# What's on @ CIOMS

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

WWW.CIOMS.CH | March 2021 | **Newsletter** | **# 33**


## Quick links



# Public consultation ongoing

## Report of the CIOMS Working Group on Clinical Research in Resource-Limited Settings

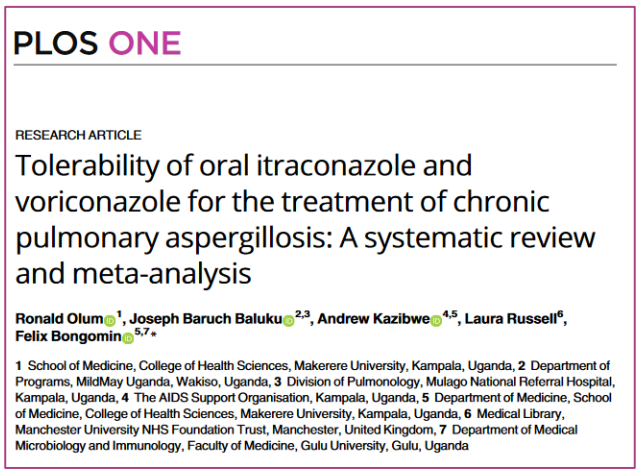
More clinical research is needed in resource-limited settings to cater for the health needs of these populations. What can governments, researchers and funders do to create a favourable environment, build capacity for research, make sure that the rights of study participants are protected, identify relevant research questions, and promote the conduct of clinical studies that bring credible results?

After three years of work, the CIOMS Working Group on Clinical Research in Resource-Limited Settings has posted its draft report and consensus recommendations on the CIOMS website for public comment.

☞ **Find the draft for comment on the Working Group's webpage here. Closing date: 12 April 2021.**


*Most clinical trials are conducted in high-income countries, where the environment is conducive to research. But people in resource-limited settings still bear the highest burden of disease globally, and medical products developed in the United States or Europe are not necessarily useful for them.*
*Map from: https://clinicaltrials.gov/ct2/search/map. Photo by Wilhan José Gomes (wjgomes) from Pixabay.*

# 2020 CIOMS award for best student paper



PLOS ONE

RESEARCH ARTICLE

Tolerability of oral itraconazole and voriconazole for the treatment of chronic pulmonary aspergillosis: A systematic review and meta-analysis

**Ronald Olum[1], Joseph Baruch Baluku[2,3], Andrew Kazibwe[4,5], Laura Russell[6], Felix Bongomin[5,7]***

**1** School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda, **2** Department of Programs, MildMay Uganda, Wakiso, Uganda, **3** Division of Pulmonology, Mulago National Referral Hospital, Kampala, Uganda, **4** The AIDS Support Organisation, Kampala, Uganda, **5** Department of Medicine, School of Medicine, College of Health Sciences, Makerere University, Kampala, Uganda, **6** Medical Library, Manchester University NHS Foundation Trust, Manchester, United Kingdom, **7** Department of Medical Microbiology and Immunology, Faculty of Medicine, Gulu University, Gulu, Uganda

Chronic Pulmonary Aspergillosis (CPA) is a fungal disease of the lungs that commonly affects patients with structural lung diseases like tuberculosis. Globally, about 3 million individuals have CPA, of whom 1.2 million have previously had tuberculosis.

Oral voriconazole and itraconazole are used as alternative first-line agents for the treatment of CPA. Patients are usually treated with one of these antifungals for many months or years, and are therefore at high risk of developing adverse events. This systematic review and meta-analysis compared adverse events and discontinuation reported for the two drugs. The study found that several adverse events were reported for both, but that itraconazole may be more tolerable than voriconazole.

Ronald's work will help guide clinicians on the selection of first- and second-line agents for the management of CPA, and educate patients on the common side effects of these two agents.

*Ronald Olum is a 23-year-old final year undergraduate student undertaking a Bachelor of Medicine and Bachelor of Surgery (MBChB) degree at Makerere University, Uganda.*

Ronald has research interests in the areas of infectious diseases, particularly tuberculosis, COVID-19, HIV and fungal diseases, as well as non-communicable diseases, mental health and medical education. He has recently completed a virtual exchange programme in global health with Yale School of Medicine in the United States and has received training from the Africa One Health University Network (AFROHUN).

Ronald has authored and co-authored over a dozen peer-reviewed journal articles and presented abstracts at regional and global conferences. Recently he has joined the editorial team of the Journal of Adolescent Health and become an external reviewer for the Partnership for Maternal, Newborn and Child Health (PMNCH).

Ronald is interested in pursuing a career in internal medicine and global health. He hopes to make contributions in reducing the intersecting dual burden of non-communicable and infectious diseases in sub-Saharan Africa.

*The annual CIOMS award for the best scientific article published by a medical student in the areas of pharmacovigilance or research ethics carries a prize of **US-$1500**. The next award applications will be accepted up to **31 October 2021** (read more here).*

2018: Connie Rees
University of Utrecht, Netherlands

2019: Mieke Foster
Deakin University, Australia

2020: Ronald Olum
Makerere University, Uganda

**2021:**
**You?**

# Update on CIOMS Working Groups

## Active Working Groups

☞ Meeting minutes are found on the groups' webpages

### Clinical research in resource-limited settings

✓ Draft report posted for public comment

### Patient involvement in the development and safe use of medicines (WG XI)

✓ Editorial phase started

### Benefit-risk balance for medicinal products (WG XII)

✓ 4th Meeting held 2-3 March 2021 (virtual meeting)

### Real-world data and real-world evidence in regulatory decision-making (WG XIII)

✓ 6th Meeting held 26 February 2021 (virtual meeting)


*The CIOMS Working Group XIII members on 17 December 2020. The CIOMS WG XIII was launched in March 2020.*

### MedDRA labelling groupings

✓ 4th Meeting held 4 March 2021 (virtual meeting)

### NEW: Severe cutaneous adverse reactions (SCARs)

✓ 1st Meeting held 2-3 February 2021 (virtual meeting)

## Starting soon

### Standards for education and training in medicines development

*Image by Nikolay Georgiev from Pixabay*

*Few medical schools worldwide include medicines development and its disciplines in their undergraduate or post-graduate syllabus. As a result, it is difficult to attract and retain qualified professionals in clinical trials and other medicines development-related activities.*

This new CIOMS Working Group will develop recommended standards of education and training for health professionals participating in medicines development. Several CIOMS member organizations—including the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP), the World Medical Association (WMA), the International Union of Basic and Clinical Pharmacology (IUPHAR) and others—have agreed to support this initiative. Work is expected to start in the second quarter of 2021.

### Good governance for research institutions

*Image by PublicDomainPictures from Pixabay*

*Today's ethical and regulatory requirements for health research are very advanced, but they say little about how research institutions can equip their researchers with the necessary resources—such as time, training, information, technical and virtual tools, and ethical and legal advice—to conduct scientific studies in line with required standards.*

The aim of this new CIOMS Working Group is to fill the gap between the required standards and the actual research environment. The first meeting is expected for the second quarter of 2021.

**Now online**

## Cumulative CIOMS Glossary

This Glossary includes the definitions from eight different CIOMS Working Group reports published in the field of pharmacovigilance (see right-hand column). Some of the early CIOMS reports formed the basis of pharmacovigilance in Europe in the 1990s. As the science and practice of pharmacovigilance have evolved over the past decades, so too have the related definitions (see the example below). For some of the definitions the glossary also shows synonyms or differences between jurisdictions.

The glossary was compiled by Stephen Heaton, Stella Blackburn and Panos Tsintis, all of whom have contributed to at least one CIOMS pharmacovigilance Working Group report. The original inspiration came from Stephen Heaton at the time of writing the CIOMS IX Report.

Version 1.0 of the cumulative glossary includes terms from the following CIOMS reports:

- Guidelines for Preparing Core Clinical-Safety Information on Drugs, Second Edition (CIOMS III and V) 1999.
- Benefit-risk balance for marketed drugs: Evaluating safety signals (CIOMS IV) 1998.
- Current Challenges in Pharmacovigilance: Pragmatic Approaches (CIOMS V) 2001.
- Management of Safety Information from Clinical Trials (CIOMS VI) 2005.
- Practical Aspects of Signal Detection in Pharmacovigilance (CIOMS VIII) 2010.
- Practical Approaches to Risk Minimisation for Medicinal Products (CIOMS IX) 2014.
- Evidence Synthesis and Meta-Analysis for Drug Safety (CIOMS X) 2016.
- Drug-induced liver injury (DILI). A consensus by a CIOMS Working Group. 2020.

Terms from additional CIOMS reports will be included in subsequent versions.

☞ CIOMS Cumulative Pharmacovigilance Glossary

CIOMS

A – B – C – D – E – F – G – H – I – J – K – L – M – N – O – P – Q – R – S – T – U – V – W – X – Y – Z

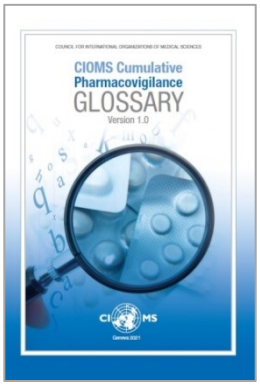
161. Risk (CIOMS IX)

**The probability of developing undesirable outcomes relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health or any undesirable outcomes with regard to the environment.**

*Combined from:*

*Lindquist, M. The need for definitions in pharmacovigilance. Drug Safety. 2007; 30: 825-830.*

*EU Guideline on good pharmacovigilance practices (GVP) – Annex I - Definitions (28 April 2014).*




Risk (CIOMS VIII)

**The probability of developing an outcome.**

Note: The term risk normally, but not always, refers to a negative outcome. When used for medicinal products, the concept of risk concerns adverse drug reactions. Contrary to harm, the concept of risk does not involve severity of an outcome. The time interval at risk should be specified.

*Modified from: Lindquist, M. The need for definitions in pharmacovigilance. Drug Safety, 2007, 30:825-830.*

Risk (CIOMS VI)

**As used in the context of adverse experiences, it is the proportion of individuals who have an event out of all those who could possibly have that event. Two groups can be compared either by taking their ratio (relative risk) or by subtracting the two risks. The latter is called an absolute risk difference.**

*Proposed by CIOMS Working Group VI.*

Risk (CIOMS IV)

**The simple, standard, epidemiological definition of risk is the probability that something will happen.**

Note: In the context of medical interventions (drugs, e.g.), the ''something'' is almost always associated with a negative event. In defining or describing a specific risk, it is always important to include information on intensity (severity, e.g.), time of the event (onset or duration), and time period over which the probability applies. Some definitions attempt to include concepts of rate, intensity and time: The probability of the occurrence of an adverse or untoward outcome and the severity of the resultant harm to the health of individuals in a defined population, associated with the use of a medical technology for a specified medical problem under specified conditions of use.

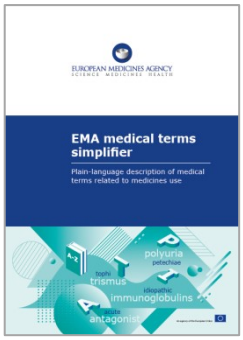
*Proposed by CIOMS Working Group IV.*

# Events and publications

Information from CIOMS partners in the areas of research ethics, medical product development and safety.

## EMA European Medicines Agency

### EMA Medical terms simplifier




This new glossary published by the European Medicines Agency (EMA) gives plain-language descriptions of medical terms commonly used to describe side effects and other terms used in medicines information and assessments of medicines.

☞ **Find the medical terms simplifier on the EMA Glossaries webpage.**

## IPRP International Pharmaceutical Regulators Programme

### Reliance:
### A smarter way of regulating medical products

This article presents the results of a survey conducted in the context of the International Pharmaceutical Regulators Programme (IPRP) on reliance approaches, and the experience and lessons learned among regulators. The paper was prepared with WHO as the lead author.

☞ **Doerr P, Valentin M, Nakashima N, *et al.* Reliance: a smarter way of regulating medical products - The IPRP survey. Expert Rev Clin Pharmacol. 2020 Dec 23:1-5. (Journal full text)**

## WHO World Health Organization

### Chronic pain management in children

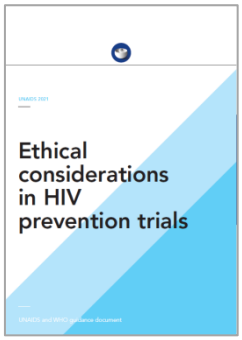
This new WHO guideline focuses on physical, psychological and pharmacological interventions to manage primary and secondary chronic pain in children 0-19 years of age. It will help countries to balance the benefits of therapies for pain relief with the harms arising from potential misuse of medications and other adverse effects of interventions for pain management.

☞ Guideline | Annexes

make medicines Child Size

*The pain management guideline is of interest for the WHO-convened Paediatric medicines Regulators' Network*

### Revised UNAIDS/WHO Ethical Guidance for HIV Prevention Trials




New, effective ways of preventing HIV must be tested in populations with a high incidence of HIV infection, where many people are vulnerable *e.g.* due to criminalization or housing instability. The revised UNAIDS/WHO ethical guidance for HIV prevention trials highlights the need to involve the local communities at all stages of the trials, to include participants regardless of age, pregnancy, gender identity or drug use, and to protect the rights, safety and well-being of the trial participants.

☞ UNAIDS/WHO. Ethical Considerations in HIV Prevention Trials. Published January 27, 2021.

**See also: van der Graaf R, Reis A, Godfrey-Faussett P. Revised UNAIDS/WHO Ethical Guidance for HIV Prevention Trials. JAMA. 2021 Jan 27. (Journal full text)**

### WHO 148th Executive Board meeting

This virtual meeting was held on 18-26 January 2021. Delegates adopted resolutions on oral health and on the social determinants of health, as well as some organizational issues.

In his closing speech, the WHO Director-General called on countries to close the financing gap of US$26 billion in 2021 for the Access to COVID-19 Tools (ACT) Accelerator. He pointed out that failure to ensure equitable access to vaccines could cost the global economy up to US$ 9.2 trillion, with almost half of that to be incurred in the wealthiest economies.

☞ Meeting documents

# What's new with COVID-19?

## WHO technical documents

**COVID-19 vaccine safety surveillance**: WHO has developed a manual on this topic, building on the principles described in the Global Vaccine Safety Blueprint, the WHO global manual on surveillance of adverse events following immunization, and the CIOMS guide to active vaccine safety surveillance.

☞ **WHO. COVID-19 vaccines: Safety surveillance manual**

**SARS CoV-2 variants** of interest (VOI) and variants of concern (VOC):

☞ **WHO working definitions**

**Impact on vaccines**: WHO has held a global consultation on how to assess the effect of SARS-CoV-2 variants on vaccine effectiveness.

☞ **Report of the WHO consultation**

## Regulatory transparency

**Clinical data made public**: To support vaccine confidence and trust in regulators, the EMA and Health Canada have published the full clinical data packages that they reviewed as part of their evaluation of COVID-19-related products. The data sets are available here:

☞ **Health Canada: Search for clinical information on drugs and medical devices**
**EMA: Clinical Data**
(requires creation of an EMA log-in account)

## Regulatory guidance

### Evaluating the impact of variants

**Vaccines**: As clinical disease endpoint efficacy studies may take too long, clinical immunogenicity studies are recommended to compare the immune response induced by the modified vaccine against the variant with that induced by the prototype vaccine against the virus upon which the prototype vaccine was based.

☞ **U.S. FDA** (Food and Drug Administration)
**EMA** (European Medicines Agency)
**Regulators from the ACCESS Consortium**
(Australia, Canada, Singapore, Switzerland, UK)

**COVID-19 tests**: This U.S. FDA guidance includes recommendations and tools for test developers to consider the impact of variants during development and to monitor test performance after authorization.

☞ **U.S. FDA Policy for Evaluating Impact of Viral Mutations on COVID-19 tests**

**Monoclonal antibody (MAB) products** against COVID-19 block the virus's attachment and entry into human cells. Different MAB products bind to different sites on the surface of the virus. The U.S. FDA recommends that sponsors collaborate to develop combination therapies that can minimize the risk of losing activity against emergent variants.

☞ **U.S. FDA guidance on monoclonal antibody products targeting SARS-CoV-2**

**Source of information in this section:** 30th WHO Regulatory Update on COVID-19. — *Images by Miroslava Chrienova **from** Pixabay*

# Conference announcement

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES
AASLD / FDA DILI CONFERENCE

## AASLD-FDA 2021 Conference on Drug-Induced Liver Injury (DILI)

**Virtual conference, 20-22 April 2021 | Conference website**

This online conference will address new developments, tools and assessment strategies in patients with underlying liver disease or cancer and in the setting of the COVID-19 pandemic. It is expected to attract an international audience of clinicians, scientists and regulatory experts.

The moderators and speakers include several members of the former CIOMS Working Group on Drug-Induced Liver Injury (DILI). In a session entitled *Perspectives in the development of best practices for different DILI scenarios,* four presentations will be dedicated to components of the 2020 CIOMS DILI Working Group report.

# News from the CIOMS Secretariat

## CIOMS cited

Davies M, Lane S, Shakir S. **Principles of benefit-risk assessment: A focus on some practical applications**. Journal of the Faculty of Pharmaceutical Medicine, 10 November 2020. (Journal full text)

Hoffmann M, Vander Stichele R, Bates DW, *et al.* **Guiding principles for the use of knowledge bases and real-world data in clinical decision support systems: report by an international expert workshop at Karolinska Institutet.** Expert Rev Clin Pharmacol. 2020;13(9):925-934. (Journal full text)

Iyer AA, Millum J, Grady C, Wendler D. **Avoiding exploitation in multinational covid-19 vaccine trials**. BMJ. 2021 Mar 4;372:n541. (Journal full text)

Maxwell L, Gilyan R, Chavan SA *et al.* **Guidance for ensuring fair and ethical broad consent for future use. A scoping review protocol**. F1000Res; 2021. 1. (Protocol)

Meurs L, Kant A *et al.* **Cohort event monitoring to assess safety of COVID-19 vaccines using patient-reported events, a protocol template from the ACCESS project**. EUPAS 38915. (Protocol)

Mouchantaf R, Auth D, Moride Y *et al*. **Risk Management for the 21st Century: Current Status and Future Needs**. Drug Saf. 2021 Feb 9. (Journal full text)

Orr E, Durepos P, Jones V, Jack SM. **Risk of Secondary Distress for Graduate Students Conducting Qualitative Research on Sensitive Subjects: A Scoping Review of Canadian Dissertations and Theses**. Glob Qual Nurs Res. 2021 Feb 12;8:2333393621993803. (Journal full text; PMC full text)

Saraiba A, Sánchez S, Santos S, Alonso M, Colella M, Legón J, *et al*. **Análisis comparativo de las pautas del consejo de organizaciones internacionales de ciencias médicas (CIOMS) 2016**. (Parte 3 de 3). [Comparative Analysis of the standards of the Council for International Organizations of Medical Sciencies (CIOMS) 2016. Part 2 of 3.] Rev Digit Postgrado. 2020; 9(3): e227. (Journal full text)

Schweim JK, Nonnemacher M, Jöckel KH *et al*. **Heterogeneity of national legislation and practice on clinical trials with vulnerable patients based on the EU Clinical Trials Directive by the example of adults permanently incapable of giving informed consent**. GMS Ger Med Sci 2021;19:Doc03. (Journal full text)

Strauss DH, White SA, Bierer BE. **Justice, diversity, and research ethics review**. Science. 2021 Mar 19;371(6535):1209-1211. (Journal full text)

*The above is a selection. On 30 March 2021, a Google Scholar search for articles mentioning "CIOMS" since 2021 yielded almost 400 results (see below). Commonly cited CIOMS publications and tools include (in no particular order):*

- *The CIOMS 2016 ethical guidelines (free);*
- *the CIOMS/RUCAM scale for causality assessment of drug-induced liver injury (discussion included here);*
- *the CIOMS-ICLAS 1985 International guiding principles for biomedical research involving animals (free);*
- *the CIOMS I form for reporting of adverse events (fillable PDF); and*
- *the CIOMS Working Group VIII report on signal detection (free).*

# Find us on the web

## Top 10 (past year)

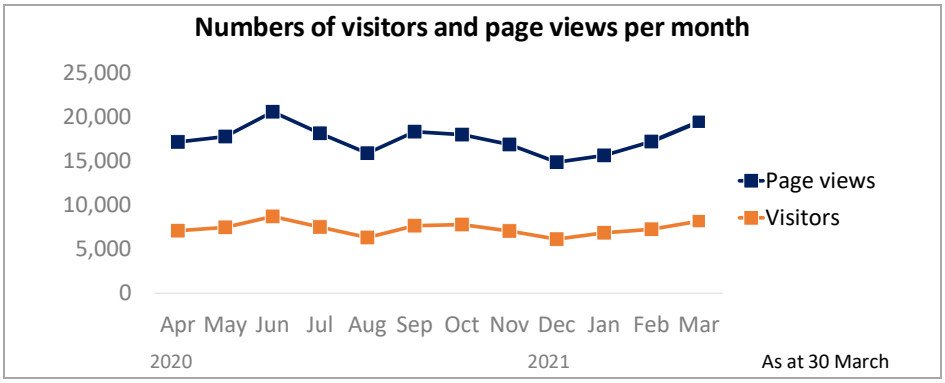
26 March 2020 – 25 March 2021

### Countries

| | | |
|---|---|---|
| 1 | United States | 22417 |
| 2 | India | 8898 |
| 3 | China | 5165 |
| 4 | United Kingdom | 3602 |
| 5 | Germany | 2565 |
| 6 | Canada | 2459 |
| 7 | Japan | 2285 |
| 8 | France | 2097 |
| 9 | Switzerland | 1681 |
| 10 | Mexico | 1396 |
| | Total visitors | 83075 |

### PDF downloads

| | | |
|---|---|---|
| 1 | CIOMS I Form for reporting of adverse events | 9196 |
| 2 | International ethical guidelines for health-related research involving humans (2016) | 2423 |
| 3 | Drug-Induced Liver Injury (2020) | 2401 |
| 4 | International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) | 1359 |
| 5 | Management of Safety Information from Clinical Trials: Report of CIOMS Working Group VI (2005) | 1196 |
| 6 | Spanish translation of the International Ethical Guidelines for Health-related Research Involving Humans (2016) | 828 |
| 7 | Guidelines for Preparing Core Clinical-Safety Information on Drugs 2nd Edition - Report of CIOMS Working Groups III and V (1999) | 771 |
| 8 | Current Challenges in Pharmacovigilance: Pragmatic Approaches – Report of CIOMS Working Group V (2001) | 753 |
| 9 | CIOMS Guide to Vaccine Safety Communication (2018) | 586 |
| 10 | Definitions and Applications of Terms for Vaccine Pharmacovigilance (2012) | 522 |

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## Upcoming meetings

**Working Group XIII Real-World Data & Evidence in Regulatory Decision-Making**

7th Working Group Meeting, 1 April 2021 (virtual meeting)

**Working Group on Severe Cutaneous Adverse Reactions (SCARs)**

2nd Working Group Meeting, 13 April 2021 (virtual meeting)

**CIOMS Annual General Meeting**

28 June 2021 (virtual meeting)
Open to representatives of CIOMS member organizations