

What's on @ CIOMS

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES



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September 2019 | Newsletter

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International events and visits

CIOMS Working Groups at the DIA 2019 Annual Meeting



DIA 2019
JUNE 23-27, 2019
SAN DIEGO, CA

CIOMS WGXI on Patient Involvement in the Development and Safe Use of Medicines



The CIOMS WGXI members at DIA 2019. **From left:** Marc Boutin (U.S. National Health Council), Kerry Leeson-Beevers (Alström Syndrome UK), Hervé Le Louët (CIOMS), Theresa Mullin (U.S. FDA), Meredith Smith (Amgen Inc), Judith Zander (U.S. FDA; session coordinator)

A forum and a round table discussion on [Current initiatives on Patient Involvement in the Medicinal Product Lifecycle](#) provided opportunities to gather additional input to the topics that will be covered by the CIOMS guidance on patient involvement. Some of the key takeaways are listed below.

- Different groups—for example patients with multiple diseases, young patients, or caretakers—need different considerations.
- Patients should be involved systematically and strategically throughout the product lifecycle.
- As resources are limited all round, stakeholders across sectors should share their resources such as surveys, templates or training, focusing on critical areas.

Patient involvement initiatives have gained ground over the last decade. The CIOMS WGXI is one of the first to bring patient representatives, regulators and industry together to produce comprehensive, global consensus guidelines.

CIOMS Expert Working Group on MedDRA Labelling Groupings (MLGs)

Clinicians and the healthcare community need clear and consistent information on adverse effects of biopharmaceuticals in reference safety information. When existing terminology, e.g. MedDRA, is not offering an appropriate option, terms must be grouped to communicate meaningful medical concepts.

As independent “one-off” approaches to such groupings are emerging, the presentation of adverse reaction can vary from label to label. The CIOMS EWG aims to develop an international approach for voluntary consideration. The group presented its work at a forum and a round table discussion titled [The Elephant in the Room: Meaningful Communication on Near Synonyms as Suspected Adverse Reactions](#).



At the DIA session on MedDRA Labelling Groupings. **Back row, from left:** Bill Gregory (Pfizer Inc), Rie Matsui (Pfizer R&D Japan), Judith Jones (PharmaLex). **Front row, from left:** Sonja Brajovic (U.S. FDA), Ilona Große Michaelis (Bayer AG).



San Diego, U.S., 23 June 2019

The International Coalition of Medicines Regulatory Authorities (ICMRA) held a plenary meeting in the margins of the DIA Global Annual Meeting. CIOMS Secretary-General Lembit Rägo was invited to attend and participated in the session dedicated to vaccines. The session was introduced by Dr Petra Dörr from Swissmedic and focused on issues related to vaccines hesitancy. Lembit Rägo spoke about the [CIOMS Guide to Vaccine Safety Communication](#) (freely available on the CIOMS website). This was followed by an update from Ms Emer Cooke from

WHO on the Organization’s activities on vaccine safety, and by a presentation Lorraine Nolan, CEO of the Health Products Regulatory Authority (HPRA) of Ireland on ways to improve trust and confidence in vaccines and vaccine programmes. The presentations were followed by questions and answers, and ended with a discussion to define next steps.

ICMRA is a voluntary coalition bringing together the leaders of regulatory authorities around the world to work together on scientific, regulatory or safety challenges.

Exploratory meeting on herbal medicines

Geneva, Switzerland, 3 September 2019



From left: Professor Xiao-He (Institute of Chinese Herbal Medicine, Beijing and Integrative Medical Department for Liver Diseases, The Fifth Medical Center of Chinese PLA General Hospital), Lembit Rägo (CIOMS), Professor Ingolf Cascorbi and Professor Michael Spedding (both International Union of Basic and Clinical Pharmacology, IUPHAR).

Many past CIOMS Working Groups have focused on various aspects of pharmacovigilance. The latest of these is dealing with Drug Induced Liver Injury (DILI). In addition to “chemical drugs”, there is an ever-increasing number and variety of traditional and complementary medicines (TCM) being used in all parts of the world, and regulators must find ways to assess which ones are safe and worthwhile to be marketed. The government of China has recently introduced tighter controls of TCM and food supplements.

Discussions have been held to explore a potential new IUPHAR-CIOMS Working Group on Herbal Induced Liver Injury (HILI), benefitting regulators in jurisdictions that do not have sufficient expertise and reference material in this area.

Two examples of plants that have been implicated with liver injury are: Green tea extract (or green tea consumed in large quantities), and kratom, a herbal extract derived from the leaves of a tropical evergreen tree (Mitragyna speciosa), which belongs to the coffee family.



Camellia sinensis (Green tea)

Image: Franz Eugen Köhler, Köhler's Medizinal-Pflanzen [Public domain]



Mitragyna speciosa (Kratom)

Image: Korthals, P.W. [Public domain]

Pharmacovigilance for non-prescription medicines

Geneva, Switzerland, 7 June 2019

The Pharmacovigilance Committee of the Association European Self-Medication Industry (AESGP) met on 7 June in Geneva. Dr Lembit Rägo, Secretary-General of CIOMS, was invited to give a presentation about CIOMS, with an emphasis on its pharmacovigilance-related activities. Upon request more detailed information was given about the recently formed CIOMS WGXI on patient involvement in development of medicines and their safe use. The presentation was followed by good discussions. Dr Rägo confirmed that CIOMS remains open to exchange views on topics of mutual interest that could merit discussion in the CIOMS environment, including establishing a CIOMS Working Group.

Legal experts on clinical trials

Copenhagen, Denmark, 24 September 2019

At the biannual [ctlegal](#) meeting, the CIOMS Secretary-General was invited to give a presentation about CIOMS and its activities in the area of clinical trials. The presentation focused on the CIOMS 2016 [International Ethical Guidelines for Health-related Research Involving Humans](#) and the ongoing [CIOMS Working Group on Clinical Research in Resource Limited Settings](#). It was followed by questions and discussion.

[ctlegal](#) (“pharmacovigilance legal”) is a membership-based forum for in-house counsel and compliance personnel at pharmaceutical companies working on clinical trial issues.

University workshop at CoRE

Singapore, 8-12 July 2019

In July CIOMS President Professor Le Louët was invited by the [Centre of Regulatory Excellence \(CoRE\)](#) of the [Duke-NUS University in Singapore](#) to give a lecture on new insights of pharmacovigilance during clinical trials. His presentation was part of a 3-day [workshop](#) for Graduate Certificate Students on clinical trial operations, biostatistical analysis and regulatory decision-making. This was followed by a pilot workshop on Multi-regional Clinical Trials for regulators from the 21 member states of the Asia-Pacific Economic Cooperation (APEC).

Discussions were also initiated with colleagues of the university on how to strengthen collaboration between CIOMS and the Duke-NUS medical school.



Looking back: Words of past CIOMS leaders

1961 – On budgets and organizations



Professor Joseph Maisin (CIOMS President 1949-55)

“If the budgets of the inter-governmental organizations run into millions of dollars and ours into thousands of dollars, at the most, it must be said that, considered on a world scale, these sums, theirs as well as ours, are ridiculously small. [...] What counts is the good will of the men who, in their laboratories, their offices or in the field contribute to

the improvement of our fate. And these men can very often be more easily mobilized through the professional organizations which they themselves created than through inter-governmental organizations whose internal machinery is vast and whose procedures are complex. But there is another good reason not to underestimate the role of our private organizations: they are free; they are not subjected to directives which are not specifically those of science.”

Professor Joseph Maisin, during the Opening of the 5th General Assembly of CIOMS.

1972–On the consequences of technological progress

“Advances in these sciences also made possible technological innovations which enormously increased the wealth of the industrial nations while recklessly and mindlessly squandering limited raw materials and polluting the biosphere with alarming rapidity and arrogant disregard. On the other hand, these same advances led to instant world communication with effects of vast consequence on the social and political structures of every person alive.”

Dr Alfred Gellhorn, in his address to the 7th CIOMS Round Table Conference.



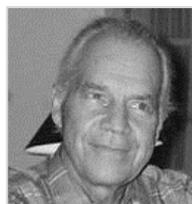
Dr Alfred Gellhorn (CIOMS President 1970-80)

1984 – On nuclear war

“I believe that everyone in this room is sensitive to the problem which faces mankind from the proliferation of nuclear weapons and the constant sword of Damocles under which all of us, our children, our grandchildren, and in fact all of mankind, live. [...] The only approach to the treatment of the health effects of nuclear explosions is primary prevention of such explosions, that is, the prevention of atomic war.”

Dr Alfred Gellhorn, at the 12th General Assembly of CIOMS, in introducing a CIOMS Resolution asking the medical profession to inform the public about the consequences of nuclear war, so as to “do its part in preventing what has been appropriately called the ‘final epidemic.’”

1987 – On affordability of health care



Dr John H. (“Jack”) Bryant (CIOMS President 1993-2003)

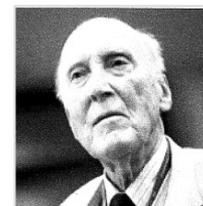
“Concern about paying for health services [...] was a recurring theme at the conference. [...] The surprise was that this problem of inadequate resources to pay for desirable or even essential health services appeared as new to some participants. This is familiar ground in the Third World and it is probably true that it should be seen as a permanent state of affairs worldwide.”

Professor John H. (“Jack”) Bryant, in his reflections on the 20th CIOMS Round Table Conference.

1993 – On “real world data”

“I had worked for many years with the rigour of experimental sciences, [...], trying to approach the ideal situation of studying the effects of a single variable. And then, in this project I was exposed to the other extreme, of a retrospective analysis of frequently incomplete and poorly documented case reports of suspicions, sent in by health professionals from different countries, [...]—in short, an unknown number of unknown variables. Hoping to find among this mass of reports cases of medical significance amounted to what Bill Inman compared to looking for nuggets of gold in a huge pile of garbage. It took me some time to convince myself that it was possible.”

Professor Jan Venulet, at the 27th CIOMS Round Table Conference.



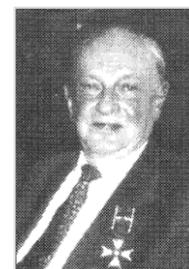
Professor Jan Venulet, member of several CIOMS Working Groups and long-standing CIOMS advisor. In 1968 he set up the WHO International Drug Monitoring Programme.

1999 – A great architect of CIOMS meetings retires

At the turn of the millennium Dr Zbigniew Bankowski retired after 25 years as Secretary-General of CIOMS.

“Dr Bankowski always manages to amass an impressive amount of brain-power at CIOMS conferences. Obviously, this is what results in the very high quality of meetings such as this one.”

Francisco Vilardell, at the 27th CIOMS Round Table Conference.



Dr Zbigniew Bankowski (CIOMS Secretary-General 1975-99) in 2001, when was awarded his country's highest honour, the Cross of the Order of Polonia.

News from the CIOMS Working Groups

CIOMS supports Uganda workshop on patient involvement

Kampala, Uganda, 27 August 2019

CIOMS supported the Uganda [Community Health and Information Network \(CHAIN\)](#) with holding a workshop on “Opportunities and Challenges of Patient Involvement in Drug Development and Safe Use of Medicines in Resource Limited Settings”. The workshop was held to seek additional input to the work of the [CIOMS Working Group XI on Patient Involvement in Development and Safe Use of Medicines](#).

CHAIN is a member of the International Alliance of Patients’ Organizations (IAPO). The workshop was co-hosted with the National Drug Authority and brought together over fifty participants involved with patients at the community, health facility and policy levels.

Patient representatives decried their non-involvement in decision making. “Communities are supposed to be involved right from the initial stages of drug development up to the end, but this is never the case. The patients’ views do not really matter”, said Moses “Supercharger” Nsubuga, an HIV patient who has been on medication since 1994.

Healthcare professionals at the workshop emphasised that patients have the right to air their views and ask questions. “In fact doctors find it encouraging to deal with informed patients”, said one participant. On the other hand, it was noted that some healthcare professionals are intimidated by empowered patients.

It was also noted that the environment in Uganda is not conducive to patient involvement. Relevant institutions are incapacitated, and information and feedback systems are inadequate. As a result, most

people are unaware of the rules and regulations in place for clinical research, there are poor health-seeking behaviours and unsafe use of medicine, and many adverse effects go unreported. This is compounded by the presence of substandard and counterfeit medicines due to weak legal enforcement systems, uncontrolled advertising for herbal medicines with unvalidated claims, and temptations for scientists to engage in unethical practices due to high poverty levels.

The workshop participants felt that foreign guidelines are not adapted to the social environment in resource-limited settings. They recommended that patients in these settings should be given tailor-made drug information and that a deliberate effort should be made to empower and meaningfully involve them in line with the [Patients’ Charter](#) of the Ministry of Health of Uganda.



Regina Kamoga (Executive Director of CHAIN and member of the CIOMS Working Group XI), addressing workshop participants. Regina noted that patients in resource-limited settings should be more involved when decisions are made on drug development and clinical research, and that the CIOMS guidance on patient involvement in the development and safe use of medicines is timely.

New Working Group: Risk-benefit balance for medicinal products



The CIOMS Working Group XII on Risk-Benefit Balance for Medicinal Products at its 1st Meeting, held on 17-18 September 2019 in Chavannes-de-Bogis near Geneva

The CIOMS Working Group XII on Benefit-Risk Balance for Medicinal Products has held its first meeting in Geneva, Switzerland. The new guideline will update the previous one published in 1998, titled *Benefit-Risk Balance for Marketed Drugs: Evaluating Safety Signals*.

New themes have emerged over the past 20 years since the first CIOMS IV guidance was published, such as the focus on patient involvement and preference; the need to integrate benefit and risk evaluations into one value judgement; and the importance of continuing to evaluate risks and benefits throughout the full medicinal product

lifecycle. New therapies have emerged; for example gene therapies and stem cell therapies, which require tailored, forward-thinking tools and complex clinical trials to help evaluate them appropriately. The fast-paced and ever increasingly complex world we live in continues to generate more and more types of uncertainties, which we must take into consideration. And additionally, regulatory initiatives are moving the field forward; new data sources are making new evaluations possible; and

innovative evaluation methodologies from academia have arrived on the scene to help us plan ahead in the best ways possible.

The general purpose of the new guidance is to bring benefit-risk management to the current day, enhance consistency and transparency in decision-making and communication, and to explain how to apply these at different junctures in the medicinal product lifecycle.

News from CIOMS partners

FDA guidance on real-world evidence

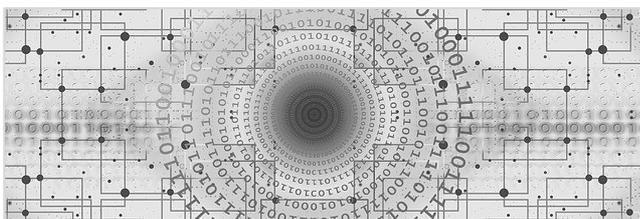
The U.S. Food and Drug Administration (FDA) has released its draft guidance for industry on [Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics](#).



Real-world data are derived from electronic health records, medical claims and billing systems, product and disease registries, or other sources such as mobile devices or patient-generated records. More and more applicants submit evidence generated from these data to demonstrate the safety and/or effectiveness of their medical products.

EC draft guidelines for trustworthy artificial intelligence

The European Commission's High-Level Expert Group on Artificial Intelligence (AI) has followed a wide-reaching consultation process in producing its draft [ethics guidelines on trustworthy artificial intelligence](#). The guidelines put forward a human-centric approach on AI and list seven key requirements that AI systems should meet in order to be trustworthy. These requirements will go through a piloting process expected to conclude with the presentation of a revised document in early 2020.



Images: Gerd Altmann from Pixabay

New publications from the German Ethics Council

- [Embryo Donation, Embryo Adoption and Parental Responsibility](#). Opinion. Berlin, Germany: German Ethics Council; 2019. (Translation of German document published in 2016)
- [Impfen als Pflicht? \(Vaccination as a duty?\)](#) 2019. (In German)

All publications of the German Ethics Council are freely available on the organization's website at: <https://www.ethikrat.org/en/publications/>

Meeting announcement

ICH public meeting on Good Clinical Practice

FDA Headquarters, Silver Spring, MD, U.S.
31 October 2019

The International Council for Harmonisation (ICH) has announced a global stakeholder meeting to solicit public input to its draft revised guideline [E8\(R1\) General Considerations for Clinical Trials](#), which— together with the subsequent revision of the [E6 Guideline for Good Clinical Practice](#)—is part of the [GCP Renovation](#).

The meeting will be hosted by the FDA and is meant for stakeholders who are impacted by guidelines but not represented directly by ICH, such as research universities and hospitals, healthcare professionals, non-ICH regulators (e.g. African regulators), research funders, patient groups, professional societies, and small and medium regional pharmaceutical companies.

Registration is free, although the number of places for the meeting is limited. More details are found on the [registration page](#).

News from WHO

WHO Paediatric Regulatory Network



Photograph: WHO/ Bangladesh

Children are our future, and much remains to be done to ensure that they have access to medicines that are adapted to their needs. More approved

therapies for children have become available in the past two decades, but additional efforts are needed to overcome the challenges of developing medicines for children globally.

In the field of paediatric medicines, international collaboration is key. WHO is therefore reactivating its **Paediatric medicines Regulatory Network**, which was initiated in 2010. This global network will help to make quality-assured medical products for children available by facilitating communication, collaboration, training and regulatory harmonization.

As part of this initiative, WHO has launched the **Paediatric community** on MedNet—the Organization’s collaborative e-platform—to share information about paediatric medical product guidelines and reference documents. The Paediatric community is proposed as a source of regulatory information on the development, approval and surveillance of paediatric medical products and to provide a forum for discussion between regulatory authorities and other relevant stakeholders.

If you have an interest in global development of paediatric medicines, you are welcome to join the WHO Paediatric Community, a consolidated online location for global guidance on paediatric medical products. You can sign up for free at <https://mednet-communities.net/pc/>

CIOMS award for best student paper



Connie Rees from the University Medical Center Utrecht in the Netherlands has received the 2018 CIOMS award of US\$ 1500 for the best scientific article published by a medical student in the areas of pharmaco-vigilance or research ethics. Connie is the joint first author of the publication titled “**The willingness to participate in biomedical research involving human beings in low- and middle-income countries: a systematic review**”, published in the journal *Tropical Medicine and International Health*.

Biomedical research with human subjects—from clinical trials for new products, such as an Ebola vaccine, to tests of generic medicines—is being conducted more and more often in low- and middle-income countries, raising ethical issues around

voluntary consent, undue inducement and the involvement of vulnerable populations. Connie reviewed data from 94 relevant articles and came up with a system to rank the reasons why people in LMIC accept or decline to participate in research.

Connie is currently completing her medical degree within the Selective Utrecht Medical Master (SUMMA) programme. Once she finishes her degree, she hopes to combine a clinical career in medicine with a career in research. Her aspirations for the future are to continue in the field of gynaecology and obstetrics, ideally with a research focus relating to maternal and global health.

Submissions are invited for the 2019 edition of the CIOMS award for the best scientific article published by a medical student in the areas of pharmacovigilance or research ethics. Applicants are expected to be medical students from a member organization of the International Federation of Medical Students’ Associations (IMFSA).

👉 Details are found on the [CIOMS website](#).

News from the CIOMS Secretariat

New staff member



On 5 August Sanna Hill joined the CIOMS team as a technical writer. Sanna has more than twenty years of experience of providing writing, editing and communications services in different fields, including for the World Health Organization.

CIOMS ethical guidelines in Japanese

CIOMS/WHO International Ethical Guidelines for Health-related Research Involving Humans (2016) in **Japanese**. This guideline now exists in eight languages (**English, French, Spanish, Portuguese, Ukrainian, Russian, Chinese and Japanese**). An Arabic translation is under preparation.



CIOMS in the media

<https://cioms.ch/cioms-in-the-media/>

Brown P., Bahri P. 'Engagement' of patients and healthcare professionals in regulatory pharmacovigilance: establishing a conceptual and methodological framework. *Eur J Clin Pharmacol*. 2019 Jun 25. doi: 10.1007/s00228-019-02705-1. [Epub ahead of print].

Van Roessel IMAA, Mazur NI, Shah SK, Bont L, Van Der Graaf R. **Post-trial Access in Maternal Vaccine Trials**. *Amer J Perinatol* 2019; 36(S 02): S41-S47.

About the CIOMS Working Group on Drug-Induced Liver Damage (DILI):

Tänapäeva meditsiini üks suurimaid väljakutseid on maksakahjustused ravimitest [One of the biggest challenges of modern medicine is drug-induced liver damage. *In Estonian*]. [Interview](#).

Ravimtekkeline maksakahjustus on tõsine probleem [Drug-induced liver damage is a serious problem. *In Estonian*]. *Lege Artis* (a journal for medical doctors in Estonia). 2019;5(3):20-1.

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Upcoming meetings

Clinical Research in Resource-Limited Settings

5th Working Group meeting , 8-9 October 2019, Extremadura, Spain

Patient Involvement in the Development and Safe Use of Medicines

4th Working Group meeting, 16-17 October 2019, Basel, Switzerland

CIOMS 86th Executive Committee Meeting and XXIIIrd General Assembly

18 December 2019, Geneva, Switzerland