What's on @ CIOMS
COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES
70 YEARS 1949 - 2019

WWW.CIOMS.CH | Special Newsletter | 11 April 2019

Highlights

This is the second of a series of special CIOMS Newsletters. As the Council celebrates its 70th Anniversary, we have asked some of its friends and partners to tell us their memories and their views of the role that CIOMS is playing in a rapidly changing world. Their contributions are included throughout this newsletter.

Anniversary message

Stuart Nightingale has worked with CIOMS for many years as a senior official at the U.S. FDA, the U.S. Department of Health and Human Services (HHS) Office of the Secretary, and as a consultant at the National Institutes of Health (NIH).

I congratulate CIOMS on the occasion of its 70th Anniversary. CIOMS is a very important and unique international organization that has provided, and continues to provide, unbiased information and guidelines in research ethics and on a variety of pharmaceutical-related safety concerns.

My first introduction to CIOMS goes back to my early work at FDA in the early 1980s, where I was exposed to CIOMS pharmacovigilance activities. Subsequently, most of my interactions with CIOMS have centered on its essential contributions to international guidelines for the protection of human research subjects, especially in the provision of comments during their revision process.

In my work, the CIOMS ethical guidelines have been important resources in developing presentations, curricula for educational workshops, and informational materials for institutional review boards and clinical investigators. The guidelines have been especially important internationally in facilitating the practical implementation of the Declaration of Helsinki**.**

CIOMS leadership and staff have been, and are, outstanding. The Secretaries-General with whom I have worked most closely, Drs Idänpään-Heikkilä and Lembit Rägo, have brought a wealth of experience from their extensive work in pharmaceuticals at WHO. This has helped in many ways, for example, in selecting impressive expert consultants to serve on working groups. In addition, Mr Sev Fluss has brought his experience at WHO and his expertise as one of the world's experts on bioethics guidelines to his role as a staff member and advisor. I recall his excellent presentation at the U.S. Holocaust Museum symposium on the anniversary of the Nuremberg Code. I have had occasion to call upon all three of them for advice on ethical issues over the years. They have been friends as well as professional colleagues.

Today, CIOMS is leading the way in transparency through its regular newsletters and public working group minutes. Transparency will become increasingly important in all facets of guideline development, and other organizations will need to emulate CIOMS.

In the future, CIOMS should continue developing guidelines targeted to the special needs of LMICs for example in emerging bioethical issues, broad consent, international data sharing, and many other areas. It is essential for CIOMS to stay closely involved with the work of ICH, WMA, and WHO. In fact, it is a testimonial to the small but excellent staff of its Secretariat that CIOMS is able to support so many well-run and productive working groups.

CIOMS membership

CIOMS was founded in 1949 as an organization to form a link between specialized international medical associations with research interests. Initially its activities were focused on the coordination of international medical congresses globally, and assistance to member organizations for the standardization of nomenclature in various medical disciplines.

In the 1960s, when fundamental changes were transforming the practice and potential of medicine, CIOMS as a non-governmental organization, with a mandate to collaborate with the United Nations and its specialized agencies, was in a position in provide a forum for representatives of different fields to make explicit the ethical and other non-technical considerations to be taken into account along with the technical ones in determining and implementing health policy.

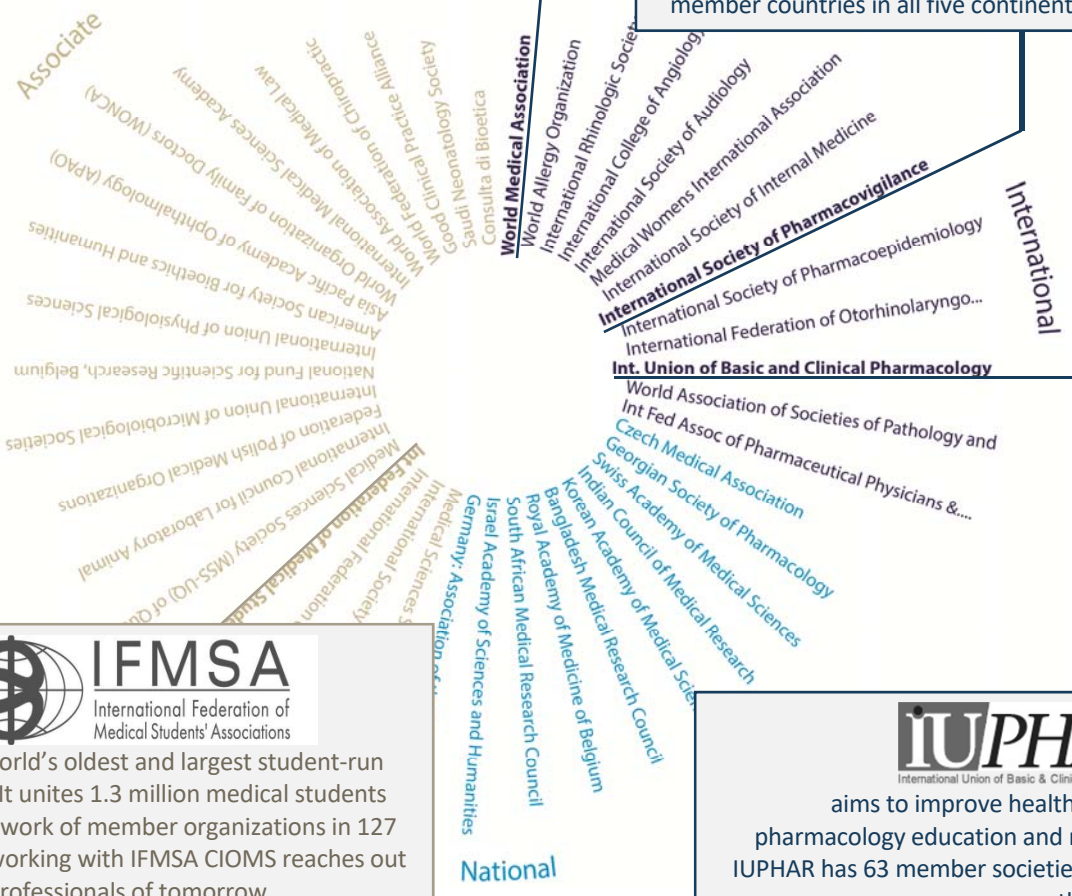
CIOMS is an associate partner of UNESCO, in official relations with the World Health Organization (WHO). Through its members CIOMS reaches out to a large part of the global health community. For example:

WORLD MEDICAL ASSOCIATION

brings together physicians from over 100 countries through their national associations.

ISoP

fosters science and learning to support the safe use of medicines. ISOP has 61 member countries in all five continents.



IFMSA International Federation of Medical Students' Associations

is one of the world's oldest and largest student-run organizations. It unites 1.3 million medical students through its network of member organizations in 127 countries. By working with IFMSA CIOMS reaches out to the health professionals of tomorrow.

CIOMS has an agreement with IFMSA to support medical student internships at WHO every year.

IUPHAR International Union of Basic & Clinical Pharmacology

aims to improve health through pharmacology education and research. IUPHAR has 63 member societies all over the world.

Message from CIOMS

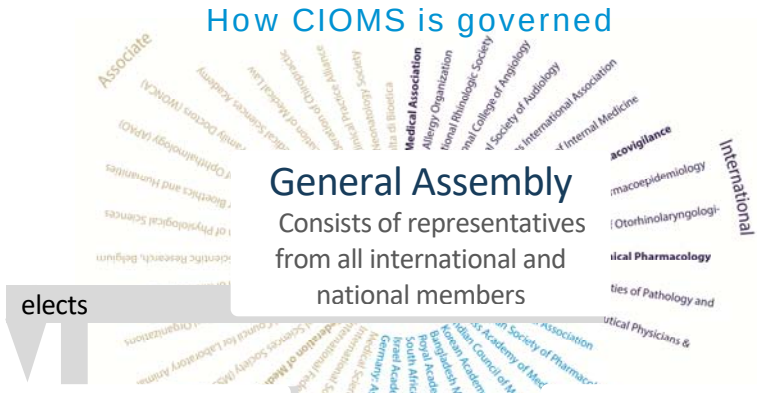
We are happy to celebrate the 70th Anniversary of CIOMS with all of our stakeholders. We are proud to lead this small but recognized influential and creative organization. On behalf of the Executive Committee and the Secretariat we would like to pay tribute to all the past Presidents, Secretaries-General, staff members, and members of the Executive Committee. It is their vision, their dedication to improving public health and their success in handling complex problems that we are celebrating. We will do our best to continue in their footsteps.

It is with tremendous gratitude that we would also like to acknowledge the contribution of all past and present members of numerous CIOMS international Working Groups. The Working Groups are the core of CIOMS!

Professor Hervé Le Louët
President

Dr Lembit Rägo
Secretary-General

How CIOMS is governed



President

Since 2016 Hervé Le Louët

Secretary-General

Since 2016 Lembit Rägo

Past Presidents

2010	Johannes JM van Delden
2003	Michel Vallotton
1993	John H (Jack) Bryant
1987	Francisco Vilardell
1980	Murillo Belchior
1970	Alfred Gellhorn
1964	Marcel Florkin
1961	Robert Cruickshank
1955	Ronald Ernest Tunbridge
1949	Joseph Maisin (Chairman of the Executive Committee)

Past Secretaries-General

2010	Gunilla Sjölin-Forsberg
2006	Gottfried Kreutz
1999	Juhana Idänpään-Heikkilä
1975	Zbigniew Bankowski
1974	Louis Verhoestraete
1971	Simon Btesh
1966	Vittorio Fattorusso
1961	Paul Albert Messerli
1950	Jean Delafresnaye

Unique topics: the Round Table conferences

In the mid-1960s, the world went through some huge political and technological developments. At the same time, biomedical scientific and technological advances were transforming the practice and potential of medicine, with unprecedented social, cultural and ethical implications.

In 1977 the World Health Assembly adopted the goal of health for all. This asserted the need for health policy to be informed by ethics and human values, indicating the field in which CIOMS could best complement the work of WHO. A particular aspect of biomedical technology—the development and safe use of medicines—became another dominant theme of CIOMS. Since the 1990s most of CIOMS working groups have focused on various aspects of pharmacovigilance.

These developments are reflected in the 30-year history of Round Table Conferences organized by CIOMS. The Council has not hesitated to take up some bold topics.

I.	Biomedical Science and the Dilemma of Human Experimentation	Paris, France	1967
II.	Heart Transplantation	Geneva, Switzerland	1968
III.	Evaluation of Drugs: WHOse Responsibility?	Liège, Belgium	1968
IV.	Medical Research: Priorities and Responsibilities	Geneva	1969
V.	Training of Research Workers in Medical Sciences	Geneva	1970
VI.	Drug Abuse: Non-Medical Use of Dependence-Producing Drugs	Geneva	1971
VII.	Recent Progress in Biology and Medicine: Its Social and Ethical Implications	Paris	1972
VIII.	Protection of Human Rights in the Light of Scientific and Technological Progress in Biology and Medicine	Geneva	1973
IX.	Medical Care and Society	Rio de Janeiro, Brazil	1974
X.	Health Needs of Society: A Challenge for Medical Education	Ulm, Germany	1976
XI.	Trends and Prospects in Drug Research and Development	Geneva	1977
XII.	Medical Ethics and the Protection of Human Rights	Cascais, Portugal	1978
XIII.	Economics and Health Policy	Geneva	1979
XIV.	Medical Ethics and Medical Education	Mexico	1980
XV.	Human Experimentation and Medical Ethics	Manila, Philippines	1981
XVI.	Health for All – a Challenge to Research in Health Manpower Development	Ibadan, Nigeria	1982
XVII.	Biomedical Research Involving Animals – Proposed International Guiding Principles	Geneva	1983
XVIII.	Health Policy Ethics and Human Values: An International Dialogue	Athens, Greece	1984
XIV.	Battered Children and Child Abuse	Berne, Switzerland	1985
XX.	Health Manpower out of Balance. Conflicts and Prospects	Acapulco, Mexico	1986
XXI.	Health Policy, Ethics and Human Values: European and North American Perspectives	Noordwijk, the Netherlands	1987
XXII.	Ethics and Human Values in Family Planning	Bangkok, Thailand	1988
XXIII.	Health Technology Transfer: Whose Responsibility?	Geneva	1989
XXIV.	Genetics, Ethics and Human Values: Human Genome Mapping, Genetic Screening and Gene Therapy	Tokyo and Inuyama City, Japan	1990
XXV.	Ethics and Epidemiology: International Guidelines	Geneva	1990
XXVI.	Ethics and Research on Human Subjects. International Guidelines	Geneva	1992
XXVII.	Drug Surveillance: International Cooperation – Past, Present and Future	Geneva	1993
XXVIII.	Poverty, Vulnerability, the Value of Human Life and the Emergence of Bioethics	Ixtapa, Mexico	1994
	The Declaration of Inuyama, a follow-up to the 1990 Conference	Inuyama and Nagayo	1995
XXIX.	Ethics, Equity and Health for All	Geneva	1997

Did you know?

Over the decades, the work of CIOMS has had a lasting impact on many areas of medical sciences.

A landmark CIOMS meeting put controlled clinical trials on the map

The meeting took place in Vienna on 23–27 March **1959** and was chaired by Austin Bradford Hill, director of the British Medical Research Council's Statistical Research Unit. The proceedings described the British concept of the controlled clinical trial and the place that it held in medicine.

See also: Bird SM. **The 1959 meeting in Vienna on controlled clinical trials – a methodological landmark**. JLL Bulletin: Commentaries on the history of treatment evaluation.

> *The conference was in itself an experiment. The meeting was a closed one, and only one hundred participants were invited. One national group, the British, was charged with the task of presenting each topic to be studied. …Originally we did not intend to publish the proceedings in English …. But the number of requests for the working documents from many countries was so great that we decided to publish in full the introductory papers in mimeographed form. This limited edition was soon exhausted, and in view of the continued demand we have decided to bring out a printed version…*
>
> ***JF Delafresnaye, First Executive Secretary of CIOMS,***
> *in the preamble to the conference proceedings*

> *As I sat on the dais in Room X of UNESCO House in Paris, about to deliver one of two introductory presentations to the "round table" of assembled experts, I felt anxious. The hall was gigantic. In addition to the front rows, occupied by scientists from near and far, there were rows upon rows of seats, each with a desk and microphone, reserved for ambassadors of the UNESCO countries, other rows for representatives of international scientific associations, and still others for the press. Booths for simultaneous translation overlooked the hall.*
>
> ***Amitai Etzioni***
> *In: Genetic Fix. New York, MacMillan Publishing Co. , Inc, 1973*

A CIOMS Round Table Conference has inspired a book

Amitai Etzioni, well-known ethicist, wrote a book based on his attendance at the XIIIth CIOMS Round Table Conference, held at the UNESCO Headquarters in Paris in **1972**.

The longest-serving CIOMS Secretary-General was in office for 25 years

Zbigniew Bankowski was Secretary-General of CIOMS from **1975** to 1999. He passed away in 2010.

> *There is much I could say about my esteemed friend. Suffice it to say that, by his personal commitment and his seemingly inexhaustible energy, he has succeeded in bringing CIOMS to the forefront of the global dialogue on ethics in health policy.*
>
> ***Hiroshi Nakajima, then WHO Director-General,***
> *at the Opening of the XXVth CIOMS Round Table Conference*

> *This was the first time that, as a result of several years of laborious and extensive international consultations, the supreme body of the United Nations – the nearest we have to a World parliament – had taken action on a matter specifically affecting the medical and allied professions.*
>
> ***Zbigniew Bankowski,***
> *in his Background Note to the 1983 CIOMS publication*

CIOMS guidelines have been adopted as a UN resolution

The CIOMS Principles of Medical Ethics relevant to the role of health personnel, particularly physicians, in the protection of prisoners against torture and other cruel, inhuman or degrading treatment or punishment were adopted by the General Assembly as an annex to UN Resolution 37/194 of 9 March **1983**.

In the leaflet supplied with your medicine, the frequency of side effects is presented according to CIOMS guidance

The frequency categories are stated as recommended in the **1990s** by the CIOMS III Working Group.

CIOMS reports formed the basis of several ICH guidelines (ICH E2A, E2C, E2D and E2F), laying the foundations for modern pharmacovigilance.

Very common	*≥ 1/10 (≥10 %)*
Common	*≥1/100 and < 1/10 (≥1% and <10%)*
Uncommon	*≥1/1000 and <1/100 (≥0,1% and <1%)*
Rare	*≥1/10000 and <1/1000 (≥0,01% and <0,1%)*
Very rare	*<1/10000 (<0,01 %)*

> *The 25-year experience of RUCAM use confirmed that the success was due to its objective, standardized, and liver-injury-specific approach structured with defined key elements derived from a series of DILI cases with positive rechallenge.*
>
> ***Danan G, Teschke R.***
> *Drug Safety. 2018;41 (8), 735–743.*

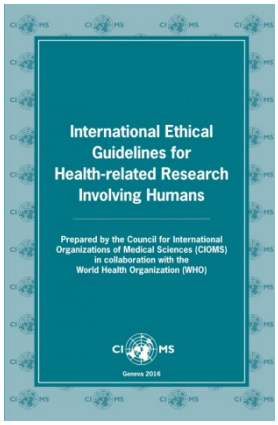
A CIOMS scale for liver injury has been used for 25 years

Launched in **1993** and partially based on the results of an international consensus meeting organized under the auspices of CIOMS, the Roussel Uclaf Causality Assessment Method (RUCAM) is the most used causality assessment tool worldwide for the diagnosis of drug-induced liver injury (DILI) and herb-induced liver injury (HILI).

In 2017 CIOMS started a new Working Group on DILI. The proceedings from this Working Group are expected to replace RUCAM.

CIOMS publications

Ethical guidelines



"CIOMS is a small organization but represents a big name in research ethics. The guidelines for the ethical evaluation of health related research guidelines are up to date, comprehensive, coherent and widely used. By providing extensive commentaries, they have proved to be a valuable tool for research ethics committees worldwide."

Johannes JM van Delden, Past President of CIOMS

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Guidelines on ethics and product development

International ethical guidelines for health-related research involving humans	2016	En Fr Es Pt Uk Ru Ch*
International Ethical Guidelines for Epidemiological Studies	2009	En
Pharmacogenetics: Towards improving treatment with medicines	2005	En
International Ethical Guidelines for Biomedical Research Involving Human Subjects	2002	En Fr Es, Pt* Cz* Ch* Jp*
Biomedical Research Ethics: Updating International Guidelines: A Consultation	2000	En
Ethics, Equity and Health for All	1997	En
Poverty, Vulnerability and the Value of Human Life	1994	En
International Ethical Guidelines for Biomedical Research Involving Human Subjects	1993	En, Cz*
Ethics and Research on Human Subjects. International Guidelines	1992	En, Fr*
International Guidelines for Ethical Review of Epidemiological Studies	1991	En, Es*
Health Manpower Out of Balance: Conflicts and Prospects	1987	En
Health Policy, Ethics and Human Values: An International Dialogue	1985	En
International Guiding Principles for Biomedical Research Involving Animals	1985	En
Biomedical Research Involving Animals: Proposed International Guiding Principles	1984	En
Principles of Medical Ethics Relevant to the Protection of Prisoners Against Torture	1983	En includes Fr Es Ar Ch Ru
Human Experimentation and Medical Ethics	1982	En

Clinical pharmacology

WHO / IUPHAR / CIOMS Clinical Pharmacology in Health Care, Teaching and Research	2012	En Jp

Clinical pharmacology is one of the core disciplines for medicines development and safe use. This position paper was composed and edited by representatives of the International Union of Basic and Clinical Pharmacology (IUPHAR), WHO and CIOMS. It is an updated and edited version of a 2010 publication and contains new chapters of special relevance to global health.

En=English; Fr=French; Es=Spanish; Pt=Portuguese; Uk=Ukrainian; Ru=Russian; Ch=Chinese; Ar=Arabic; Cz=Czech; Jp=Japanese
*=Not (yet) available through the online ordering system. Please contact info@cioms.ch

Pharmacovigilance

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CIOMS Guide to Vaccine Safety Communication	2018	En
CIOMS Guide to Active Vaccine Safety Surveillance	2017	En
Development and Rational Use of Standardised MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA	2016	En Jp
Evidence Synthesis and Meta-Analysis for Drug Safety **(CIOMS X)**	2016	En
Practical Approaches to Risk Minimisation for Medicinal Products **(CIOMS IX)**	2014	En, Jp*
Definition and Application of Terms for Vaccine Pharmacovigilance	2012	En
Practical Aspects of Signal Detection in Pharmacovigilance **(CIOMS VIII)**	2010	En Ch
Development Safety Update Reports (DSUR): Harmonizing the Format and Content for Periodic Safety Report during Clinical Trials **(CIOMS VII)**	2006	En, Jp*
Management of Safety Information from Clinical Trials **(CIOMS VI)**	2005	En, Jp*
Development and Rational Use of Standardized MedDRA Queries (SMQs): Retrieving Adverse Drug Reactions with MedDRA	2004	En
Current Challenges in Pharmacovigilance: Pragmatic Approaches **(CIOMS V)**	1999	En
Guidelines for Preparing Core Clinical Safety Information on Drugs (second edition) **(CIOMS III and V)**	1999	En
Reporting Adverse Drug Reactions: Definitions of Terms and Criteria for Their Use	1999	En
Benefit-risk balance for marketed drugs: Evaluating safety signals **(CIOMS IV)**	1998	En
Guidelines for Preparing Core Clinical Safety Information on Drugs **(CIOMS III and V)**	1995	En
Drug Surveillance: International Cooperation Past, Present and Future **(XXVIIth Round TableConference)**	1994	En
International Reporting of Periodic Drug Safety Update Summaries **(CIOMS II)**	1992	En
International Reporting of Adverse Drug Reactions **(CIOMS I)**	1987	En
Monitoring and Assessment of Adverse Drug Effects **(CIOMS I)**	1985	En, Es*
Safety Requirements for the First Use of New Drugs and Diagnostic Agents in Man	1983	En

En=English; Jp=Japanese; Ch=Chinese. *=Not available via online ordering. Please contact info@cioms.ch

"For more than 20 years I have been involved in adverse drug reaction detection, analysis and reporting. The CIOMS criteria have been the most valuable resource for causality assessment and standards for pharmacovigilance."

Petra Thürmann (IUPHAR, and CIOMS Executive Committee member

"CIOMS has a rich history of bringing together a fair balance of industry and government stakeholders and other relevant parties to develop consensus approaches to gnarly pharmacovigilance and ethics issues. Many of the CIOMS consensus recommendations and principles have been adopted by regulators for protection of study subjects and patients around the globe. I am proud to have been an active contributor to several Work Groups."

Bill Gregory, Pfizer

International nomenclature of diseases

In 1975 CIOMS and WHO jointly undertook the International Nomenclature of Diseases project. More than 20,000 synonymous terms were listed in a total of 11 published volumes, 7 of which can still be ordered through the CIOMS website.

"I was part of five of the early CIOMS safety working groups. The reports of these working groups formed the direct basis for several of the ICH guidances on product safety surveillance and on-going assessment. The benefit of the CIOMS forum was as a neutral, comprehensive "think tank" in which stakeholders could develop trust in each other and discover their common ground. With that trust and common ground recognition, we were able to develop documents that expressed strategic goals, specific process ideas and consensus aspirations. ICH, given its regulatory imprimatur, was then able to take these ideas and change them from aspirations into the actual way that these issues are addressed globally."

Murray ("Mac") Lumpkin, Bill & Melinda Gates Foundation, Senior U.S. FDA official at the time of his involvement in the CIOMS Working Group

Where to from here?

I took a fond farewell of CIOMS in Geneva at the end of 2015. I am grateful to have seen, during my time in office, three WG reports being published and four initiated. The main pillar of these publications was the excellent contribution of involved experts.

The very friendly working climate at CIOMS encouraged new initiatives, and it is with great satisfaction and happiness that I have seen the recent commencement of the new CIOMS WG on patient involvement at all steps during the life-cycle of a medicine. The three other new CIOMS WGs initiated since my departure – Drug Induced Liver Injury, Clinical Research in Resource-Limited Settings and MedDRA Labeling Groupings – are also covering highly relevant and very important topics.

There are a lot of motivating topics in need of global harmonization but also an increased number of interested actors willing to take a lead. The strengths of CIOMS is the platform itself, involving all stakeholders, the global perspective involving all regions of the world, and the close collaboration with UNESCO and WHO. Over the years there has also been a fruitful collaboration with the International Conference on Harmonization (ICH), and since 2016 CIOMS is an ICH observer.

The future of CIOMS looks promising although it includes challenges. I am convinced that CIOMS will seize its opportunities. ***I wish all experts involved in CIOMS activities and the dedicated staff at the CIOMS Secretariat a successful future!***

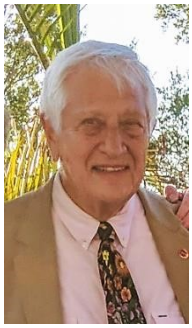
Gunilla Sjölin-Forsberg, Immediate Past Secretary-General

It was an honour for me to work with industry and regulatory colleagues who were willing to set aside personal and institutional beliefs in order to agree on the best standards for managing and reporting drug safety information. The working groups under CIOMS perform an invaluable service by providing unbiased, scientifically- and ethically-based advice.

In that spirit, for purposes of making presentations over the years on the work of CIOMS, I created a disclaimer which for me summarizes what CIOMS is all about:
"CIOMS Does Not Have any Official Regulatory or Other Authority. It Influences and Persuades by the Strength of its Ideas and its Credibility."

May it continue to serve!

Arnold J Gordon, Pharmaceutical Consultant



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