Patient involvement in drug development and safe use

Safety and Legal Support of Medicinal Products: from Development to Medical Use
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Content

- How it started?
- Why patient involvement in drug development
- Moving from occasional involvement into system of being involved
- What is CIOMS?
- CIOMS Working Group XI – Patient Involvement in Drug Development and Safe Use
- Conclusions

How patient involvement started (1)?

- For many decades patient involvement in new drug development has been largely focused on/limited to participation in *clinical trials*
- It dealt with important *ethical considerations* and legal issues protecting study participants
- Ethical issues:
  - Nurenberg Code 1947
  - WMA Declaration of Helsinki 1963, latest 2013 (7th revision)
  - CIOMS - International Ethical Guidelines for Health-related Research Involving Humans, first 1982, latest 2016
  - Belmont Report 1979
  - The Office for Human Research Protections (OHRP) is a small office within the US Department of Health and Human Services (DHHS) - 2000

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How patient involvement started (2)?

HIV/AIDS crisis in 1980s and 1990s

- First HVD drug approved in late 1980s – at large extent due to urgent advocacy efforts by people living with HIV/AIDS in Europe and in United States

Patients getting more and better organized in 1980s

- Patients with rare diseases setting up their organizations like National Organization for Rare Diseases (NORD) in 1987 in US

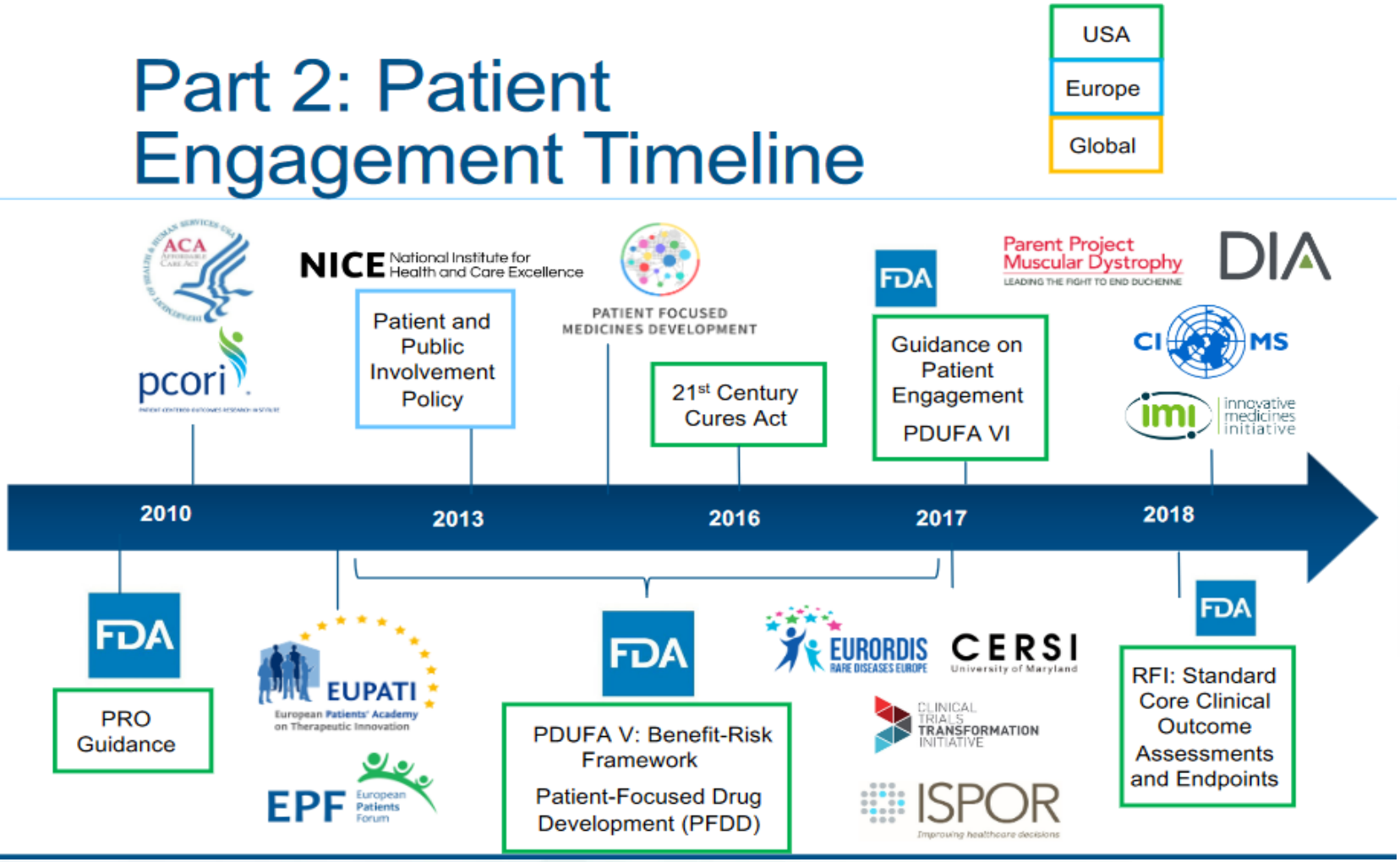
Part 1: Patient Engagement Timeline

USA
Europe
Global

Source: Marc M. Boutin , DIA San Diego June 2019

Pro – Patient Reported Outcomes
PDUFA – Prescription Drug User Fee Act
RFI – Request for Information

Part 2: Patient Engagement Timeline



Source: Marc M. Boutin , DIA San Diego June 2019

Why patient involvement is important?

- **Patients are uniquely positioned to inform the work of medicines regulators**
- Informing Assessment of Benefit-Risk
    - US FDA has learnings from over 5 years and 25 meetings focused on hearing about the experiences of patients living with serious chronic disease
- **Relationships with patients can impact the quality of clinical development programs**
    - Take-Aways from patients' shared experiences and their interests related to participation in clinical trials
- **Engaging patients can yield many opportunities for better quality development and better insight into Benefit-Risk**

Increasing incorporation of patient perspectives in clinical trials

❑ Explaining Value, Enhancing Awareness and Access

- ✓ Patients awareness of opportunities to participate in trials
- ✓ Factors considered in the decision to participate

❑ Design and Conduct of Patient-Centric Trials

- ✓ Challenges and burdens patients experience while participating in trials?
- ✓ How challenges can vary for adult versus pediatric patients
- ✓ Patient-engaged approaches and best practices

❑ Post-Trial Communications and Engagement

- ✓ Learning about trial outcomes

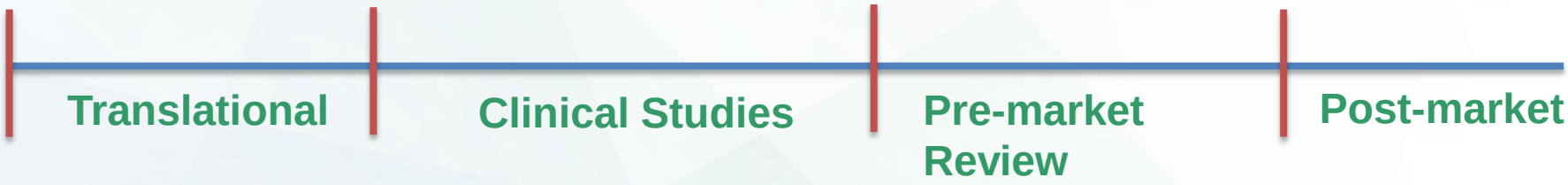
Further integrating patient perspective into medicines development and decision making

What impacts (burden of disease and burden of treatment), matter most to patients and how to measure them?

What aspects of clinical trials can be better tailored to meet the patients who (might) participate in the trial?

How to better integrate patient reported outcome data or elicited patient preferences into Benefit-Risk (BR) assessments?

How to best communicate the medicine related information to patients and prescribers? How to best manage risk?



Acronym & Logo

Council for International Organizations of Medical Sciences

- ***Founded in 1949 by WHO and UNESCO***
- ***In official relations with WHO***
- ***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

Organization

Executive committee

President: Prof. Hervé Le Louet - since Nov. 29, 2016 (member of PRAC)

Vice president: Prof. Samia Hurst (Swiss academy of sciences)

Secretary-General: Dr Lembit Rägo (CIOMS secretariat, former WHO Regulatory Unit Head)

<= 12 representatives (mostly from national and international members)

Secretariat

Secretary-General Dr. Lembit Rägo (since April 18, 2016) and team; located in Geneva (close to WHO und UN Palais des Nations)

Mandate: „day to day management in conformity with statutes and directions of executive committee“

CIOMS

Members Organizations - General Assembly

International Organizations (13)

National Organizations, Associate Members (12)

Associate Members (19)

Collaborations

Partners: Authoritative, international organizations dealing with related topics

e.g. WHO, PAHO/AMRO, ICH, IFPMA

Members (all in all – 44), Collaborations

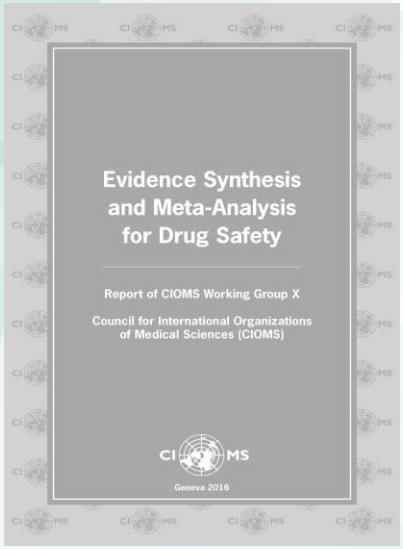
Member International*	Member National*	Member Associate*	Collaboration**
World Medical Association	Belgium - Comité des Académies Royales de Médecine	Medical Sciences Society (MSS-UQ) of Queensland University, Haiti	WHO
International Society of Pharmacovigilance (ISoP)	Indian Council of Medical Research (ICMR)	American Society for Bioethics and Humanities	UNESCO
International Society of Pharmacoepidemiology (ISPE)	Czech Medical Association	World Organization of Family Doctors (WONCA)	ICH
International Union of Basic and Clinical Pharmacology (IUPHAR)	Association of the Scientific Medical Societies in Germany	International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)	International Federation of Pharmaceutical Manufacturers Associations (IFPMA)
International Society of Internal Medicine	Israel – The Israel Academy of Sciences and Humanities	International Federation of Clinical Chemistry and Laboratory Medicine (ICLAS)	International Society of Pharmacovigilance (ISoP)
..... 8 others	..... 6 others	..... 14 others	..... and others

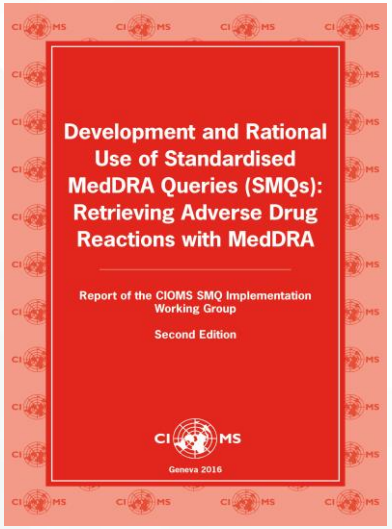
Pharmacovigilance: Working Groups

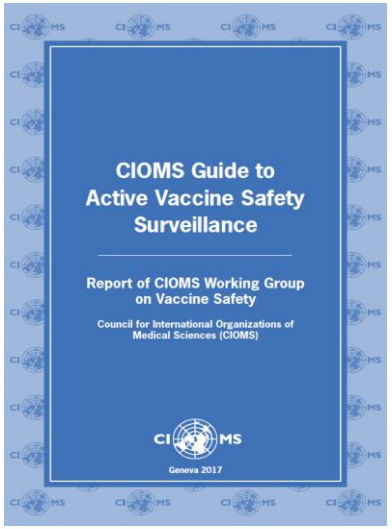
Working Group	Period (some examples)	Report / Year
CIOMS I	-	International Reporting of Adverse Drug Reactions (1990)
CIOMS II	-	International Reporting of Periodic Drug Safety Update Summaries (1992)
CIOMS III	-	Guidelines for Preparing Core Clinical Safety Information on Drugs (1995)
CIOMS IV	01/1995 – 07/1997	Benefit-risk balance for marketed drugs (1998); Revision started 2019
CIOMS V	04/1997 – 08/2000	Current Challenges in Pharmacovigilance: Pragmatic Approaches (1999)
CIOMS WG on SMQs	05/2002 -	Development and Rational Use of Standardized MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA (2004)
CIOMS VI	03/2001 -10/2004	Management of Safety Information from Clinical Trials (2005)
CIOMS VII	-	Development Safety Update Reports (DSUR): Harmonizing the Format and Content for Periodic Safety Report during Clinical Trials (2006)
CIOMS VIII	-	Practical Aspects of Signal Detection in Pharmacovigilance (2010)
CIOMS/WHO WG	11/2005 – 10/2010	Definition and Application of Terms for Vaccine Pharmacovigilance (2012)
CIOMS IX	-	Practical Approaches to Risk Minimisation for Medicinal Products (2014)
CIOMS X	06/2011 – 07/2015	Evidence Synthesis and Meta-Analysis for Drug Safety (2016)
CIOMS SMQ Implementation WG	(05/2002) – 2018/19	Development and Rational Use of Standardised MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA (2016)
CIOMS WG to Vaccine Safety	2013 -2016	CIOMS Guide to Active Vaccine Safety Surveillance (2017) CIOMS Guide to Vaccine Safety Communication (2018)
CIOMS WG on DILI	2017 – ongoing	

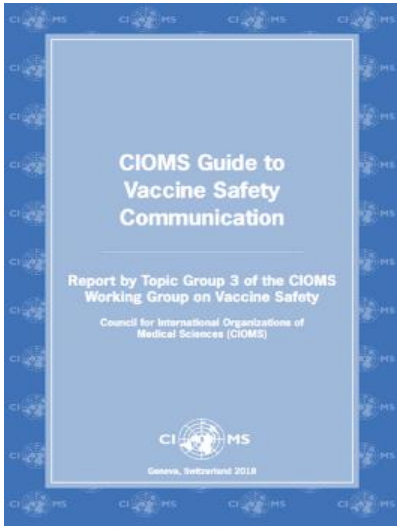
Pharmacovigilance: Recent Safety Publications

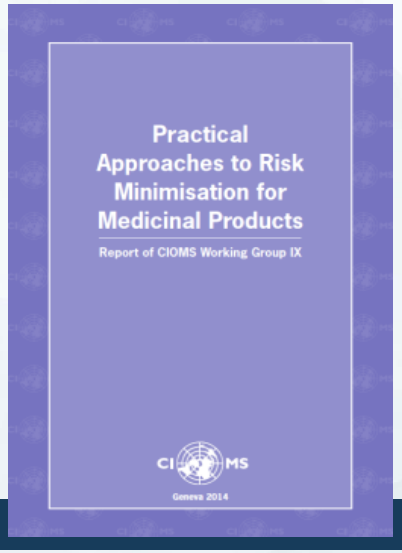
https://cioms.ch/shop/product-category/recently-published/

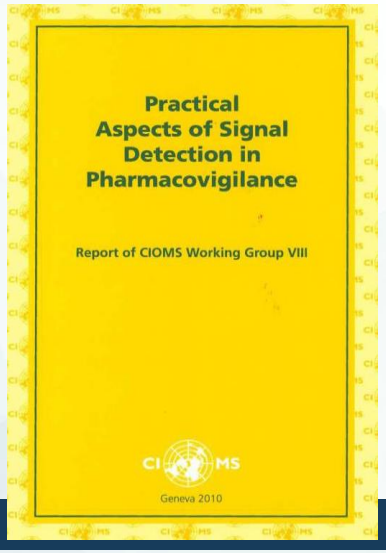


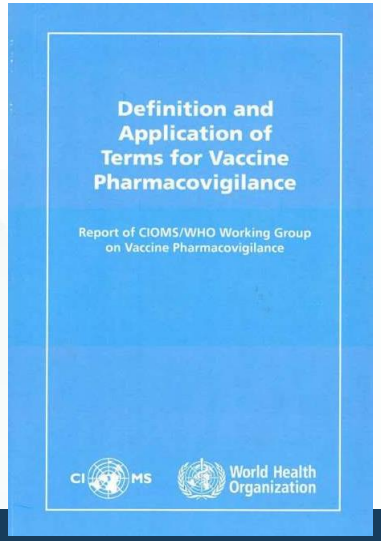












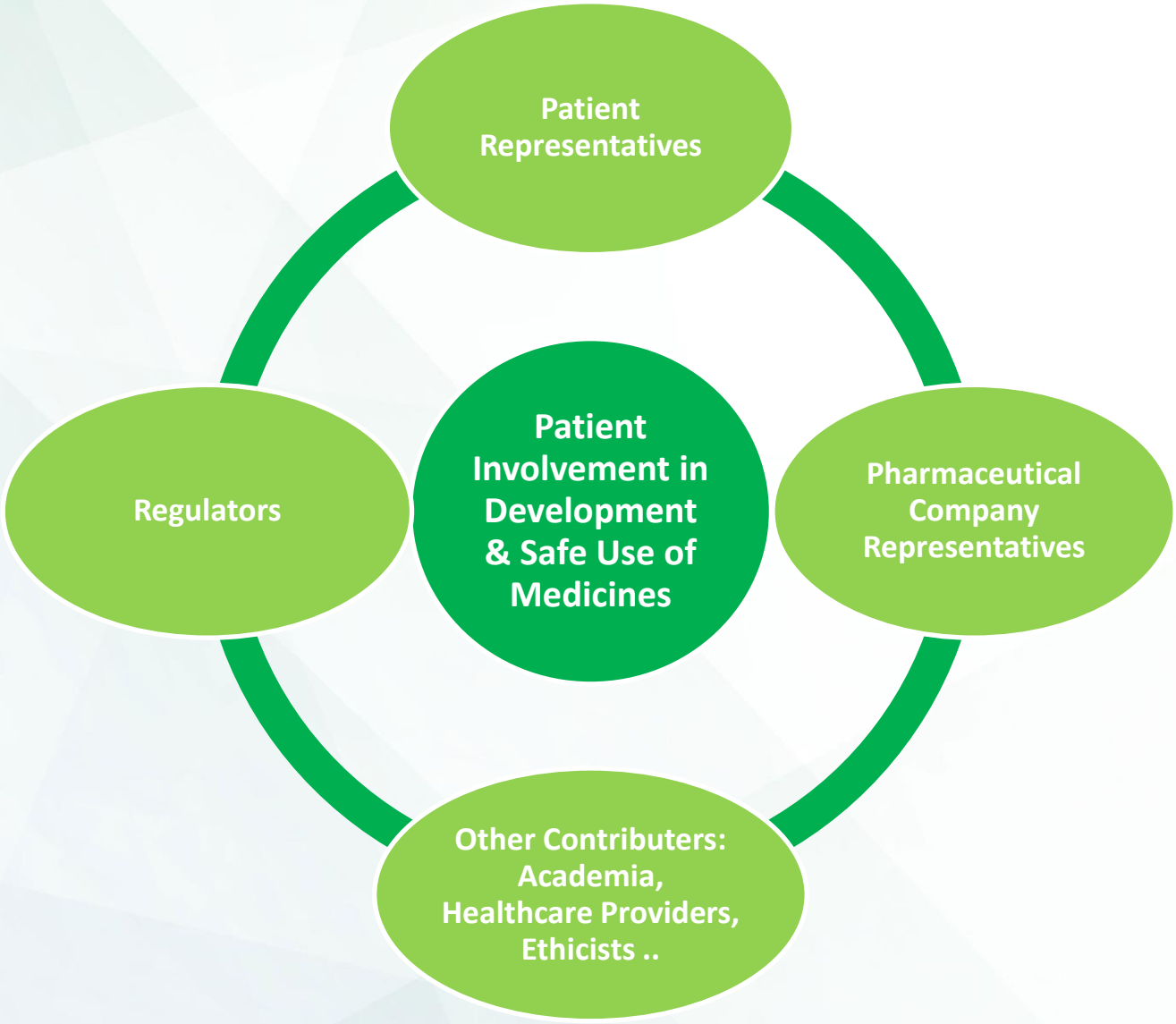
CIOMS Working Groups are Core:
Composition (1)

- CIOMS Working Groups are international – they try to involve experts from different countries and regions
- CIOMS Working Groups are usually composed of all important stakeholders, in many cases of
  - Regulators
  - Academia
  - Industries
  - WHO (as member/observer of the group)
  - …
- They involve also representatives of interested in the topic CIOMS member organizations
- In some working groups representatives from organizations such as ICH could also participate e.g. ICH secretariat in CIOMS WG on MedDRA Standardized Queries (SMQs)

Working Groups – core of CIOMS
Ongoing Working Groups (2)

- Six WGs ongoing:
  - *WG on Implementation (IWG) of Standardised MedDRA Queries (SMQs) (started 2004)*
  - *CIOMS Working Group on Drug Induced Liver Injury (DILI) (started 2017)*
  - *CIOMS Working Group on Clinical Research in Resource Limited Settings (started 2017)*
  - *CIOMS Working Group on Patient Involvement in Development and Safe Use of Medicines (April 2018)*
  - *CIOMS Expert Working Group on MedDRA Lebeling Groupings (MLGs) (April 2019)*
  - *Revision of CIOMS IV : Benefit-Risk Balance for Marketed Drugs: Evaluating Safety Signals (September 2019)*

CIOMS WG XI: Patient Involvement in Drug Developement and Safe Use



CIOMS Guidance Document

- First global guidance document on this topic
- Patient involvement in the whole life cycle of medicines

- Recognition of the importance of patient involvement
- 'Meaningful Engagement'
- Recognising the benefit of working together for the benefit of patients and their carers

CIOMS WG has 2 subgroups: Group 1 : Pre-marketing

Overview of the proposed chapters

Chapter 1 – Introduction

- 1.1. Set the scene: historical context
- 1.2. Why this book now?
- 1.3. Some concepts to consider
- 1.4. What is meant by engagement
- 1.5. Whom to engage?
- 1.6 How to engage?
- 1.7. Other ways patient stakeholders might inform drug development and advance treatments in their disease area
- 1.8. Overview of topics covered in this book

Continued….

Chapter 2 – The landscape of patient engagement in the development and safe use of medicines

- 2.1. A Brief history of patient involvement in the development and safe use of medicines
- 2.2. Current landscape of patient involvement in medical product development
- 2.3. Current landscape of patient involvement in the safe use of medicines
- 2.4. Emerging landscape in safe use of medicines: what are they [each?] currently doing or planning to do?
- 2.5. Patient involvement in low- and middle-income countries
- 2.6. Future opportunities

Continued….

Chapter 3 – Guiding principles and considerations for patient involvement.

- 3.1. Chapter outline
- 3.2. Principles for working with patients and patient organizations – independence of patients and other experts – COI, transparency …. (3.2.1. … 3.2.7)
- 3.3. Perspective of patients and advocates on involvemnent with drug development and safe use. Mutual respect among stakeholders ...
- 3.4. Positioning patients as partners and mutual benefit
- 3.5. Training and education of stakeholders
- 3.6. Contracts and communication
- 3.7. Compensation and fair market value
- 3.8. Measuring patient engagement
- 3.9. Applicable case studies

Continued….

Chapter 4 – Patient involvement in advancing treatments for their disease

- 4.1. Unmet needs
- 4.2. Early Development
- 4.3. Clinical Development relationship / involvement of patients and IRBs
  - 4.3.1. Individual choices
  - 4.3.2. The main actors in clinical development
  - 4.3.3. Why engaging with patients in clinical development?
  - 4.3.4. … 4.3.7
- 4.4. Regulatory review
  - 4.4.1. …. 4.4.7

Group 2 : Post-marketing phase

Chapter 5 – Guiding principles for patient involvement in patient product labeling

5.1. Introduction

- Communicating benefit & risk information
- Initiatives to improve quality of information
- Evaluating the effectiveness of labelling
- Future direction

5.2. Communicating drug benefit and risk information to patients

5.3. Sources of medicinal product benefit-risk information for patients

- 5.3.1. Product labeling
- 5.3.2. Additional risk minimization materials
- 5.3.3. Promotional materials provided by drug companies
- 5.3.4. Other sources of patient-targeted medicinal product benefit-risk information

Continued….

5.4. Initiatives to improve the quality of patient labeling

5.5. What constitutes high quality, ‘patient-centered’ patient labeling?

5.6. Principles for patient engagement in the development of patient labeling

5.7. Evaluating the effectiveness of patient labeling

5.8. Future directions for patient labeling

Continued ….

Chapter 6 - Opportunities for patient involvement in additional risk minimization

6.1 Introduction to Risk Minimization

6.2 Description of Risk Minimization

6.3 Regulatory Aspects of Additional Risk Minimization

6.4 Determining the Need for Additional Risk Minimization

6.5 Patient Involvement with Risk Minimization Measures

6.6 Patient Organizations Involvement in Additional Risk Minimization Measures *Chapter 6 Team to decide it this topic is included*

6.7 Ethical Considerations Regarding Patient Involvement in Additional Risk Minimization Measures *Chapter 6 Team to decide if this topic is included*

Continued ….

Chapter 7 - Guiding principles for patient participation in the generation and utilization of safety and effectiveness data

7.1. Executive summary

7.2. Introduction

7.3. Current environment

- 7.3.1. Sources of data
- 7.3.2. ….

7.4. Data linkage

7.5. Sharing of data and rules of engagement

7.6. The patient's perspective (writing led by a patient)

7.7. Gaps, needs, and untapped opportunities

7.8. Challenges

7.9. Future directions

7.10. Conclusions and recommendations

7.11. Appendixes

Continued ….

Chapter 8 - Patient involvement in developing safety issue/ crisis/time-bound communications regarding medicinal products

8.1. Scope/Introduction

8.2. Patient Involvement

8.3. Content

8.4. Type of issues

8.5. Type of distribution

8.6. Type of communication

Continued ….

Chapter 9 - Guiding principles for patient participation in therapeutic decision-making

9.1. Main body

- 9.1.1. Introduction
- 9.1.2. Landscape of patient initiatives
- 9.1.3. Rules of engagement
- 9.1.4. Patient involvement during drug development
- 9.1.5. Patient involvement in pharmacovigilance
- 9.1.6 Patient involvement in benefit-risk
- 9.1.7. Key stakeholders
- 9.1.8. Future directions
- 9.1.9. Conclusions and recommendations

Continued ….

9.2. Appendices

APPENDICES:	
• Glossary	(To be drafted by the Glossary subteam)
• Ethical considerations	(WG member comment: Bioethicist needed)
• Stakeholder feedback (meetings and surveys): Patient organizations; healthcare professional organizations; pharmaceutical companies	(This will show experiences and benefits of patient involvement as perceived by each type of stakeholder. It could be linked to the introduction and landscape of patient initiatives.)
• Practical examples of patient involvement in the medicines' lifecycle	Examples should be used throughout the main body of the report. Where more detail would be useful to the reader, detailed examples can be presented in the Appendix.

WG XI Open meeting on 30 April 2019

https://cioms.ch/open-meeting-patient-involvement-development-safe-use-medicines/

OPEN MEETING ON PATIENT INVOLVEMENT IN DEVELOPMENT AND SAFE USE OF MEDICINES

Geneva, Switzerland

30 April 2019

OPEN MEETING ON PATIENT INVOLVEMENT IN DEVELOPMENT AND SAFE USE OF MEDICINES

The CIOMS Working Group XI is developing guidance on patient involvement in the development and safe use of medicines. An open event will be held ahead of the 3rd WG meeting to present the group's work and obtain input from patient organizations and other stakeholders.

Schedule

Register Now

Speakers:

Kaisa Immonen
European Patient Forum

Marc Boutin
U.S. National Health Council

Kerry Leeson-Beevers
Alström Syndrome UK

Theresa Mullin
U.S. Food and Drug Administration

Corinna Schaefer
German Agency for Quality in Medicine (AEZQ) / World Medical Association

Isabelle Moulon
European Medicines Agency

CIOMS WG XI

Progress at https://cioms.ch/working_groups/working-group-xi-patient-involvement/

Progress

- 1st meeting held on 19-20 April 2018, Geneva, Switzerland (minutes)
- 2nd meeting held on 23–24 October 2018, Berlin, Germany (minutes)
- **Open meeting on patient involvement in development and safe use of medicines, 30 April 2019 (report, with links to presentations)**
- 3rd meeting held on 1-2 May 2019 in Geneva, Switzerland (minutes)
- 4th meeting held on 16-17 October 2019 in Basel, Switzerland (minutes to follow)

The CIOMS Working Group on Patient Involvement, at its 2nd Meeting in Berlin, Germany

Conclusion

However, working for public health has a problem:

No matter how good you are

you can always do better!