CIOMS: past, present, future

International Society of Pharmacovigilance 17th Annual Meeting
15-18 October, Liverpool

Dr Lembit Rägo
Secretary-General
Council for International Organizations of Medical Sciences

Content

- What is CIOMS?
- CIOMS history
- How it works?
- Important publications
- Ongoing and new potential WG
- Conclusions

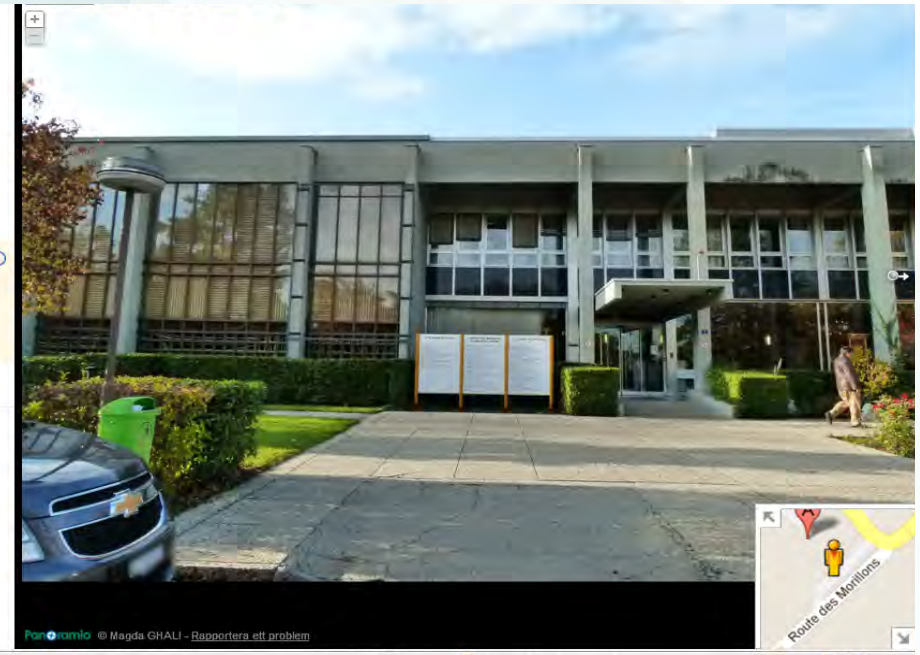
Acronym & Logo

Council for International Organizations of Medical Sciences

- ***Mission Statement***

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

Council for International Organizations of Medical Sciences (CIOMS) –
offices in WCC building in Geneva, Switzerland (CIOMS - left, WHO – right)



CIOMS in short

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

- In official relations with WHO + Associate Partner of UNESCO

- ... for WHO, health authorities, academic organizations, pharmaceutical industry and other concerned stakeholders
  ➢ an organization of medical science organizations

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

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 - General Assembly

International Organizations (12)

National Organizations, Associate Members (11)

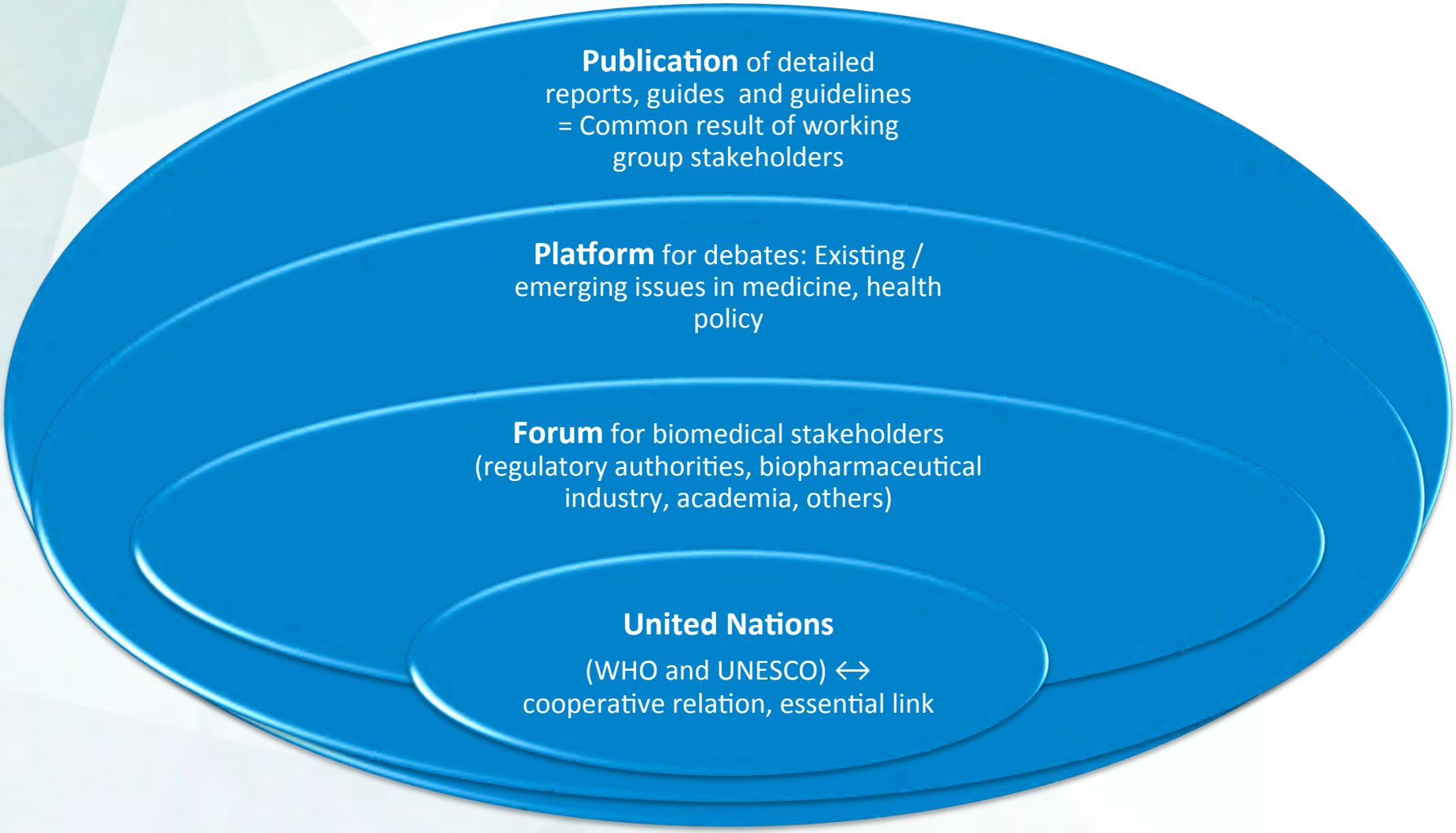
Associate Members (19)

Collaborations

Partners: Authoritative, international organizations dealing with related topics

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

Mandate


Publication of detailed reports, guides and guidelines = Common result of working group stakeholders
Platform for debates: Existing / emerging issues in medicine, health policy
Forum for biomedical stakeholders (regulatory authorities, biopharmaceutical industry, academia, others)
United Nations
(WHO and UNESCO) ↔ cooperative relation, essential link

7

Historic landmarks

Programs, Activities

Bioethics

Since 1967; 1. CIOMS Round Table Conference "Biomedical Science and the dilemma of Human Experimentation") Issuance of significant guidelines; latest revision 2016

Focus on "low and middle income countries"; translation into various languages

Pharmaco-vigilance

1986 first PV Working Group, 13 more working group reports until today

Several ICH Guidelines are based on results of CIOMS Working Groups

Product Develop-ment

Trends and Prospects in Drug Research and Development, Proceedings of the 11th CIOMS Round Table Conference, Geneva, Switzerland, 8-9 December 1977. Ed. Z. Bankowski, J.F. Dunne, published by Scrip World Pharmaceutical News, London, 1978.

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

Pharmacovigilance: Working Groups

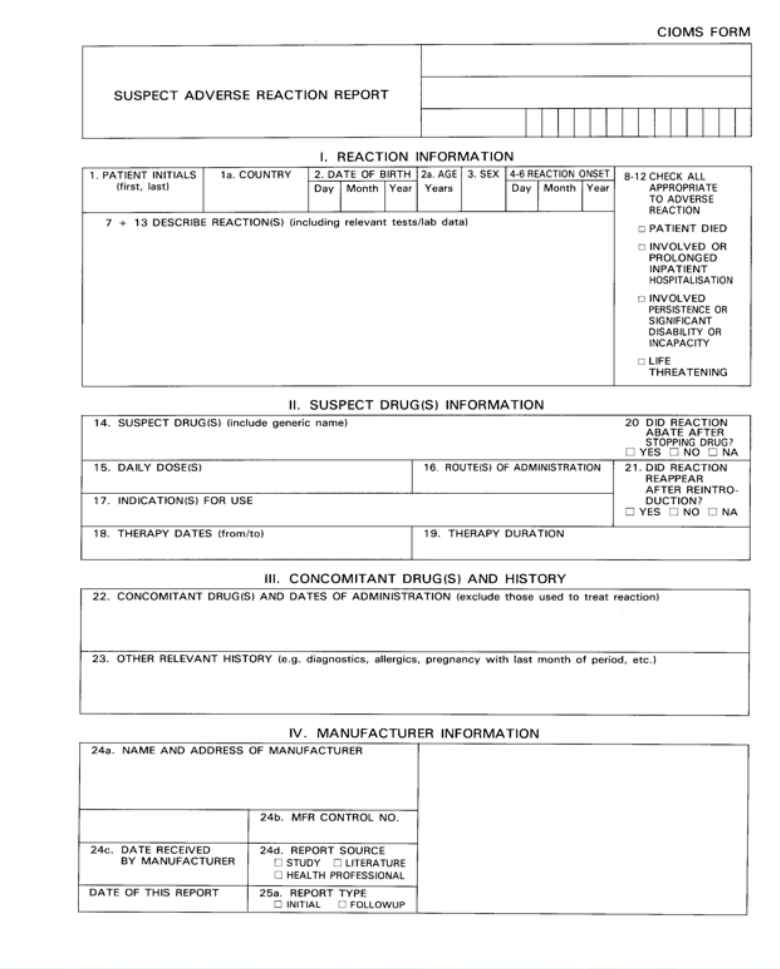
Working Group	Period (some examples)	Report / Year
CIOMS I	-	International Reporting of Adverse Drug Reactions (1990)
CIOMS II	-	International Reporting of Periodic Drug Safety Update Summaries (1992)
CIOMS III	-	Guidelines for Preparing Core Clinical Safety Information on Drugs (1995)
CIOMS IV	01/1995 – 07/1997	Benefit-risk balance for marketed drugs (1998)
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 (2017/2018?)

Impact on ICH Guidelines

CIOMS pharmacovigilance guidelines served as a basis for several ICH guidelines. Some examples:

Working Group	ICH Guideline
CIOMS WG I und II Reports (1990, 1992)	ICH-E2A (1994): Clinical Safety Data Management – Definitions and Standards for Expedited Reporting
CIOMS IA (1992)	ICH E2B: Clinical Safety Data Management – Data elements for transmission of individual case safety reports
CIOMS WGs II und III (1992, 1995)	ICH-E2C (1996): Clinical Safety Data Management – Periodic Benefit-Risk Evaluation Reports (PBRER)
CIOMS WG V (2001)	ICH-E2D (2003): Post-Approval Safety Management – Definitions and Standards for Expedited
CIOMS WG VIII Report (2006)	ICH-E2F (2010): Development Safety Update Reports

Impact - CIOMS Form



CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE Years	3. SEX	4-6 REACTION ONSET Day	Month	Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)										☐ PATIENT DIED ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION ☐ INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)		20 DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA
17. INDICATION(S) FOR USE		
18. THERAPY DATES (from/to)	19. THERAPY DURATION	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

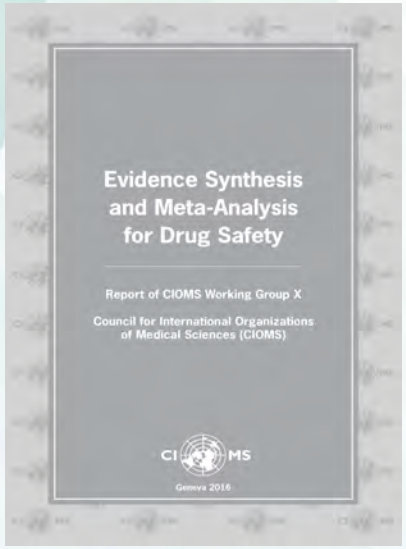
24a. NAME AND ADDRESS OF MANUFACTURER		
	24b. MFR CONTROL NO.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE ☐ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL	
DATE OF THIS REPORT	25a. REPORT TYPE ☐ INITIAL ☐ FOLLOWUP	

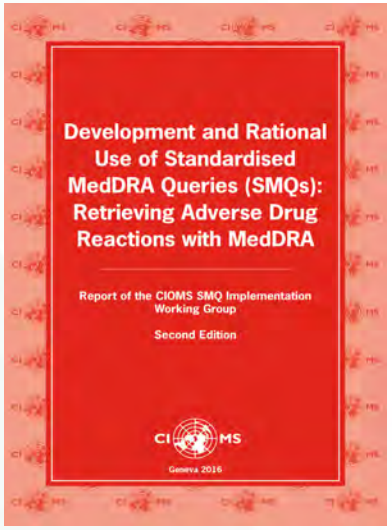
CIOMS Reporting Form I

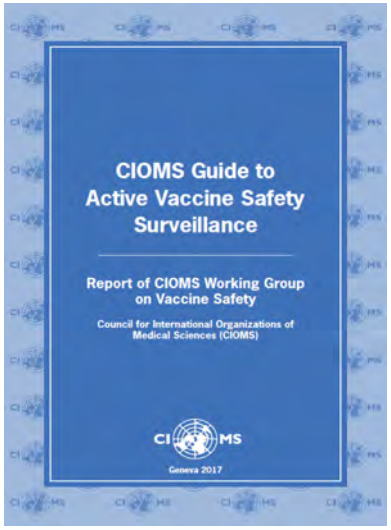
- Part of 1. pharmacovigilance WG report (International Reporting of Adverse Drug Reactions; initial 1987, final 1990)
- Served as a minimum standard for reporting of adverse drug reactions of licensed drugs
- Served as a template for upcoming national forms
- Accessible on CIOMS Homepage

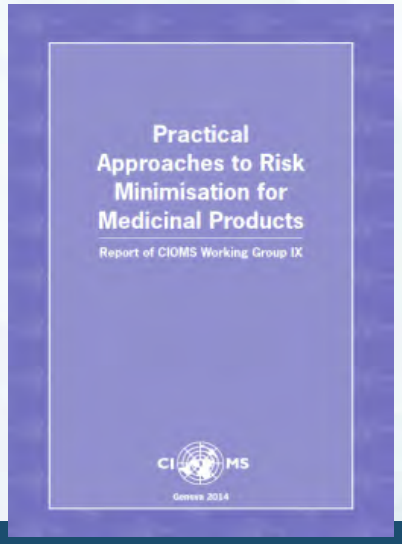
Pharmacovigilance: Recent Publications

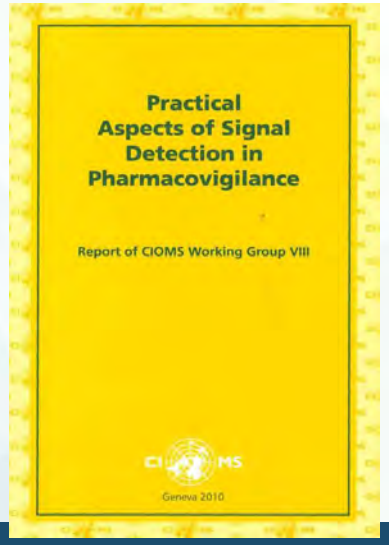
https://cioms.ch/shop/product-category/recently-published/

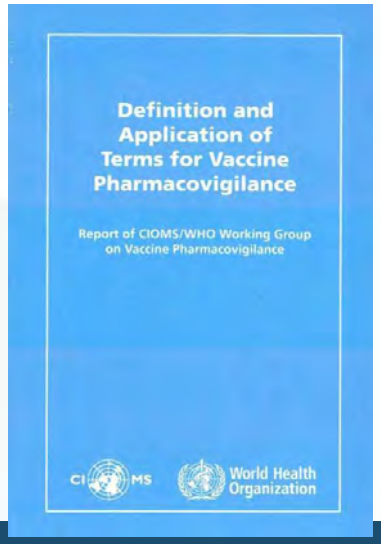








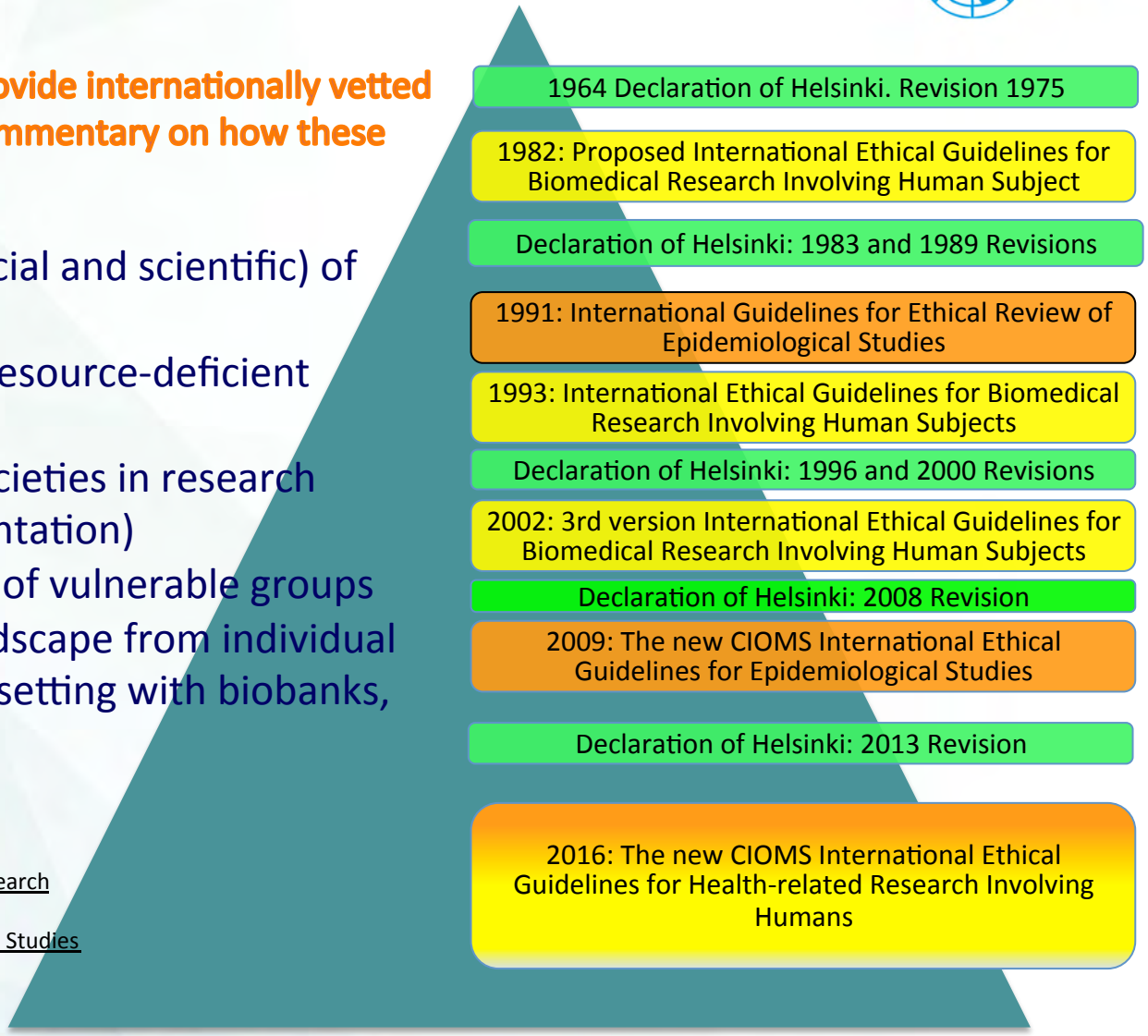




History of Ethical Guidelines

The aim of the guidelines is to provide internationally vetted ethical principles and detailed commentary on how these principles should be applied … *

- Emphases: Values (both social and scientific) of research for health
- Fair benefit of research in resource-deficient setting
- Enhanced integration of societies in research (from planning to implementation)
- Modified view on inclusion of vulnerable groups
- Conversion of research landscape from individual projects to infrastructural setting with biobanks, data banks *

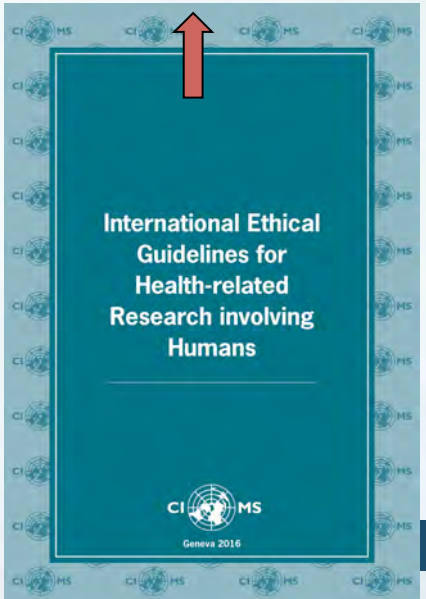


Declaration of Helsinki

CIOMS Ethical Guidelines / Biomedical Research

CIOMS Ethical Guidelines / Epidemiological Studies

Bioethics: Latest Guidelines 2016



#	Title of Guideline	#	Title of Guideline
1	SCIENTIFIC AND SOCIAL VALUE AND RESPECT FOR RIGHTS	14	TREATMENT AND COMPENSATION FOR RESEARCHRELATED HARMS
2	RESEARCH CONDUCTED IN LOW-RESOURCE SETTINGS	15	RESEARCH INVOLVING VULNERABLE PERSONS AND GROUPS
3	EQUITABLE DISTRIBUTION OF BENEFITS AND BURDENS IN THE SELECTION OF INDIVIDUALS AND GROUPS OF PARTICIPANTS IN RESEARCH	16	RESEARCH INVOLVING ADULTS INCAPABLE OF GIVING INFORMED CONSENT
4	POTENTIAL INDIVIDUAL BENEFITS AND RISKS OF RESEARCH	17	RESEARCH INVOLVING CHILDREN AND ADOLESCENTS
5	CHOICE OF CONTROL IN CLINICAL TRIALS	18	WOMEN AS RESEARCH PARTICIPANTS
6	CARING FOR PARTICIPANTS' HEALTH NEEDS	19	PREGNANT AND BREASTFEEDING WOMEN AS RESEARCH PARTICIPANTS
7	COMMUNITY ENGAGEMENT	20	RESEARCH IN DISASTERS AND DISEASE OUTBREAKS
8	COLLABORATIVE PARTNERSHIP AND CAPACITY-BUILDING FOR RESEARCH AND RESEARCH REVIEW	21	CLUSTER RANDOMIZED TRIALS
9	INDIVIDUALS CAPABLE OF GIVING INFORMED CONSENT	22	USE OF DATA OBTAINED FROM THE ONLINE ENVIRONMENT AND DIGITAL TOOLS IN HEALTH-RELATED RESEARCH
10	MODIFICATIONS AND WAIVERS OF INFORMED CONSENT	23	REQUIREMENTS FOR ESTABLISHING RESEARCH ETHICS COMMITTEES AND FOR THEIR REVIEW OF PROTOCOLS
11	COLLECTION, STORAGE AND USE OF BIOLOGICAL MATERIALS AND RELATED DATA	24	PUBLIC ACCOUNTABILITY FOR HEALTH-RELATED RESEARCH
12	COLLECTION, STORAGE AND USE OF DATA IN HEALTHRELATED RESEARCH	25	CONFLICTS OF INTEREST
13	REIMBURSEMENT AND COMPENSATION FOR RESEARCH PARTICIPANTS		

Example: Guideline #16

RESEARCH INVOLVING ADULTS INCAPABLE OF GIVING INFORMED CONSENT

Section 1 (89 words):

Adults who are not capable of giving informed consent must be included in health-related research unless a good scientific reason justifies their exclusion. As adults who are not capable of giving informed consent have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. At the same time, they may not be able to protect their own interests due to their lack of capacity to provide informed consent. Specific protections to safeguard the rights and welfare of these persons in research are therefore necessary.

..... Total 419 words

Commentary on Guideline #16 **1132 words**

Clinical Pharmacology in Health Care, Teaching and Research

- This joint publication with WHO and IUPHAR is an update of an old WHO TRS No 446 from 1970 on Clinical Pharmacology
- Contains also model core curricula for undergraduate and postgraduate training
- It has been translated into several languages such as Japanese, Korean and Russian
  - *The book is available free to download from CIOMS website*

New CIOMS website

Since July, 2017

Newsletter turned into quarterly

Since 2017

What's on @ CIOMS

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

WWW.CIOMS.CH June 2017 | Newsletter # 18

CIOMS LAUNCHES NEW WEBSITE

After several months of work with our website designers Inslab, CIOMS is pleased to announce the launch of its new website.

In addition to the online bookshop which allows payment by credit card, the website has many new features including:

- Readability on smartphones and tablets
- Instant access from Working Group pages to their publications
- Membership area with login for CIOMS members giving access to documents and allowing for annual fees to be paid online
- Expanded history of CIOMS linking to its many publications
- More information about CIOMS areas of work
- Availability of some older CIOMS publications
- CIOMS in the media

HIGHLIGHTS

- CIOMS launches new website
- CIOMS Working Group on Drug Induced Liver Injury
- Earlier publications available again

MEMBERSHIP

INTERESTING FACTS ABOUT CIOMS

June 2017 | Newsletter #18 1

What's on @ CIOMS

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

WWW.CIOMS.CH September 2017 | Newsletter # 19

NEW CIOMS WORKING GROUP

A new CIOMS Working Group (WG) on Practical Guidance to Clinical Product Development Research in Resource-Limited Settings (or Good Practices for Clinical Research in Resource-Limited Settings) will start later this year. CIOMS is organizing a working group (WG) of senior scientists from academia (including representatives of its member organizations), drug regulatory authorities, the pharmaceutical industry, public-private partnerships for product development (PPP/PD) to analyse the situation of clinical research in resource-limited settings (RLS) with the focus on, but not limited to, randomized controlled clinical trials (RCT). The WG will develop a consensus on relevant scientific, regulatory, ethical and administrative issues and propose pragmatic recommendations for improvement of the environment and good practices for social acceptance, planning, assessing, performing and interpreting randomized controlled clinical trials.

The WG is also intended to review how to benefit more from electronic health records (EHR) and how to prevent mistakes which make the use of EHRs difficult for clinical research in RLS. As usual, it is up to the WG to decide the final scope, directions and outcome of the WG. However, it is believed that these criteria/guidelines to be created could be used by all parties involved in policy-making, planning, designing, assessing and carrying out clinical research (including but not limited to RCT in RLS, notably by Ministries of Health/regulators/health technology assessors, industry, public-private partnerships and academia worldwide)

HIGHLIGHTS

- Public consultation on new Vaccines Communication Guide is still open
- New Working Group on Clinical Research in Resource-Limited Settings
- French translation of Ethical Guidelines now available

Lignes directrices internationales d'éthique pour la recherche en matière de santé impliquant des participants humains

The French translation of *International ethical guidelines for health-related research involving humans, 2016* : is now available in the CIOMS online bookshop. *Translations into other languages are also underway.*

4th International Neonatal & Maternal Immunization Symposium.

The Secretary-General of CIOMS, Dr Lembit Rägo (LR), participated in the 4th International Neonatal & Maternal Immunization Symposium - INMIS 2017 (more at http://www.inmis.org/) on 10–12 September in Brussels, Belgium. INMIS is a useful forum to bring together scientists, clinicians and public health experts from all continents to present, discuss and debate the opportunities and challenges that maternal and neonatal immunization can bring.

September 2017 | Newsletter #19 1

Current CIOMS Working Groups

- Standardized MedDRA Queries (SMQs) Implementation Working Group (IWG) – with modifications since 2004. This CIOMS activity has been conducted in cooperation with the ICH MedDRA Management Board, the MedDRA Maintenance and Support Services Organization (MSSO), the Japanese MedDRA Maintenance Organization (JMO) and other stakeholders

- Working Group on Vaccines Safety – no meetings since 2016 but still oversees finalization of *CIOMS Guide to Vaccines Safety Communication (final public consultation ended 11 October 2017, expected to be published January 2018)*

- Drug Induced Liver Injury (DILI) Working Group – 1st meeting April 27-28, 2017, Geneva; 2nd meeting 14-15 November in Malaga, 2017

- Clinical Research in Resource Limited Settings – 1st meeting 20-21 November, 2017, Geneva

New Potential Working Groups and Initiatives

- Patient involvement in the development and safe use of medicines. Draft concept note under consultation, potential CIOMS XI
- In vitro Diagnostics (IVD) Safety. Draft concept note under consultation
- Several other topics considered and under discussion…
- E-training modules about new CIOMS ethical guidelines under development
- Supporting WHO training activities with relevant CIOMS guides e.g. on vaccines pharmacovigilance, MedDRA implementation etc.
- **CHANGING ENVIRONMENT** may also offer CIOMS additional challenges, and hopefully more opportunities

Changing environment

- How it affects CIOMS' major areas of work?

Unmet medical needs –

- … are various, and may vary
  - ✓ rare diseases and oncology are important, but what about infections diseases including emergencies like Ebola (No 1 concern?)
  - ✓ what about cardiovascular diseases (No 1 killer in many countries, but few breakthrough new medicines)
  - ✓ or Alzheimer's disease/dementia (46.8 million worldwide in 2015, is believed to be close to 50 million people in 2017, reaching 75 million in 2030) – new data shows somewhat less aggressive increase …
  - ✓ relative over-representation of new drugs for oncology and rare diseases

- … are often, but not always, given priority by regulators
- Is present Global cooperation on product development and approval enough to meet unmet needs?
- Is emergency preparedness we have enough?

Expedited patient access to medicines

- What type of medicines we, patients, need? (in developed world up to 70 % of population have at least one prescription annually, elderly often 10+ different)

- Hope based medicines
- Belief based medicines
- Evidence based medicines

- …
- "We define *scientific evidence* as data or information derived from research that uses robust and reliable scientific methodologies, and seeks as far as possible to eliminate or minimise biases. Scientific evidence is subject to check and challenge and the evidence base for any medicine may evolve with the generation of further research data."

Ref.: *Academy of Medical Sciences. Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines. June 2017*
https://acmedsci.ac.uk/file-download/44970096

Expedited patient access to medicines

- How should society judge the safety and efficacy of drugs?
- In 2015 England's chief medical officer asked the Academy of Medical Sciences to undertake a review
- The report "Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines" was published in 2017

Ref.: *Academy of Medical Sciences. Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines. June 2017*
https://acmedsci.ac.uk/file-download/44970096

The report

Trust - evidence vs experience?

… surveys showed that only about one-third (37%) of the public said they trusted evidence derived from medical research, but around two-thirds (65%) trusted the experiences of friends and family.

The report explores how the generation, trustworthiness and communication of scientific evidence can be improved to strengthen its vital role in decisions by patients, carers, healthcare professionals and others about the benefits and harms of medicines …

UK Academy of Medical Science's 12 recommendations

- Involve patients, carers, and the public in research
- Address gaps in training in research methods and statistics
- Enhance the recognition of robust research findings
- Ensure best use is made of new sources of evidence
- Publish research findings
- Develop frameworks for declaring and managing interests
- Develop best practice guidelines for academia-industry relationships
- Improve the content of patient information leaflets
- NHS Choices should be a central repository of information on the benefits and harms of medicines
- Improve the reporting of scientific evidence in the media
- Support joint decision making between healthcare professionals and patients
- Continue dialogue and engagement with patients and the public

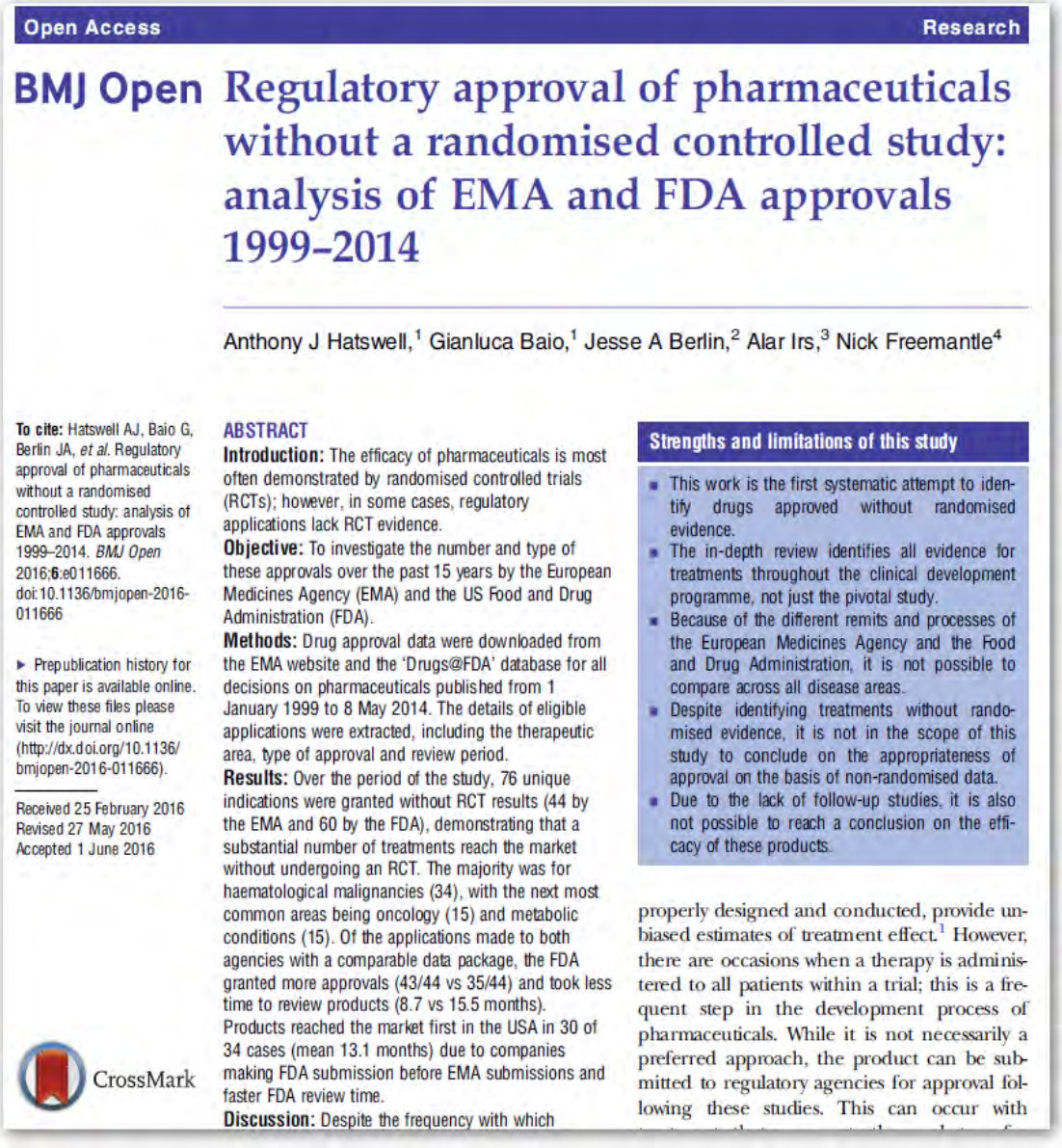
Rapidly changing environment for research and development of new medicines…

- With “social media” developing real producers of quality news have suffered – challenge for vaccines and medicines safety
- With “big data” use concepts emerging some say randomised controlled trials (RCT) can be replaced with alternative evidence from “real world data” …
  - *Urgent need for research on utility and usability, and consensus on potential new approaches and methodologies*

- People are extremely worried about their privacy and personal data related to digital health records
- At the same time people give up substantial amount of their privacy without much hesitations to all types of social media, businesses
  - *Rapid exponential increase of all type of digital data about us with little use for health and product development research?*

Approvals without RCT on increase

- Can we carry out all RCTs we need for regulatory approval?
- Regulatory approval without RCTs?
- Likely increasing trend but poses also risks that need to be addressed
- Electronic Health Records and databases – lot of hope and still little use?
- Could EHR be effectively used to monitor efficacy and safety of new medicines?



Open Access Research

BMJ Open

Regulatory approval of pharmaceuticals without a randomised controlled study: analysis of EMA and FDA approvals 1999–2014

Anthony J Hatswell,[1] Gianluca Baio,[1] Jesse A Berlin,[2] Alar Irs,[3] Nick Freemantle[4]

To cite: Hatswell AJ, Baio G, Berlin JA, *et al*. Regulatory approval of pharmaceuticals without a randomised controlled study: analysis of EMA and FDA approvals 1999–2014. *BMJ Open* 2016;**6**:e011666. doi:10.1136/bmjopen-2016-011666

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2016-011666).

Received 25 February 2016
Revised 27 May 2016
Accepted 1 June 2016

ABSTRACT

Introduction: The efficacy of pharmaceuticals is most often demonstrated by randomised controlled trials (RCTs); however, in some cases, regulatory applications lack RCT evidence.

Objective: To investigate the number and type of these approvals over the past 15 years by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA).

Methods: Drug approval data were downloaded from the EMA website and the 'Drugs@FDA' database for all decisions on pharmaceuticals published from 1 January 1999 to 8 May 2014. The details of eligible applications were extracted, including the therapeutic area, type of approval and review period.

Results: Over the period of the study, 76 unique indications were granted without RCT results (44 by the EMA and 60 by the FDA), demonstrating that a substantial number of treatments reach the market without undergoing an RCT. The majority was for haematological malignancies (34), with the next most common areas being oncology (15) and metabolic conditions (15). Of the applications made to both agencies with a comparable data package, the FDA granted more approvals (43/44 vs 35/44) and took less time to review products (8.7 vs 15.5 months). Products reached the market first in the USA in 30 of 34 cases (mean 13.1 months) due to companies making FDA submission before EMA submissions and faster FDA review time.

Discussion: Despite the frequency with which

Strengths and limitations of this study

- This work is the first systematic attempt to identify drugs approved without randomised evidence.
- The in-depth review identifies all evidence for treatments throughout the clinical development programme, not just the pivotal study.
- Because of the different remits and processes of the European Medicines Agency and the Food and Drug Administration, it is not possible to compare across all disease areas.
- Despite identifying treatments without randomised evidence, it is not in the scope of this study to conclude on the appropriateness of approval on the basis of non-randomised data.
- Due to the lack of follow-up studies, it is also not possible to reach a conclusion on the efficacy of these products.

properly designed and conducted, provide unbiased estimates of treatment effect.[1] However, there are occasions when a therapy is administered to all patients within a trial; this is a frequent step in the development process of pharmaceuticals. While it is not necessarily a preferred approach, the product can be submitted to regulatory agencies for approval following these studies. This can occur with

Review of medicines safety evidence –

not easy to understand for outsiders, nor to "fly safe" for insiders

Number of articles in PubMed

(Search was carried out 8.10.2017)

Formulated combined query	Number of articles
Electronic health records/databases and *pharmacovigilance*	146/109
Longitudinal health records and *pharmacovigilance*	13
Spontaneous reporting and *pharmacovigilance*	570
Electronic health records/databases and *signal detection*	76/49
Longitudinal health records and *signal detection*	10
Spontaneous reporting and *signal detection*	187
Electronic health records/databases and *medicines safety*	277/0
Longitudinal health records and *medicines safety*	8
Spontaneous reporting and *medicines safety*	141
Electronic health records/databases and *vaccines safety*	113/87
Longitudinal health records and vaccines safety	5* (all 2015-2017)
Spontaneous reporting and *vaccines safety*	88

Future of expedited access to new medicines - 4D?

__D__igital Governance, __D__igital Citizen, __D__igital Health Care and __D__igital Patient

- How is this changing further the way we do pharmacovigilance?
- Can 4D speed up research and development of new medicines?
- Can emerging and developing economies learn from mistakes done by Europeans and Northern-Americans in creating more research friendly and efficient digital health care
- …

Regulators and access to medicines

- Regulators seen by many parties as obstacle to access
  - *Part of the problem, and not part of the solution*
- Regulatory approvals (registration, MA)
  - Based on science – not easy to understand
  - Need considerable specialized scientific capacity, if done properly
  - Relative lack of transparency
  - Take time
  - … and may not lead to access automatically (HTA agencies decision needed for reimbursement)
- Regulatory approvals (MA) and removals (withdrawals)
  - *Damned if you do it, damned if you don't!*

Shifting the regulatory paradigm during the history

- Pharmaceutical manufacturing follows more Global market and business logics - Globalization is ongoing and likely there is no alternative
- Development of new technologies – from genome research to nanotechnologies, from stem cell research to high tech diagnostics solutions
- From "population" treatment to more "personalized" treatment, personalized or precision medicine, but … *What Happens When Underperforming Big Ideas in Research Become Entrenched? Joyner et al., JAMA July 28, 2016*
  - http://jama.jamanetwork.com/article.aspx?articleid=2541515

- New drugs for orphan diseases – but affordability a big issue
- Regulators and HTA – regulatory approval does not necessarily mean access to new products; talking to each other more, but still a lot of more needed
- Increased patient involvement in regulatory affairs – product approval (orphan diseases/drugs), including pharmacovigilance

2014 – first ever Global level call for strengthening regulatory systems

SIXTY-SEVENTH WORLD HEALTH ASSEMBLY WHA67.20

Agenda item 15.6 24 May 2014

Regulatory system strengthening for medical products

The Sixty-seventh World Health Assembly,

Having considered the report on regulatory system strengthening; [1]

Welcoming the efforts of the Director-General, and recognizing the pivotal role that WHO plays in supporting countries in strengthening their regulatory systems of medical products for human use, [2] and in promoting equitable access to quality, safe, efficacious, and affordable medical products;

Recalling the Constitution of the World Health Organization, which affirms that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition;

Recalling also United Nations General Assembly resolution 67/81 on global health and foreign policy, which, inter alia, recognized the importance of universal coverage in national health systems, especially through primary health care and social protection mechanisms, in the provision of access to health services for all, in particular for the poorest segments of the population;

Recalling further resolutions WHA45.17, WHA47.17, WHA52.19, WHA54.11, WHA59.24, WHA63.12, and WHA65.19, all of which encompass aspects of the need to promote the quality, safety, efficaciousness and affordability of medicines, including blood products;

Can all national regulators …

- fully assess and inspect all the (new innovative) products that come to their markets?
- In theory, and only in theory, YES
- But who can pay the bill?
- Thus, in practice, NO
  - ✓ Reality is that "regulatory bodies" range from staff point of view virtually from 1 person up to 3000+ !
  - ✓ Most WHO Member States are …small, or very small countries; "big fish" – minority, but
- How regulators can best contribute to the public health with the resources they have?
- How to build confidence in scientific safety and efficacy assessments carried out by other parties?
- **Of all regulatory functions perhaps pharmacovigilance is the one that carried out "locally" can add more value than others …**

Concluding remarks

- The future of regulation is a lot more in increased use of innovation and science, new methodologies and new data sources, collaboration, harmonization and convergence.

- Harmonization and convergence alone cannot help, but can form a solid basis for the new regulatory paradigm to evolve in the future -
  - *Doing “locally” what nobody is doing/can do for you, (added value), cooperate and rely in a transparent systematic way on other regulatory decisions, and decide in which area you invest to specialize to be a scientific "top class player" contributing to the Regional/Global Regulatory Network*

- CIOMS is following the changing regulatory paradigm and tries to help with dealing the topics that could give “added value”

Conclusions

- We are looking forward to work closely with all our constituencies, stakeholders and partners for renewing CIOMS and identifying new potential topics for CIOMS working groups
- We are ready to listen and see how we can improve ourselves or help
- We remain open for constructive ideas and proposals
  - *Working for public health has one important feature – no matter how good you are, you always can do better*