What's on @ CIOMS
COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

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Council for International Organizations of Medical Sciences (CIOMS) addresses new challenges of protecting humans participating in health-related research by issuing new guidelines

Progress towards a world where all can enjoy optimal health and health care is only possible due to various kinds of research, including research involving humans. This research needs to be conducted according to the highest possible ethical standards such as the ethical principles set forth in the CIOMS Guidelines. Research practices will always change and new challenges will emerge. Ethical guidelines need to be updated to match the needs of the changing environment in order to offer the best possible protection of humans participating in health-related research.

Several reasons prompted the revision and merging the two latest existing CIOMS ethical guidelines, from 2002 and 2009, respectively. The most important reason was to increase *emphasis on the scientific and social value of research*: the prospect of generating the knowledge and the means necessary to protect and promote people's health. Many stakeholders rely on the results of research for activities and decisions that impact individual and public health, welfare, and the use of limited resources. Therefore, it is mandatory to ensure that research addresses important and unsolved questions to improve health and increase the reliability of scientific information, promote efficient translation and reduce research waste.

The underlying importance of *social value* is another major effort to clarify considerations of fairness in research conducted in low-resource settings. For example, CIOMS now lists the obligation to make available interventions proven effective in research as part of a broader obligation to care for participants' health needs. This broader obligation also requires that before a study begins, researchers and sponsors make plans for transitioning participants who continue to need treatment after their participation in research to appropriate health services.

The second reason was to make the CIOMS guidelines more sensitive to ethical issues that arise across *the whole lifecycle of translation from basic to clinical research,* since the ethical acceptability of research fundamentally depends on addressing important questions for improving health.

There were other challenges such as how better to clarify what counts as *fair benefits of research* in low-resource settings, how to address the increased *need to engage communities* from the planning to the implementation phase of research, and how to reflect a better global paradigm shift in thinking about *inclusion of potentially vulnerable groups*. An additional new challenge that needed attention was *the increase in the collection, storage and use of bodily material and health-related data.*

As a response to changing environment of research involving humans, the scope of the 2002 guidelines has been broadened from "biomedical

research" to "*health-related research*" as biomedical research would not cover research with health-related data. Nearly all former guidelines underwent major revisions and several new guidelines were created.

These guidelines, written in close collaboration with the World Health Organization (WHO), are highly regarded for their clear ethical principles and detailed and nuanced commentaries. Many authoritative declarations, reports and guidance documents, such as the World Medical Association's Declaration of Helsinki and UNESCO's Universal Declaration on Bioethics and Human Rights have had a prominent role in the development of the CIOMS guidelines. The aim of the CIOMS guidelines has been to indicate how the ethical principles that should guide the conduct of biomedical research involving humans, as set forth in the Declaration of Helsinki, could be effectively implemented, particularly in low- and middle-income countries (LMICs).

The final draft of the new guidelines was made available to all CIOMS member organizations before the CIOMS 83rd Session of the Executive Committee and XXII General Assembly on 29 November 2016 in Geneva, Switzerland. Following the presentation of the work done on the new CIOMS ethical guidelines by the CIOMS President, Professor Johannes van Delden, the Executive Committee adopted the new CIOMS International Ethical Guidelines for Health-Related Research Involving Humans. The XXII General Assembly endorsed the decision of the Executive Committee to adopt the new guidelines.

On the same day after the CIOMS General Assembly, a press event dedicated to the new CIOMS International Ethical Guidelines for Health-Related Research Involving Humans was organized in the Geneva Press Club. The press event was moderated by Dr Lembit Rägo, CIOMS Secretary-General, and had three distinguished speakers. Dr Marie-Paule Kieny, Assistant Director-General of WHO, addressed in her speech the importance of the new CIOMS International Ethical Guidelines. Dr Hans-Jörg Ehni from the World Medical Association (WMA) gave in his presentation reflections on the new guidelines from the WMA perspective, concluding that CIOMS guidelines are not contradictory to WMA's Declaration of Helsinki (DoH). He said that these guidelines should be seen as complimentary to DoH. Professor Johannes van Delden, immediate past President of CIOMS and the Chairman of the CIOMS International Working Group drafting these new CIOMS guidelines, explained in his presentation how the drafting process of the Guidelines went through challenges to the success by addressing all major issues that were identified to need either new or revised guidance. The CIOMS Secretariat is planning to make the presentations made during this press event available on the CIOMS website. This press event can be viewed on YouTube at

https://www.youtube.com/watch?v=vcn8ic_F2dM

(Clockwise from left to right: Hans-Jörg Ehni, Lembit Rägo, Johannes van Delden, Marie-Paule Kieny)

On 6 December a good short overview of the reasons and rationale behind the new CIOMS ethical guidelines entitled "Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans" by J. Van Delden and R. Van der Graaf was published online by the Journal of the American Medical Association (JAMA) at

http://jamanetwork.com/journals/jama/fullarticle/2592245.

On the same day the text of the new CIOMS **International Ethical Guidelines for Health-related Research involving Humans** was made public for the first time at http://www.cioms.ch/ethical-guidelines-2016/. However, it should be noted that this text is still subject to layout copy editing and is not the very final version as it would appear in print. CIOMS will replace the current web posted text with the final text as soon as it becomes available.

Finally, new guidelines are of limited value if they are not disseminated and implemented. CIOMS considers the implementation of these new international guidelines very important. A specific implementation plan will be drafted and financed. The CIOMS Executive Committee has already approved in its 29 November session a specific budget to support implementation activities. CIOMS will work on implementation issue closely with its stakeholders and partners, most importantly with WHO involving its headquarters and regional offices. One of the very important aspects of the new guidelines implementation is making them available in other languages in addition to English. CIOMS has already granted rights to translate the guidelines into Japanese, and it is anticipated that with the help of the Pan American Health Organization (PAHO – also WHO's Regional Office for Americas) the guidelines are being translated into Spanish. CIOMS is also looking forward to find partnerships through which the guidelines could be translated further, first of all into French and Japanese.

NEW PRESIDENT OF CIOMS

CIOMS is pleased to announce that Professor Hervé Le Louet has been elected as the President of CIOMS. Hervé Le Louet is Professor of clinical Pharmacology. He is currently the head of Pharmacovigilance Federation and the Co-chair of the Pharmacoepidemiology unit of Paris University Hospitals (AP-HP). He is a hepatologist by training and a PhD in Pharmacogenetics from the Paris University. He worked on liver metabolism assessment in patients with different liver conditions and on the drug induced mitochondria toxicity. He also worked on serious cutaneous adverse reactions (SCAR), especially on causality assessment for Steven Johnson Syndrome and Toxic Epidermal Necrolysis. He is dedicated to learning activities in several universities worldwide. He is a co-opted member by the European Commission of the Pharmacovigilance Risk Assessment Committee (PRAC) at the *European Medicines Agency.* He is a member of the European Network of Centers of Pharmacoepidemiology and Pharmacovigilance (ENCEPP) and is an Honorary Consultant for Uppsala Monitoring Centre (WHO). He was the advisor of the Minister of Health and Social Security. He is the immediate Past President of the International Society of Pharmacovigilance (ISoP). He was elected as the President of the Council for International Organizations of Medical Sciences (CIOMS) on 29 November 2016.

Professor Hervé Le Louet

CIOMS 83rd Executive Committee and XXII General Assembly Meeting, 29 November 2016

The 83rd CIOMS Executive Committee and XXII General Assembly meeting was held on 29 November 2016.

The Committee approved the new statutes of CIOMS to become a new association registered in Switzerland.

The following new officers and members of the CIOMS Executive Committee were elected:

President: Prof Hervé Le Louet

Vice-President: Prof Samia Hurst

World Medical Association: Dr Otmar Kloiber

World Association of Societies of Pathology and Laboratory Medicine: Dr Roberto Verna

Indian Council of Medical Research: Dr Roli Mathur

Czech Medical Association: Prof Jaroslav Blahos

The next CIOMS Executive Committee meeting will take place in Geneva on 28 November 2017.

CIOMS MEMBERSHIP

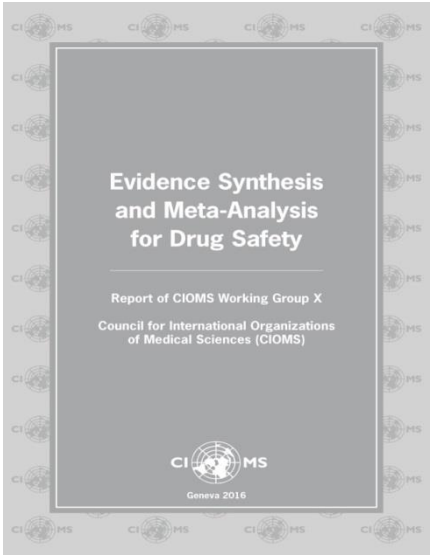
CIOMS currently has a total of 44 members (13 international, 12 national and 19 associate). This year CIOMS welcomed 2 new members: Saudi Neonatology Society and Indian Council of Medical Research. The International Association of Bioethics cancelled their CIOMS membership. An application from the Georgian Society of Pharmacology is currently being reviewed.

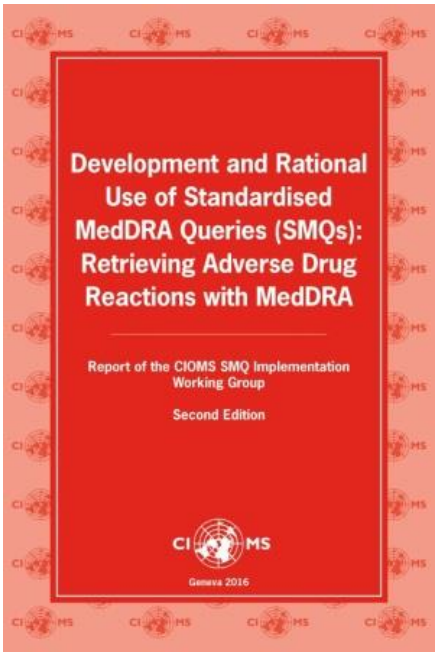
Benefits of CIOMS membership

Recently attempts have been made by the CIOMS Secretariat to add benefits to its members. Additional information about CIOMS activities and future plans are provided by distributing a CIOMS Newsletter twice a year. Future plans to add benefits to CIOMS membership include providing all members with one hard copy of CIOMS publications free of charge and sending all members a CIOMS Newsletter on a quarterly basis (effective from Q3 2017). New members who join would receive copies of those publications that were printed 12 months before their joining date. Since 2016, the Secretariat has informed CIOMS members on a regular basis about major developments in WHO by distributing WHO Executive Board and World Health Assembly agendas with relevance to CIOMS constituencies background papers. Due to its status (an NGO in official relations with WHO) the CIOMS Secretariat is also able to raise concerns, or issue statements of support, from its member organizations. The CIOMS Secretariat is exploring how to improve the information flow about UNESCO activities to its member organizations. As of June 2016, CIOMS has been an ICH observer. CIOMS can also inform its members on a high level about the developments in ICH, in particular about the topics that are related to medical sciences. CIOMS can also be the voice of its members relating ICH technical guidelines when needed. In Q2 2017, a survey is planned to be carried out with the aim of listening to views from member organizations on how to communicate better with members as an added value to CIOMS membership.

New CIOMS Publications

CIOMS published the following two new publications in August 2016:





Collaboration with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

The ICH Assembly held during 15-16 June 2016 in Lisbon, Portugal, discussed under agenda item 3: Membership and Observership Applications. The Assembly approved in Lisbon the observership application from CIOMS on the basis of the recommendation of the ICH Management Committee. CIOMS is listed as an ICH observer among other international organisations with an interest in pharmaceuticals such as the European Directorate for the Quality of Medicines & HealthCare (EDQM), the International Pharmaceutical Excipient Council (IPEC) and the United States Pharmacopeia (USP). Thus, until today, CIOMS is virtually the only organization that represents the medical sciences among ICH observers. More details about changing ICH membership can be found at http://www.ich.org/about/membership.html.

The MedDRA Management Board (MB) during its meeting in Osaka, Japan in November 2016 acknowledged the significant efforts of the Council for the International Organizations of Medical Sciences (CIOMS) Standardised MedDRA (see more about MedDRA at http://www.ich.org/products/meddra.html) Queries (SMQs) Implementation Working Group (IWG) and renewed the Memorandum of Understanding between ICH and CIOMS for a further year for development of new SMQs. Five SMQs will go into production in March 2017 for MedDRA Version 20.0. In addition, the Board noted the publication of the second edition of the CIOMS SMQ Implementation Working Group (IWG) report, Development and Rational Use of Standardised MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA (http://www.ich.org/ichnews/press-releases/view/article/meddra-management-board-osaka-japan-november-2016.html).

The CIOMS Secretary-General has started to attend ICH Assembly meetings since the Lisbon meeting in June 2016 that was followed by the Osaka meeting in November 2016. The ICH Assembly meetings are a good platform for information exchange and learning about increasingly numerous and complex activities, not only in the ICH environment, but also those that meet in the margins of ICH such as the International Pharmaceutical Regulators Forum (IPRF, see more at https://www.i-p-r-f.org/index.php/en/).

Last, but not least, since April 2016, CIOMS has also started to inform its member organizations about the ICH activities on a high level. The CIOMS Secretariat is ready to increase the feedback from its stakeholders to ICH as many of the ICH guidelines do influence medical research in the future. The CIOMS Secretariat is happy to answer any questions from its member organizations regarding ICH.

CIOMS is looking ahead to establish new Working Groups in 2017

The CIOMS Secretariat is working with stakeholders on a Working Group (WG) proposal "*Pragmatic approaches in pharmacovigilance and risk management including patient involvement*". The new draft concept paper is based on two concept papers from 2015 (Considerations for applying good vigilance practices to patient reported safety data within the pharmaceutical regulatory process and academia, and Considerations on evidence-based communication to and interaction with patients and other stakeholders during the pre- and post-authorization stages of drug development) which, due to a rapidly changing environment, had to be modified and updated. Some activities in line with these working groups work was already undertaken by other parties (e.g., specific to patient reporting MedDRA terminology creation by MSSO, some activities funded by EU under Innovative Medicines Initiative, etc.). To address the new challenges and eliminate some duplication between the two project proposals, a new merged concept paper was created through a number of informal consultations. If successful, this could be CIOMS Working Group XI.

During 2016 two new additional concept papers emerged for WGs. The first is dedicated to drug-induced liver injury (*DILI – Drug Induced Liver*

Injury - A need for new recommendations – draft distributed in advance). It is of interest to mention that this reflects continuity, as CIOMS has historically provided guidance on some aspects of DILI. Professor Hervè Le Louet, the newly elected CIOMS President, led the creation of this concept paper which is now in the phase of active consultation with major stakeholders.

The second proposal is to organize a Working Group to develop a consensus on methodologies for development and maintenance of *Drug Groups of Special Interest*. Various pharmacodynamic, pharmacokinetic and chemical structure properties of drugs influence their clinical effects and interactive capacity, leading to both desired and beneficial effects, but also adverse reactions. There is often a need to group drugs sharing properties of interest, e.g., regarding the potential for development of certain adverse reactions or injury, sharing the same clinical indications, chemical particulars or particulars of metabolism. The groupings are used to compare drugs that share a particular predefined characteristic, or to explore drug properties. This may apply for analyses during the entire life cycle of a drug. This call for action is to support a common approach and consensus for the methodology to produce DGSIs for a specific need and to complement established classification systems. In addition to the above-mentioned WG concept papers, several other projects, such as the one concerning some aspects of pharmacogenomics/personalized medicine and in vitro diagnostics safety, are in different stages of development. Finally, the recent CIOMS Executive Committee endorsed the above-mentioned WG proposals, including the one in collaboration with ICLAS (see section on ICLAS collaboration) and asked the Secretariat to continue consultations with the aim of getting some proposals finalized and new Working Groups established.

Collaboration with the International Council for Laboratory Animal Science (ICLAS)

CIOMS has long-standing collaboration and joint activities with the International Council for Laboratory Animal Science (ICLAS) (www.iclas.org). For example, in 2011 it was decided that CIOMS would collaborate with ICLAS towards a publication formulating CIOMS Basic Principles for Biomedical Research Involving Animals. This process was finalized and the final version was published as a joint publication on both websites in 2013. During September 2015 CIOMS received a questionnaire from ICLAS and a reply was sent expressing the support of a continuous collaboration like in the past. In 2016 the ICLAS President approached the CIOMS President with the proposal of establishing a new joint working group. The CIOMS Secretary-General has been in contact with ICLAS and performed substantive consultation with many interested and concerned parties, notably from industry and regulators. The last meeting was in November 2016 in the margins of ICH meetings in Osaka. The ICLAS concept paper was discussed with EFPIA experts and some regulators. The work to explore further rationale of setting up a new joint working group will continue. This includes a potential to link it with some other initiatives already ongoing or planned (such as a recent relevant project proposal under the EU Innovative Medicines Initiative umbrella).

UPDATE ON CIOMS WORKING GROUPS

MedDRA Working Group Meeting: Geneva, 6—7 September 2016

The 10th meeting of the MedDRA* Implementation Working Group took place at the CIOMS offices in Geneva on 6—7 September 2016, attended by 16 representatives from regulatory and pharmaceutical organizations. This current Working Group has been meeting twice every year since 2012, though the WG has existed since 2002. Some of the original members are still active today in the ongoing revisions of MedDRA.

This was the first meeting of the WG since the new edition of *Development and Rational Use of Standardised MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA* was published in August and WG members were pleased to receive their complimentary copies and have a chance to see the finalization of several years of work on this topic.

Thereafter the meeting focused on discussions around maintaining, reviewing and updating SMQs (Standardised MedDRA Queries). On the Tuesday evening, the Group enjoyed a special visit to the mediaeval town of Yvoire in France *(photo below)* followed by perch from Lake Geneva. The Group will reconvene again in March 2017. This Working Group activity is carried out according to the Memorandum of Understanding that exists between ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) and the MedDRA Management Board.

*Medical Dictionary for Regulatory Activities

(L-R): Yu Wada, Judith Jones, Sue le Roux, Aniello Santoro, Miki Ohta, Lembit Rägo, Yutaka Nagao, Tomas Moraleda, Bill Gregory, Norbert Paeschke, Yu Tanaka, Silvia Bader-Weder, Hitomi Takeshita, Christiane Michel

CIOMS Working Group on Vaccine Safety

The CIOMS Working Group on Vaccine Safety has finalized the main deliverable from its collaboration: The CIOMS Guide to Active Vaccine Safety Surveillance (Guide). The Guide addresses the situation facing many resource-limited countries' national immunization programs and regulatory authorities around the globe when a new vaccine is being introduced into a country for the first time ever and vaccine safety needs to be assured. Under the auspices of CIOMS, and addressing objective #8 of the World Health Organizations's Global Vaccine Safety Initiative regarding public-private information exchange, the working group served as an information exchange between academia, regulatory, public health, and industry stakeholders, as well as a "think-tank" to develop and propose new approaches in the field. Taking into consideration resources already in the field (e.g., WHO's Manual on surveillance of adverse events following immunization, 2014, which covers passive vaccine safety surveillance), the Guide focuses on how to determine when active vaccine safety surveillance is warranted based on what baseline safety data are available for the vaccine in question and if significant knowledge gaps in vaccine safety exist.

The present era has seen a drastic change of conditions, with earlier introduction into resource-limited countries of new vaccines — such as vaccines against rotavirus and human papillomavirus — as well as new vaccines targeting diseases endemic to regions. New vaccines anticipated for introduction in the coming years include dengue, malaria, typhoid, TB, and HIV vaccines and newly-licensed vaccines with expanded coverage recommendations including those to prevent HPV, influenza, Herpes zoster, meningococcal and pneumococcal diseases.

This CIOMS publication more than any other in recent history has focused on the special needs of the country level organizations responsible for developing strategies and implementing new vaccination programs into resource-limited environments. The Guide offers a practical step-by-step approach and a graphic algorithm to aid immunization professionals and decision-makers in determining the best course of action when confronting such challenges. The Guide provides a structured process, a source list for evaluating the extent of data resources, and several case studies for review.

The specified target audience for the Guide meant that some new concepts and approaches were vetted extensively by WHO among their regional and country level colleagues and the input received was incorporated into the materials and final document. The CIOMS Working Group and its Editorial Board were asked to concentrate on style and formats that would create CIOMS guidance most accessible to professionals at country-level who are often facing significant challenges and demands on

their time and resources. The resulting CIOMS Guide to Active Vaccine Safety Surveillance should serve as a practical document to help the planning and decision-making process when a country prepares for the launch of a new vaccine into their country.

The Guide will be published in early 2017 in both paperback and digital versions available on the CIOMS website, and through WHO.

CIOMS SECRETARIAT

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UPCOMING MEETINGS

11th Working Group on MedDRA IWG Meeting, Geneva, Switzerland,

22-23 March 2017

84th CIOMS Executive Committee Meeting, Geneva, Switzerland,

28 November 2017