Group XI:
Patient involvement in the development, regulation and safe use of medicines
Started in April 2018

Objective	To discuss benefits of patient involvement during the whole life-cycle of a medicine, from early development through regulatory process and post-marketing use until (potential) retirement - life-cycle approach
Composition	International, with involvement of patient representatives, regulators (including US FDA and EMA), industry, academia and various international/national organizations including WHO
Transparent process	All full WG meeting minutes made public, public meetings organized for input, public consultation of the final text with structured analysis and use of comments
Content	Ethical considerations, executive summary, 11 chapters with annexes and numerous case studies, a very comprehensive glossary
Accessibility	The publication will be a ‘public good’ – an open access online publication with limited hard copies at a price of 1 CHF + postal costs

Some general remarks

Most of the work based on scientific literature search

- Few patient organisations publish their work / engagement
  - Ignores important stories / facts that founded modern patient advocacy
  - Testimonies from patient advocates difficult to include in the report, as a “reference” would be systematically requested
  - Some “grey literature”, but very limited
- When published, often initiated by a pharma company

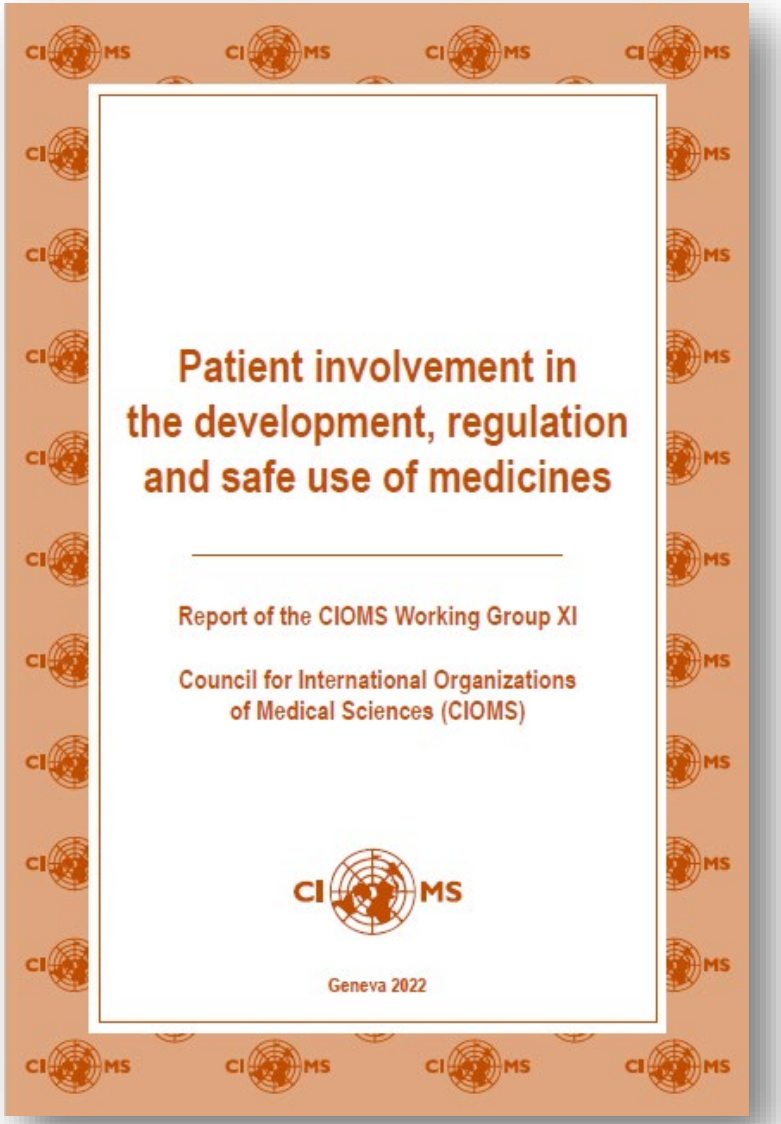
All references are in English language

- References from USA / UK authors are abundant
- Difficulties to bring in other experiences
- Yet, some efforts to open the working group to advocates from all world regions

Composition of the working group was well balanced when it started, but this changed over time

- Difficult to maintain the involvement of public bodies / patient advocates throughout the 3 years with same intensity
- When industry people usually are tasked to contribute

Report Content (download here)



Chapter 1. Introduction

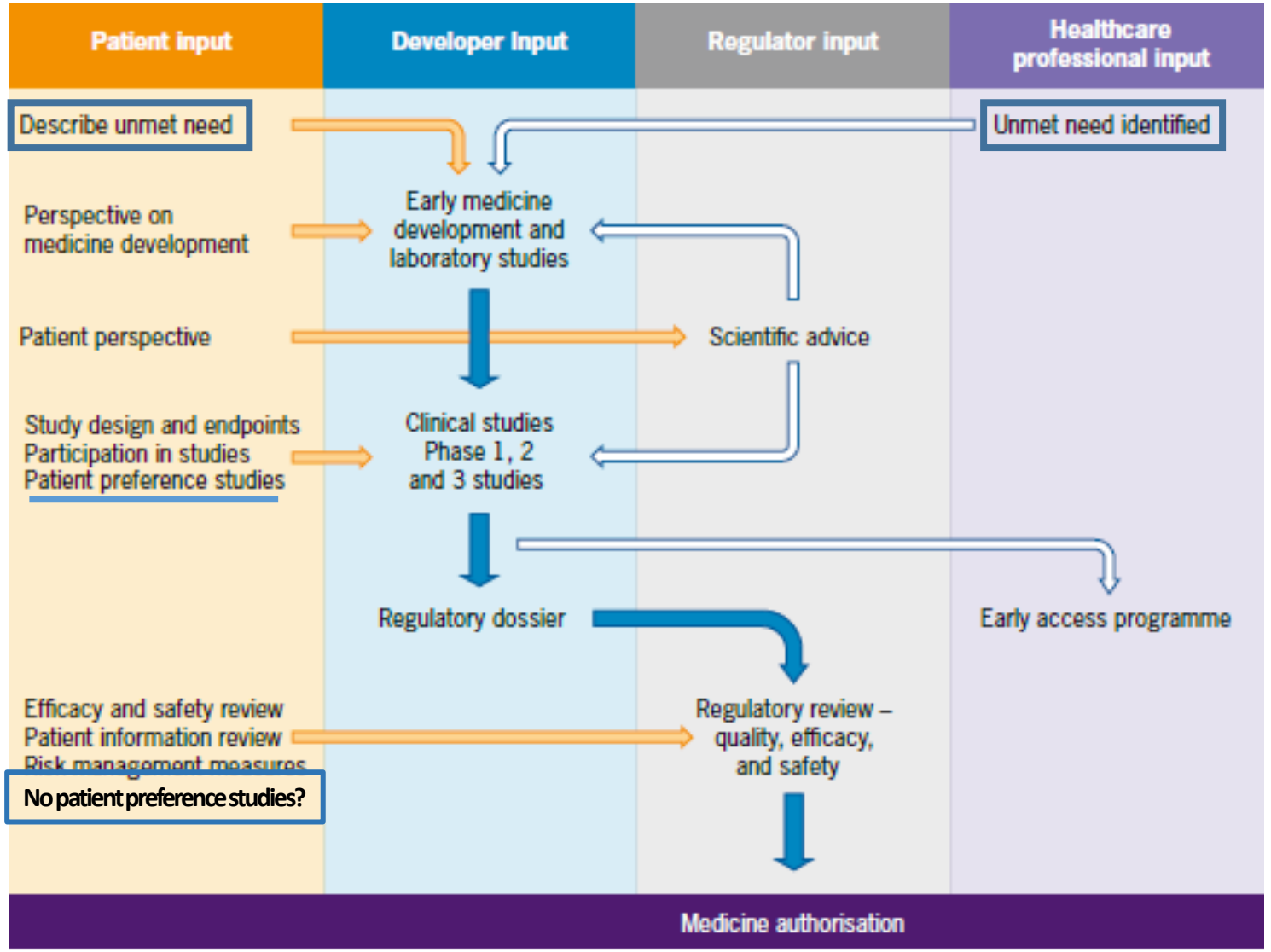


Figure 1a: Patient involvement during a medicine lifecycle: ***pre-authorisation***

Source: CIOMS Working Group WG XI

Illustration

- CAB meeting with Agouron, 1996 | Nelfinavir, new HIV protease inhibitor | CAB cost: $50,000 | RoI: >10,000 x

- Phase I IPK/PD results, study 510

1.5 g/day: effective
10% loose stools (grade 2)

2.25 g: more effective

3.00 g: even more effective
30% loose stools – no grade 3 or 4

- Agouron and clinicians chose 2.25 and 3.00 g or higher for phase III

CAB disagreed

1.5 and 2.25 preferred

Finally 2.25 and 2.5 in phase III

- Authorised in 1998 at 2.25 or 2.5/day

Patients were staying longer on treatment than expected. Dose adjustment ++, several strengths

Children could be treated for 1st time, well tolerated. Demand > offer - tensions

Surplus of 500 Mio$ sales 1st year compared to Agouron's estimates

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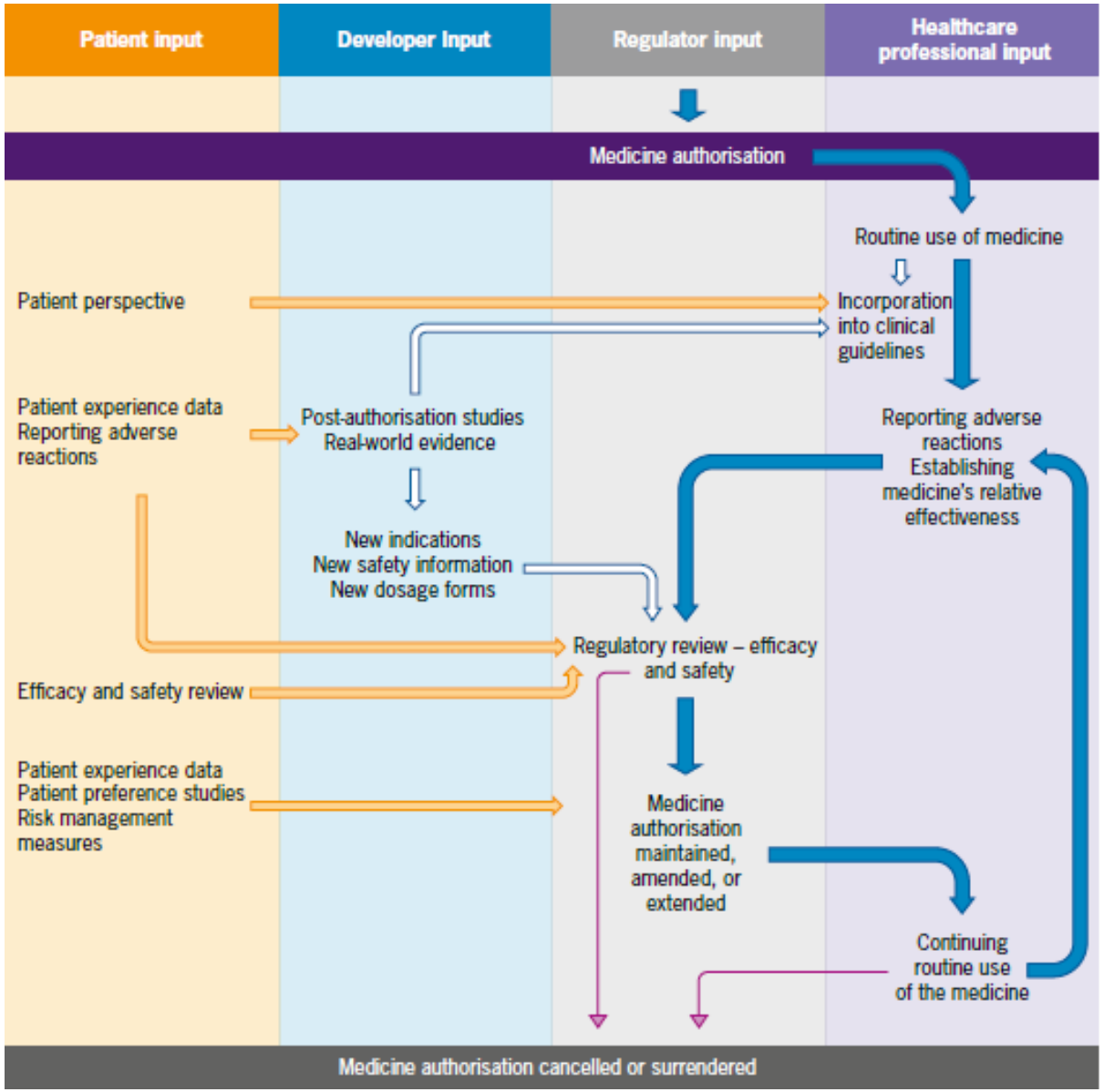

Figure 1b: Patient involvement during a medicine lifecycle: ***post authorisation***

Source: CIOMS Working Group WG XI

Chapter 2. Landscape: key points

1. Patient advocates, especially members of the HIV/AIDS and rare disease communities, advanced the role of patients in the development and regulation of treatments.

2. Patients, pharmaceutical companies and medicine regulators have collaborated to overcome real and perceived regulatory, cultural and communication barriers to patient engagement in medicines development.

3. Case examples of patient involvement in the development, regulation and use of medicines demonstrate considerable benefit to all parties: a win-win situation.

4. The cultural shift to greater involvement of patients needs to continue by deepening involvement of patients in areas such as:
   a. Identifying patient-related treatment outcomes;
   b. Participating in regulatory review;
   c. Contributing to constructing, reviewing and disseminating medicines information;
   d. Monitoring medicines safety by making direct contribution to reporting and assessing side effects.

Chapter 3. Guiding principles

Chapter 4. Table 3. Stakeholder collaboration examples on introducing, improving, and using medicines

Ongoing →

Stage:	Unmet need	Early development	Clinical development	Regulatory review	Healthcare delivery Safety monitoring	Health & data communication
Patients	• Form patient organisations • Produce information for patients about their disease • Conduct / contribute to early research • Create patient registries • Create biosample banks • Develop research priority setting partnerships, *e.g.* James Lind Alliance (see section 5.3.7)	• Establish research priorities • Describe living with disease • Describe standard of care – may not be treatments available (likely to be some variability) • Describe being treated • Describe needs, goals and wants	• Develop patient-relevant outcomes • Contribute to protocol design • Contribute to benefit-risk profile • Co-create / review research plans • ASTERIX (Advances in Small Trials dEsign for Regulatory Innovation and eXcellence) • Co-create / review information for patients • FDA MyStudies App	• Contribute to dossiers / reviews • Members of scientific committees • EMA involvement • FDA collaborative process • User-test patient leaflets and some risk management materials	• Learn about treatments • Contact developers about promising products for compassionate use • Talk about treatments and goals with HCP • Tell HCP / sponsor / regulator about side effects • Engage conversations with developers following a safety signal once the product is on the market. This may be the first dialog between patients and drug developers.	• Co-create / review non-promotional information • Co-create / contribute (to) good information guidance
Healthcare professionals	• Establish clinical guidelines • Characterise disease • Develop natural history studies	• Talk with / listen to patients about their needs, goals, and wants	• Inform patients about clinical trials and ensure they are making an informed choice • Discuss with patients their interest and eligibility for clinical trials • Support patients throughout the trial and give regular feedback • Talk about standard treatment	• Give input on current treatment regimens	• Learn about safe and appropriate use of product • Report side effects promptly • Engage with patients to establish treatment guidelines	• Co-create / review / distribute non-promotional materials
Developers	• Joint research priority partnership, *e.g.* The James Lind Alliance (see section 5.3.7)	• Discuss with patients their needs, goals, and wants • PFMD	• Co-create with patients or request patient review of research plans; incorporate needed changes • Co-create with patients or request patient review of information for patients; incorporate needed changes • Developers contact patient organisations to recruit for clinical trials (should not be the first interaction with patients) • Provide clinical trial feedback to patients (make accessible)	• Include patient input in dossiers • Propose patient-oriented labelling	• Monitor safety and effectiveness of treatments in patient-friendly ways • Involve patients in risk minimisation planning and activities; see also CIOMS Working Group IX report	• Co-create non-promotional information per guidance
Regulators	• Early dialogue/hearing with patients and patient groups (*e.g.* EMA's Innovation Task Force and FDA's Patient Listening Sessions) • Involvement in orphan designation • Involvement in scientific advice	• Invite / attend public discussions of patients' diseases, treatments, needs, goals, and wants • FDA CDER PFDD • EMA multistakeholder workshops • Talk with sponsors and patients about development plans	• Co-create with patients and provide guidance on including patients' input in treatment development • FDA CDER PFDD • EMA patients & consumers • EMA scientific advice • Talk with sponsors and patients about development plans and risk minimisation • Include patients as members of scientific committees, *e.g.* EMA paediatric committee PDCO, committee for orphan medicine	• Include patient input in review of dossiers • EMA scientific committees review process • Include user-testing for patient leaflets and relevant risk management materials	• Monitor safety and effectiveness of treatments in patient-friendly ways • EMA PV stakeholder forum • FDA RWE Framework • Hold public hearings for input	• Co-create / provide guidance on including patients' input in non-promotional information • EMA review of documents

Source: CIOMS Working Group WG XI

An interesting success already (out 6/09/22)

- In major conferences worldwide
  - CoRE Scientific Conference 2022: 'Patients as Partners for Health' in Singapore (Lembit, Juan, François)
  - Reuters Pharma event Nice, 11th of October (Estelle Jobson)
  - Operationalise Early Access Programmes 19 Oct, London (François)
  - European Pharmacovigilance Congress 10th November, Milan
  - PVNET 8th November, New York

- First month: 1,193 downloads
- 500 hard copies sent out
- Promoted by International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine

In short

This report is a success: it proposes universal recommendations for the involvement of patients

This report is a progress: it can be used by private and public organisations who haven't yet started involving with patients as the case was not fully "demonstrated"

A broad dissemination will ensure the success of the work done and its conclusions

The report is a hope: the hope that you will enrich it with more experiences, more demonstration of how useful it is to engage with you all. The hope you will publish more!