Content

What is CIOMS?

✓ Organization, links with other international organizations
✓ Areas of work and Working Groups

CIOMS Working Group XI: *Patient Involvement in Drug Development and Safe Use*

✓ Background and scope
✓ WG processes, progress
✓ Draft content
✓ Examples of selected chapters
✓ Plans for future

Conclusions
What is CIOMS?
Council for International Organizations of Medical Sciences

Founded in 1949 by WHO and UNESCO
In official relations with WHO and 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 in short

Organization located in Geneva:
A. International
B. Nongovernmental
C. Not-for-Profit

Forum for discussion and neutral platform to elaborate new ideas in medical product development, pharmacovigilance and research ethics (bioethics)

... for WHO, health authorities, academic organizations, pharmaceutical industry and other concerned stakeholders

CIOMS:
an umbrella organization of medical science organizations
Core of activities: Technical Working Groups

Run-time: Mostly 2-4 years, or even more than 10 years (SMQs)

Impact: Legally not binding, yet significant influence on healthcare community (including decision makers and other organizations with impact); can also be transformed to be legally binding when embodied in regional/national legislation
COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

Associate partner of UNESCO - in official relations with WHO.

The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949. CIOMS represents a substantial proportion of the biomedical scientific community through its member organizations, which include many of the biomedical disciplines, national academies of sciences and medical research councils. CIOMS mission is to advance public health through guidance on health research including ethics, medical product development and safety.

NEW FREE ONLINE TRAINING
for 2016 Ethical Guidelines for Health-related rese
Members, links with other international organizations
CIOMS membership
Recent new members (2018)

New international member of CIOMS
The International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP)

New national member of CIOMS
Bangladesh Medical Research Council
CIOMS is ICH Observer since 2016

### MEMBERS

#### Founding Regulatory Members
- EC, Europe
- FDA, US
- MHLW/PMDA, Japan

#### Founding Industry Members
- EFPIA
- JPMA
- PhRMA

#### Standing Regulatory Members
- Health Canada, Canada
- Swissmedic, Switzerland

#### Regulatory Members
- ANVISA, Brazil
- CFDA, China
- HSA, Singapore
- MFDS, Republic of Korea

#### Industry Members
- BIO
- IGBA
- WSMI

### OBSERVERS

#### Standing Observers
- IFPMA
- WHO

#### Legislative or Administrative Authorities
- CDSCO, India
- CECMED, Cuba
- COFEPRIS, Mexico
- INVIMA, Colombia
- MCC, South Africa
- National Center, Kazakhstan
- Roszdravnadzor, Russia
- TFDA, Chinese Taipei
- TGA, Australia

#### Regional Harmonisation Initiatives (RHIs)
- APEC
- ASEAN
- EAC
- GHC
- PANDRH
- SADC

#### International Pharmaceutical Industry Organisation
- APIC

#### International Organisation regulated or affected by ICH Guideline(s)
- Bill & Melinda Gates Foundation
- CIOMS
- EDQM
- IPEC
- PIC/S
- USP
CIOMS pharmacovigilance guidelines served as a basis for several ICH guidelines. Some examples:

<table>
<thead>
<tr>
<th>Working Group</th>
<th>ICH Guideline</th>
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<tbody>
<tr>
<td>CIOMS IA Report (1992)</td>
<td>ICH E2B: Clinical Safety Data Management – Data elements for transmission of individual case safety reports</td>
</tr>
</tbody>
</table>

*ICH - The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
Collaboration with CIOMS on SMQs (1)

- **SMQs** (Standardised MedDRA Queries) are tools developed to facilitate **retrieval of MedDRA-coded data** as a first step in investigating drug safety issues in pharmacovigilance and clinical development.

- Developed in collaboration with **ICH Observer CIOMS since 2003**.
  - Currently, 105 SMQs currently available to users.
    - SMQ **Opportunistic infections** finalised and will be released in March 2020.
    - **Two other SMQs under final stages of development and planned for release in September 2020**
      - SMQ **Progressive multifocal leukoencephalopathy (PML)**
      - SMQ **Immune-mediated/autoimmune disorders**
Areas of Work and Working Groups
### Pharmacovigilance: Working Groups

<table>
<thead>
<tr>
<th>Working Group</th>
<th>Period (some examples)</th>
<th>Report / Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIOMS I</td>
<td>-</td>
<td>International Reporting of Adverse Drug Reactions (1990)</td>
</tr>
<tr>
<td>CIOMS II</td>
<td>-</td>
<td>International Reporting of Periodic Drug Safety Update Summaries (1992)</td>
</tr>
<tr>
<td>CIOMS III</td>
<td>-</td>
<td>Guidelines for Preparing Core Clinical Safety Information on Drugs (1995)</td>
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<tr>
<td>CIOMS VI</td>
<td>03/2001 - 10/2004</td>
<td>Management of Safety Information from Clinical Trials (2005)</td>
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<tr>
<td>CIOMS VIII</td>
<td>-</td>
<td>Practical Aspects of Signal Detection in Pharmacovigilance (2010)</td>
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<tr>
<td>CIOMS IX</td>
<td>-</td>
<td>Practical Approaches to Risk Minimisation for Medicinal Products (2014)</td>
</tr>
<tr>
<td>CIOMS WG on DILI</td>
<td>2017 – ongoing</td>
<td>-</td>
</tr>
</tbody>
</table>
Pharmacovigilance: Recent Safety Publications

https://cioms.ch/shop/product-category/recently-published/
CIOMS reaches out in many languages
Introducing the course

Learning objectives

This course will help you to grasp and to navigate the 2016 CIOMS International Ethical Guidelines for Health-related research.

At the end of the course you will ...

- be able to navigate the Guidelines in order to find the Guidelines applicable to your case.
- have a comprehensive idea of the topics described in the Guidelines.
- understand the position of CIOMS on specific issues, such as the use of placebo or the level of acceptable risks.
Ongoing Working Groups today

Five WGs ongoing:
• CIOMS Working Group on Drug Induced Liver Injury (DILI) (started 2017)
• CIOMS Working Group on Clinical Research in Resource Limited Settings (November 2017)
• CIOMS Working Group on Patient Involvement in Development and Safe Use of Medicines (April 2018) – WG XI
• CIOMS Expert Working Group on MedDRA Labeling Groupings (MLGs) (April 2019)
• Revision of CIOMS IV : Benefit-Risk Balance for Marketed Drugs: Evaluating Safety Signals (September 2019) – WG XII

New WGs 2020:
• CIOMS Working Group on Real World Evidence and Real World Data in Regulatory Decision (March 2020) – WG XIII
• CIOMS Working Group on Severe Cutaneous Adverse Reactions (SCARS) – Q3 2020
Part 2: Patient Engagement Timeline

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

The CIOMS Working Group XI on Patient Involvement in the Development and Safe Use of Medicines was launched in April 2018 with an ambition to cover the whole product life-cycle – from early development until retirement from the market. It includes participants from patient organizations, industry, regulators, academia and the World Medical Association. All F2F meeting minutes are made public.

Progress

1st meeting held on 19-20 April 2018, Geneva, Switzerland (minutes available)
2nd meeting held on 23–24 October 2018, Berlin, Germany (minutes available)
3rd meeting held on 1-2 May 2019, Geneva, Switzerland (minutes available)
- Open meeting held on 30 April 2019, Geneva, Switzerland
4th meeting held on 16-17 October 2019, Basel, Switzerland (minutes available)
5th meeting to be held on 1-2 April 2020, Utrecht, Netherlands
6th meeting to be held in October 2020, Amsterdam, Netherlands

https://cioms.ch/working_groups/working-group-xi-patient-involvement/
CIOMS Working Group on Patient Involvement in the Development and Safe Use of Medicines (since April 2018)

The CIOMS Working Group on Patient Involvement
4th Meeting in Basel, Switzerland.
Draft content for the future guidance (1)

Chapters

1. Introduction;

2. Landscape of patient involvement in the development and safe use of medicines;

3. Guiding principles and considerations for patient engagement;

4. Patient involvement in advancing treatments for their disease;

5. Patient involvement in patient product labelling;

6. Opportunities for patient involvement in additional risk minimization measures;

7. Patient participation in the generation and utilization of safety and effectiveness data;

8. Patient input in developing safety issue communications regarding medicinal products;

9. Challenges and opportunities in patient involvement in resource-limited settings;

Chapter 6 Opportunities for Patient Involvement in Additional Risk Minimisation

Description of Risk Minimisation

**Purpose:**
- Optimise a product’s benefit-risk profile
- Enhance safe use
- Preserve patient access

**Types:**

<table>
<thead>
<tr>
<th>Routine</th>
<th>Additional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate for most products</td>
<td>Reserved for specific products / risks</td>
</tr>
<tr>
<td>• Product Label</td>
<td>• Communication / Educational Measures</td>
</tr>
<tr>
<td>• Packaging</td>
<td>• Controlled Product Distribution and Use</td>
</tr>
<tr>
<td>• Prescription Status</td>
<td></td>
</tr>
</tbody>
</table>

Regulatory Aspects of Additional Risk Minimisation

Current regulatory landscape for EU, USA, and Japan
Case examples of patient involvement with regulators for additional risk minimisation planning

Determining the Need for Additional Risk Minimisation

Description of pharma adaptation of Failure Mode and Effects Analysis (FMEA) and opportunities for including patient perspective
Chapter 6. Opportunities for Patient Involvement in Additional Risk Minimisation

Patient Involvement in the Design, Implementation and Effectiveness of Additional Risk Minimisation Measures (aRMMs)

Additional Risk Minimisation Process Steps

**DESIGN**
- Tool Specifications
  - Purpose
  - Stakeholder
  - Function

**DEVELOPMENT**
- Create Prototype
  - Format
  - Content
  - Usability (Human Factors) Testing

**IMPLEMENTATION**
- Tool Distribution
  - Local healthcare setting
  - Feasibility
  - Burden
  - Digital Options

**EFFECTIVENESS**
- Tool Assessment
  - Deployment
  - Knowledge
  - Behavioral Impact
  - Burden

Patient input can inform design of aRMMs to promote behaviors/actions to minimize risk.

Patients’ ideas or feedback can optimise tool prototypes and enhance health literacy of content.

Patient input can help customise implementation on country level and lessen burden on healthcare setting.

Patients can provide input on design and conduct of aRMMs effectiveness evaluations and participate in evaluation activities.
Draft content for the future guidance (3a)

Chapter 7. Patient participation in the generation and utilization of safety and effectiveness data

Overview

Sources of data, entities with which patients interact, and the existing rules of engagement are reviewed. Followed by critical appraisal of gaps, needs, and opportunities. Specific challenges and promising future directions are highlighted, followed by a set of recommendations.

Current environment

Sources of data

- Adverse Event Spontaneous reporting
- Real-World Evidence: Post-authorisation safety studies (PASS), Health Economics and Outcomes Research (HEOR) Studies, Patient Surveys, Risk Management Registries
- Expanded access programs and compassionate use programs
- Qualitative Studies (Structured Interviews and Focus Groups)
- Industry Medical Information Systems
- Internet Posts/Social media
- Personal sensors and wearable devices (new forms of data)
Draft content for the future guidance (3b)

Chapter 7. Patient participation in the generation and utilization of safety and effectiveness data

… …

Data linkage

Sharing of data and rules of engagement

The patient’s perspective

Gaps, needs, and untapped opportunities
Mobilizing patients, caregivers, and patient families as advocates for open access to patient benefit-risk data. Increasing patient engagement in regards to providing their data.

Challenges
Legal requirements, Global Environment on Data Privacy, large volume data, societal attitudes towards industry and regulators/government partnering with patients
Draft content for the future guidance (4)

Chapter 8. Patient input in developing safety issue communications regarding medicinal products

Scope - Definition of An Urgent Communication

Patient involvement

Content

Type of issues
- Crisis Communication in Clinical Trials
- Crisis Communications for Marketed Products
- Crisis Communications for Generics

Type of distribution

Type of communication
- Clarification
- Additional communication
- Educational
- Contact for information
- Links for communication
- Patient organisations to assist in communication
- Vulnerable patients
Gaps / additional topics identified

- Resource-Limited Settings challenges and opportunities
  - CHAIN Uganda workshop
  - Resource-Limited Settings subgroup: India, Iraq, Cameroon, Ghana, Malawi, Argentina, and Brazil

- Therapeutic decision-making contributions

- Bioethicists subgroup

- Case studies worldwide to broaden scope

- Considerations for special populations such as those with rare diseases, disabilities, and multiple co-morbidities, as well as various pediatric patients

- Patient involvement in benefit-risk considerations
Draft content for the future guidance (6)

Considerations for communication and distribution
Glossary – Most pertinent terms from the stakeholder perspectives
Easy to read – Content structure, flow, navigation, infographic, high-level recommendations
Implementation strategy – Reach target readership

Differentiators of CIOMS’ approach
Comprehensively combines all existing initiatives;
Capitalises on the outstanding work completed to date.

Feedback from the field
Real sense of excitement from for example:
CIOMS Open Meeting on Patient Involvement in Development and Safe Use of Medicines
DIA 2019 Global Annual Meeting;
DIA 2019 Annual Canadian Meeting;
European Medicines Agency (EMA) Patients’ and Consumers’ Working Party (PCWP)
   22 European organisations representing patients
DIA 2020 Euro meeting
… public consultation (early 2021?) before finalisation
A lot of progress has been made in learning how the best to benefit from patient involvement in the process of drug development and safe use.

However, working for public health has a problem:

No matter how good you are, you can always do better!