

# **Report of the Division of Clinical Pharmacology**

## **IUPHAR Executive Meeting Basel May 2012**

Since the last IUPHAR Executive Meeting in Paris October 2011, The Division of Clinical Pharmacology (DCP) officers have held four Skype conferences in December 2011 and February, March and April 2012

### **Pharmacoepidemiology**

The DCP officers consider it is important to have activity in this area and have been exploring possibilities for formation of a Subcommittee for Pharmacoepidemiology. Several suggestions have been made for individuals to lead this development. After somewhat prolonged discussions, the first individual approached eventually declined. Other approaches are currently being made by Petra.

The Division has proposed a symposium on geriatric pharmacoepidemiology for the 2013 meeting of ISPE and this has been accepted. There may be no expense to IUPHAR.

### **Relationship with FIP**

We see an obvious affinity between the division and clinical pharmacy activities in FIP. Patrick is currently exploring opportunities for collaboration between our societies.

### **Relationship with ASCPT**

Darrell Abernethy has made some tentative approaches to ASCPT regarding for example joint symposia at their meetings. Forming a relationship has proved difficult and is not being pursued at present.

### **Focussed Regional Conferences**

The Section of Pharmacogenetics is planning a conference "Pharmacogenetics in South-America" in Rio de Janeiro, Brazil. This is a Meeting of the Latin-American Pharmacogenetics Network, the FDA and the Brazilian Pharmacological Society (Guilherme Kurtz Suarez). The IUPHAR Section of Pharmacogenetics chaired by Ingolf Cascorbi will host one keynote lecture held by Magnus Ingelman-Sundberg and a symposium on "Recent Progress in the Pharmacogenomics of Drug Transporters" with Deanne Kroetz, Matthias Schwab and himself as speakers. The conference will be on June 28/29 2012. The CPD initially explored whether this might be a RFC but it did not meet the criteria. Nevertheless, IUPHAR has agreed to provide support for the symposium organised by Ingolf Cascorbi to the extent of US\$5,000 equally shared between IUPHAR and the CPD.

A meeting is tentatively to be held in 2015 in perhaps Hong Kong jointly sponsored by the SEAWP group and the BPS. This may meet the criteria for a RCP.

### **Clinical Pharmacology Publication**

This is an "update" of the 1970 WHO report on the relevance and importance of the discipline of clinical pharmacology to improving the use of drugs in the delivery of health care. A preliminary version of the current document was published as "Clinical Pharmacology in Research, Teaching and Health Care- Considerations by IUPHAR, the International Union of Basic and Clinical Pharmacology" in Basic and Clinical Pharmacology and Toxicology (BCPT) 2010, Volume 107, pages 531 – 559.

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The preliminary version, with three extra chapters, has been exhaustively and carefully edited by Don Birkett on behalf of the DCP, and then by Michael Orme and Folke Sjoqvist, the editors of the original document. While the document addresses mainly the physician clinical pharmacologist, careful attention has been paid to acknowledging the multidisciplinary nature of the broader discipline of clinical pharmacology and the contributions to the discipline by a wide range of professional groups involved with improving the use of medicines in the delivery of health care.

A high-level consortium, comprising IUPHAR, CIOMS and WHO, have agreed to jointly publish the document. It will be professionally laid out and attractively printed both as web-based and printed versions. A number of organisations have generously agreed to provide the finance for this (Swedish and British societies, WHO, CIOMS and IUPHAR, the latter through its DCP).

The document is getting a final edit by Michael Orme and Folke Sjoqvist and this will be sent to the officers of IUPHAR for approval. It will then have a final “polish” in early May before being sent for printing.

### **COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES (CIOMS)**

CIOMS has enthusiastically agreed to become a member of the consortium publishing the clinical pharmacology document. For this reason, and in general, it is valuable for IUPHAR to become a member of CIOMS. CIOMS, affiliated with WHO, is a peak and influential organisation in the medical sciences. Membership will provide an opportunity to be active in their activities and working groups and provides a valuable avenue into WHO itself. The aims and activities of CIOMS are important to IUPHAR, in particular our clinical division, being in the fields of ethics of human research, adverse drug reactions, epidemiology and disease nomenclature. Members and associate members include important international and national bodies - for instance ISPE and ISOP are members among other major international medical societies.

The officers of IUPHAR have agreed that it should become a member of CIOMS and this is currently being progressed by Lynn and others. The annual fee of US\$200 will be paid by the DCP. A statement of the structure and functions of CIOMS is attached to this report (See Addendum 2).

### **IUPHAR Website**

Petra Thuermann has been in close contact with Lynn regarding the organisation of the new IUPHAR website. The Division wishes to use a private section for development work and to develop a comprehensive range of educational materials for free use. This activity is ongoing.

### **WCP 2014**

The Division officers have been concerned about appropriate clinical pharmacology content of WCP 2014. They will take part in the Scientific Advisory Meeting in Basel and are preparing a list of possible clinical pharmacology content.

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### **SubCommittees of the Division of Clinical Pharmacology**

The two current DCP subcommittees are the Subcommittee for Clinical Pharmacology in Developing Countries (Lars Gustafsson) and the Subcommittee for Geriatric Clinical Pharmacology (David LeCouteur). Brief reports from these Subcommittees are below.

#### ***SubCommittee for Geriatric Clinical Pharmacology***

The SC had 4 skype/telephone conferences, one with Lembit Rägo to explore the original plan, namely an Essential medicines List for the Elderly. However, due some open positions at WHO and a general uncertainty for planning, this idea will not be followed in the near future.

The Symposium of Geriatric Pharmacoepidemiology was planned by the SubCommittee. The SubCommittee will follow up this symposium by writing a paper on the subject of Geriatric Pharmacology and will develop documents for a curriculum and prescribing. The symposium programme was as follows:

#### **When pharmacoepidemiology gets old: use of medicines in geriatric patients**

Darrell Abernethy: Age and comorbidity of patients in clinical trials versus “real patients”

Sarah Hilmer: Understanding interactions between medicines and geriatric syndromes: the role of pharmacoepidemiology

Sirpa Hartikainen: Sedative drug load in the elderly and adverse outcomes

Petra Thürmann: Prescribing of potentially inappropriate medication – a quality indicator for drug prescription?

#### ***Subcommittee for Clinical Pharmacology in Developing Countries***

See Addendum 1

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## Addendum 1

### Report on activities for “Subcommittee for Clinical Pharmacology in Developing Countries” (July 1, 2012 to March 31, 2011) and planning 2012-2013.

#### 1. Subcommittee members

The following colleagues serve as members of the subcommittee since 2007:

Professor MD and Dean, Grace Gonzaga, Dep. of Clinical Pharmacology, Medical School of the University of Santo Tomo, Manila, The Philippines. E-mail [gracegarayblasgonzaga@yahoo.com](mailto:gracegarayblasgonzaga@yahoo.com).

Professor MD, senior consultant, Lars L Gustafsson (Chairman), Division of Clinical Pharmacology (C1-65), Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital, SE-141 86 Stockholm Sweden. Email: [lars-l.gustafsson@ki.se](mailto:lars-l.gustafsson@ki.se), phone 46-8-58581066 (58581067 secretary), fax 46-8-58581070

Professor MD R L Jayakody, Chairman, Dep. of Clinical Pharmacology, University of Colombo, Sri Lanka. E-mail: [jayakodyrl@hotmail.com](mailto:jayakodyrl@hotmail.com).

Professor MD Mahmoud Khayyal, Dep. of Pharmacology, Azhar university, Cairo, Egypt (Joined August 2008, Chairman Clinical Pharmacology Section of Egyptian Society of Pharmacology).E-mail: [khayyal@hotmail.com](mailto:khayyal@hotmail.com).

MD PhD Philip Sasi, Chairman Dep. of Clinical Pharmacology, Muhimbili University Health College, Dar-es-Salaam Tanzania. E-mail: [psasi@muhas.ac.tz](mailto:psasi@muhas.ac.tz).

Professor MD Akin Sowunmi, Dep. of Pharmacology & Therapeutics, University of Ibadan, Nigeria. E-mail: [akinsowunmi@hotmail.com](mailto:akinsowunmi@hotmail.com).

Professor MD Mabel Valsecia, Dep. of Clinical Pharmacology, Corrientes University Argentina. E-mail: [mwalsecia@med.unne.edu.ar](mailto:mwalsecia@med.unne.edu.ar)

MD PhD Paul Waako, Chairman Dep. of Pharmacology & Therapeutics, University Health College of Medical Sciences, Makerere University, Kampala Uganda. Mail: [pwaako@chs.mak.ac.ug](mailto:pwaako@chs.mak.ac.ug)

Professor Andrew Walubo, Dep. of Pharmacology, University of the Free State, Bloemfontein, South Africa. E-mail: [waluboa.md@ufs.ac.za](mailto:waluboa.md@ufs.ac.za).

Professor MD Fan-Dian Zeng, Dept. of Pharmacology, Tongji Medical College of Huazhong, University of Science and Technology, People Reepublic of China. E-mail: [fdzeng@163.com](mailto:fdzeng@163.com).

Since Worldpharma in Copenhagen 2010 new members have joined the group:

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Professor MD PhD, Prof Milica Prostran, Dep of Clinical Pharmacology and Toxicology, School of Medicine, University of Belgrade, Dr Subotica 4, PO Box 840, 11129 Belgrade, Serbia. Phone: ++381-11-3643-381, fax: ++381-11-3643-397, mobile: ++381-66-8300-014, e-mail:  
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Professor MD Adrian Llerena, Clinical Pharmacology, University of Extremadura, Badjoz, Spain. E-mail: [allerena@unex.es](mailto:allerena@unex.es) (He regretted that he could attend but he want to be member of the group).

Four senior colleagues serve as advisors: Professor Chris van Boxtel ([cvboxtel@upcmail.nl](mailto:cvboxtel@upcmail.nl)), Amsterdam, The Netherlands; Professor Folke Sjöqvist ([folke.sjoqvist@ki.se](mailto:folke.sjoqvist@ki.se)), Stockholm, Sweden, Professor Anthony Smith ([Anthony.Smith@newcastle.edu.au](mailto:Anthony.Smith@newcastle.edu.au)), Newcastle and professor Joan-Ramon Laporte ([irl@icf.uab.es](mailto:irl@icf.uab.es)), Barcelona, Spain.

**2. Work plan for the Subcommittee** A work plan for 2007-2012 has been developed. It was summarized with planned activities for 2011-12 in our report to IUPHAR February 14<sup>th</sup> 2011. It is followed to a great extent.

### 3. Review of activities July 1, 2011 to March 31, 2012

#### 3.1. Participation in the development of the IUPHAR document on the discipline *Clinical Pharmacology*

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The strategic IUPHAR-document on the discipline clinical pharmacology is being revised and will be published in a joint version by IUPHAR, CIOMS (Council for International Organizations of Medical Sciences) and WHO. The subcommittee has communicated the draft widely and given input during 2011 and 2012 on the version that is soon final. Drs Walubo and Gustafsson have contributed as authors of specific chapters. Subcommittee members have used their contacts to assure feed-back from colleagues in developing and emerging countries. Professor Folke Sjöqvist is in charge of editing this version together with the Clinical Division of IUPHAR.

### **3.2 Secure drug distribution meeting organized by Ministry of Health, Tanzania, September 16, 2011**

Lars L Gustafsson and professor Björn Pehrson Royal Institute of Technology in Stockholm were invited to a Ministry of Health to a meeting in Tanzania on how to support secure drug distribution by IT-based solutions. Lars L Gustafsson represented the subcommittee. Proceedings from the meeting is presently being approved by the Ministry of Health. Several research groups in Africa are involved to further develop and test integrated IT-based solutions for drug ordering ordering and continuous medical education. African and European research groups have formed an alliance to advocate for and test pilot installations of high-speed fiberoptic based communication in countries situated at Lake Victoria in East Africa. College of Health Sciences at Makerere University is involved in these pilot projects through its Deputy Dean professor Celestino Obua (Department of Pharmacology & Therapeutics) and the subcommittee through its chairman.

### **3.3. Pharmacokinetic/dynamic course for HIV- and antimalarial drugs organiaed by Makerere University and Karolinska Institutet in collaboration with IUPHAR**

The joint Makerere University and Karolinska Institutet research course was carried out during two weeks in October 2012. It was organized in collaboration with our Subcommittee. A total of 15 participants were admitted and 11 graduated successfully. The design of the course is available on request ([Lars-L.Gustafsson@ki.se](mailto:Lars-L.Gustafsson@ki.se)). Members of the subcommittee in collaboration with the organizing group is willing to assist and help colleagues planning to do a similar course in Africa, Asia or Latinamerica. The subcommittee plans to apply for funding to assist experts to establish a similar course elsewhere in Africa, Asia or Latinamerica (course plan enclosed) if there is an interest.

### **3.4 Suggested program at World Congress in Pharmacology and Clinical Pharmacology 2014 in South Africa**

The subcommittee has given detailed suggestions for symposias and themes for the Congress. In addition we have answered the questionnaire about the focus for the congress considering needs in research and education in clinical pharmacology in developing and emerging countries. Dr Walubo in our group is member of the Scientific Committee. The following symposias and/or themes were suggested by the Subcommittee through its chairman in consultation with the members of the group (February 2012).

1. INITIATIVES FOR RATIONAL USE OF MEDICINES IN AFRICA
  - a. How irrational is the use of medicines in Africa?
  - b. Initiatives in East Africa for improved undergraduate training in pharmacology and clinical pharmacology

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- c. Impact of Drug and Therapeutics Committees in West Africa
  - d. Regional and effective initiatives for monitoring quality of drug therapy in Africa South of Sahara
2. **OPEN, GLOBAL DRUG DISCOVERY AND CLINICAL DRUG DEVELOPMENT-a panacea to improve therapy of neglected diseases**
    - a. Neglected diseases: success or failure in drug discovery during the past 20 years?
    - b. New innovative molecular and clinical targets for drug therapy of neglected diseases
    - c. Status and future: open networks for drug discovery
    - d. Status and future: open networks for clinical drug development
  3. **PROS, CONS AND IMPACT OF CLINICAL DECISION SUPPORT SYSTEMS IN DRUG THERAPY**
    - a. Technical and knowledge based limitations: what clinical problems can be addressed and what can't
    - b. Decision support systems in resource strained countries
    - c. Ways to increase clinical usage of decision support systems
    - d. Future development-new databases, graphical interfaces and one signal per drug
  4. **INFORMATION TECHNOLOGY IS TRANSFORMING THE PHARMACOLOGICAL SCIENCES**
    - a. **Future in research in basic and clinical pharmacology**
    - b. **Future in undergraduate teaching and training**
    - c. **Future in clinical pharmacological services**
    - d. **Future technological and society breakthroughs: how will pharmacologists in resource poor settings collaborate locally, regionally and globally**

### **3.5. WHO initiated global course on "Interface management of pharmacotherapy" aiming for collaboration between primary and hospital care**

WHO headquarter office in Geneva (Dr Richard Laing) has taken initiative to a global course and site visit to study and discuss methods for improving selection, communication and adherence using the experience about the Wise List from Stockholm as the basis for the course (*Gustafsson LL, Wettermark B, Godman B, Andersén-Karlsson E, Bergman U et al. The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. Basic Clin Pharmacol Toxicol 2011;108:224-33*). The Drug and Therapeutics Committee in Stockholm in collaboration with clinical pharmacology at Karolinska Institutet is arranging this course and site visit (*Interface management of pharmacotherapy: promoting hospital-primary care collaboration for Rational Use of Medicines" September 11-13, 2012*). The target group is in total 25-30 leaders of either Drugs and Therapeutics committees or managers of healthcare around the globe. IUPHAR subcommittee members and its chairman Lars L Gustafsson have been involved in designing the course to it is relevant for developing and emerging countries in line with the priorities of the Subcommittee.

### **4.Exploration of options for funding**

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So far costs for meetings, travels and administration have been covered by individual members of the subcommittee or their home institutions. The clinical division of IUPHAR has declared that some travel expenses can be covered yearly. This is considered for our activities 2012 and onwards. To raise major and sustainable funds the subcommittee will focus on one or two major activities.

On behalf of the subcommittee

Lars L Gustafsson, MD, PhD  
Professor, senior consultant  
Chairman "Subcommittee for Clinical Pharmacology in Developing Countries  
Division of Clinical Pharmacology, Department of Laboratory Medicine  
Karolinska Institutet, Stockholm Sweden

**Attachment: Course plan kinetic-dynamic course focusing on HIV/AIDS and malaria drug therapy  
Makerere University-Karolinska Institutet, Kampala October 2011**

**Attachment 1: Course plan for pharmacokinetic/dynamic course focusing on HIV/AIDS and malaria  
drug therapy in Kampala, Uganda October 2012 (joint Makerere University and Karolinska  
Institutet in IUPHAR Subcommittee)**

 [Stäng](#)



### KURSPLAN FÖR KURS PÅ FORSKARNIVÅ

Kurskod

2494

Kursens svenska benämning

Klinisk farmakokinetisk/farmaokodynamisk forskningskurs-fokus på läkmedelsbehandling av HIV/AIDS och malaria

Kursens engelska benämning

Clinical pharmacokinetics/pharmacodynamics research course- focus on HIV/AIDS- and antimalarial drug therapy

Antal högskolepoäng

4.5

Kursansvarig institution



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Institutionen för laboratoriemedicin

## Nivå

Forskarnivå

## Särskild behörighet

Insight into basic aspects of pharmacokinetics and pharmacodynamics as provided by web based teaching courses (e.g. A First Course in Pharmacokinetics and Biopharmaceutics by David Bourne- available at <http://www.boomer.org/pkin/>) or corresponding knowledge is recommended.

## Betygsskala

Godkänd/Underkänd

## Kursens lärandemål

- Critical insights and understanding how to evaluate design and results of pharmacokinetic/dynamic studies of HIV- and antimalarial drugs.
- How to design and plan for performing pharmacokinetic/-dynamic studies including sampling schedules for evaluation of drug concentrations and pharmacological and outcome effects
- Theory and practice of pharmacokinetic/-dynamic data analysis and modelling using rich data
- Understanding of the principles for population pharmacokinetic/-dynamic modelling using sparse data sampling strategies
- Documented capacity to calculate and understand pharmacokinetic/-dynamic parameters

## Kursens innehåll

This is a course that has been recommended to be included in World Health Program at Karolinska Institutet

### BASIC LECTURES MALARIA

Pathology, Clinical endpoints, Variables for PK-PD modeling, Overview of current pharmacological treatments

### BASIC LECTURES HIV/AIDS

Pathology, Clinical endpoints, Variables for PK-PD modeling, Overview of current pharmacological treatments

### LITERATURE STUDIES ON PK-PD MODELLING OF DRUGS USED TO TREAT HIV/AIDS AND MALARIA

To summarize and discuss :

Study population and selected demographic covariates, Treatment regimens and principles for dose individualization, Clinical endpoints used for PK-PD modeling, Bioanalytical methods, Selection of PK model, Selection of PK-PD model, Performance of PK-PD model, Conclusions and usefulness of results

### LITERATURE STUDIES ON RATIONALE FOR CURRENT DOSING REGIMENS OF SELECTED HIV/AIDS AND ANTIMALARIAL DRUGS

To summarize and discuss

Studies performed to support dosing principles, Quality of studies, Available data in subgroups (males, females, children, impaired renal or hepatic function), Suggestions for supplementary studies

### CONCEPTS IN PK MODELLING

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Purpose of modelLing, PK variables and their physiological correlates, Model selection, Compartmental vs. non-compartmental methods, Population models, Assessment of model performance

### CONCEPTS IN PK-PD MODELLING

Purpose of modelLing, PD variables and their physiological correlates, Model selection, Time dimension in PK-PD models, Assessment of model performance

### MATHEMATICAL CONCEPTS

Types of data (dichotomous, categorical, continuous), Logarithms and exponential functions, Regression functions (linear, nonlinear, logistic), Distribution fitting, Parametric and nonparametric statistical tests

### HANDS-ON TRAINING IN PK AND PK-PD MODELLING OF GIVEN DATA

Organizing the database, Graphical and statistical methods to explore data, Transformation of data  
Setting up aims of modeling, Model selection, Evaluation of model performance (CI for parameters, correlations, AIC), Statistical evaluation of results

### CONSIDERATIONS FOR DESIGN OF PK-PD EVALUATIONS IN TREATMENT STUDIES

Sampling of PK and PD data, Analysis plan, Sample size

## Arbetsformer

Lectures, group work, PK-PD calculations, demonstrations and literature review/seminars. Except for teachers/lecturers the course will have tutors with about 5 students each.

This is a joint research course between Karolinska Institutet and Makerere University. It will be part of Global Health Program at Karolinska Institutet.

Observe that the 3 course weeks contains 3 days of home based work with literature review and evaluations, 2 weeks run in Kampala (Makerere University or at Karolinska Institute, Stockholm (affiliated)) and with 2 days for home examination. The course centre will be in Kampala but it will be video linked with high-resolution technique (Clinical Pharmacology, Huddinge) and with local leadership and practical calculation classes at Karolinska Institutet. This is a joint course between Makerere University (Dep of Pharmacology & Therapeutics) and Karolinska Institutet (Clinical Pharmacology, Laboratory Medicine).

Costs for travel and housing have to be covered by participant/participating home institution.

## Obligatoriska moment

Lectures, groups work, calculations, demonstrations and seminars are obligatory. If a student fail to participate in all moments it is required that the students document knowledge/understanding and document that he/she has calculated and analyzed data.

Maximum 22 participants at main course site (Makerere University).

Markus Jerling MD PhD associated to Clinical Pharmacology/Laboratory Medicine is course leader with professor

Lars L Gustafsson, professor, Karolinska Institutet as course director.

Main teachers include Urban Hellgren, associate professor and Anders Sönnberg, professor at

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Karolinska Institutet, Stockholm Sweden and Celestino Obua, associate professor, Pharmacology & Therapeutics, Makerere University, Kampala Uganda

The course will recruit well-known experts in the field from Sweden, Europe and Uganda. At the main campus in Uganda we will have about 6 junior staff for practical instructions and about 2 and one coordinator in Stockholm. Experts in the area of pharmacokinetics/pharmacodynamics from drug industry, from academia and from registration bodies (i.e. European Medicines Agency, Medical Products Agency in Sweden) will be invited to lecture.

Information is given by University Secretary Margit Ekström (margit.ekstrom@ki.se), Clinical Pharmacology, Dep of Laboratory Medicine, Karolinska Institutet or by Associate professor Celestino Obua (cobua@chs.mak.ac.ug) Dep of Pharmacology & Therapeutics, Makerere University

The curriculum will be

### Examination

Literature reviews and home examination.

### Kurslitteratur och övriga läromedel

1. Principles of Clinical Pharmacology, Second Edition [Hardcover] by Arthur J. Atkinson Jr. (Editor), Darrell R. Abernethy (Editor), Charles E. Daniels (Editor), Robert Dedrick (Editor), Sanford P. Markey (Editor)

2. A First Course in Pharmacokinetics and Biopharmaceutics by David Bourne-available at <http://www.boomer.org/pkin/>

3. Prepared course material

4. Literature articles provided and recommended

Fastställande av arbetsgruppen för kurser på forskarnivå i enlighet med delegation från Styrelsen för forskarutbildning (2001-12-19).

Datum för fastställande

Datum för revidering

### Kursansvarig

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Ej satt

### Kontaktpersoner

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### ADDENDUM 2 – Structure and Activities of CIOMS

#### COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

c/o World Health Organization - CH-1211 Geneva 27 (Switzerland)

#### About CIOMS

The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949. In 2009 CIOMS was celebrating the 60<sup>th</sup> anniversary of its creation.

Through its membership, CIOMS is representative of a substantial proportion of the biomedical scientific community. The membership of CIOMS in 2010 includes over 55 international, national and associate member organizations, representing many of the biomedical disciplines, national academies of sciences and medical research councils. The main objectives of CIOMS are:

- To facilitate and promote international activities in the field of biomedical sciences, especially when the participation of several international associations and national institutions is deemed necessary;
- To maintain collaborative relations with the United Nations and its specialized agencies, in particular with WHO and UNESCO;
- To serve the scientific interests of the international biomedical community in general.

To achieve its objectives, CIOMS has initiated and coordinates the following main long-term programmes:

- Bioethics
- Health Policy, Ethics and Human Values - An International Dialogue
- Drug Development and Use
- International Nomenclature of Diseases

#### Extract about CIOMS from the CP document chapter on Governments

In particular, the Council for International Organizations of Medical Sciences (CIOMS) was founded under the auspices of WHO and the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1949. In the late 1970s, CIOMS set out, in cooperation with WHO, to prepare guidelines 'to indicate how the ethical principles that should guide the conduct of biomedical research involving human subjects, as set forth in the Declaration of Helsinki, could be effectively applied, particularly in developing countries, given their socioeconomic circumstances, laws and regulations, and executive and administrative arrangements'. The most important of the publications of CIOMS is its International Ethical Guidelines for Biomedical Research Involving Human Subjects, first published in 1993. The updated version was published in 2002 [46] and is designed to be of use, particularly to low-resource countries, in defining the ethics of biomedical research, applying ethical standards in local circumstances, and establishing or redefining adequate mechanisms for the

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ethical review of research involving human subjects. Although mainly targeting ethics committees, sponsors and investigators, the CIOMS guidelines, to which several clinical pharmacologists have contributed, have influenced governments thinking about clinical research, especially in resource-poor settings.

### CIOMS Working Groups

A broad range of drug safety topics has been covered by CIOMS via working groups. Senior scientists from regulatory authorities, pharmaceutical industry and academia have joined together in order to develop consensus guidelines within areas such as international reporting of adverse drug reactions (CIOMS I reporting form), periodic drug safety update summaries and development safety update report, core clinical safety information on drugs, terminology of ADRs, standardised MedDRA queries and pharmacogenetics. There have also been joint working groups together with WHO covering drug development research and pharmacovigilance in resource-poor countries and vaccine pharmacovigilance.

### DRUG DEVELOPMENT AND USE

#### Safety requirements for the use of drugs

This program was initiated in the early 1980s in the light of the benefits that society as a whole derives from modern drugs and vaccines. At the same time, society must be prepared to accept the possibility of remote risks to the individual as the corollary of modern medical care and further therapeutic progress; without this realization, the basis of contemporary drug development will ultimately founder. Moreover, society must be assured that a responsible and committed effort is undertaken to minimize drug-induced injury, and that the risks of such injury compare favorably to those accepted in other aspects of daily life.

#### Assessment and monitoring of adverse drug reactions and pharmacogenetics

Eight CIOMS working groups have proposed recommendations within areas such as international reporting of adverse drug reactions -including the introduction of the standardized *CIOMS I reporting form*", international reporting of periodic drug-safety updates, core clinical safety information on drugs, evaluation of benefit/risk balance, current challenges of pharmacovigilance, management of safety information from clinical trials and development safety update report (DSUR) and signal detection in pharmacovigilance. Seven of these are previously published and the outcome of Working Group VIII on signal detection is presently being published (for more detailed description of the Working groups see under the heading of "Working groups" and "Publications").

In addition there are Working Groups dedicated to pharmacogenetics, standardised MedDRA Queries (SMQs), reporting and terminology of adverse drug reactions and two joint CIOMS-WHO Working Groups); vaccine pharmacovigilance, drug development research and pharmacovigilance in resource-poor countries

### BIOETHICS

The remarkable progress of biomedical sciences and biotechnology, and its applications in medical practice, are confronting our societies with new ethical dilemmas, extending from traditional medical ethics to the many emerging areas of bioethics.

The particular contribution of CIOMS in this field has been the issuance of international guidelines for the application of ethical principles in various key areas. Specific reference should be made to the International Ethical Guidelines for Biomedical Research Involving Human Subjects (developed in conjunction with WHO), which superseded Proposed Ethical Guidelines (1982) and were published in 1993. They have been very widely

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utilized, particularly in low-resource countries. In 1999-2002 the Guidelines were revised and updated. CIOMS published in 2002 the new text of the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* which are available on the CIOMS website. Moreover, translations of the Guidelines have been made into French, Spanish, Portuguese, Chinese, Japanese, Korean and Vietnamese.

A chapter by Professor Juhana E. Idänpään-Heikkilä and Mr Sev Fluss, CIOMS, describing the 2002 Guidelines has been included in *The Oxford Textbook of Clinical Research Ethics*.

In 1991 CIOMS issued the *International Guidelines for Ethical Review of Epidemiological Studies*. In 2003 CIOMS initiated the revision of these Guidelines by establishing a multidisciplinary Core Group which has collected comments on the draft revision of the guidelines from various institutions, organizations and individual experts involved in ethics and epidemiological research. CIOMS published in 2009 the new revised and updated text.

Specific reference should also be made to the "Principles of Medical Ethics Relevant to the Protection of Prisoners Against Torture", prepared by CIOMS at the invitation of WHO and adopted by the United Nations General Assembly in March 1983.

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Z. Bankowski & J.H. Bryant, Eds.

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Z. Bankowski & N. Howard-Jones, Eds.

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Health Manpower out of Balance: Conflicts and Prospects

Z. Bankowski & A. Mejia, Eds.

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Ethics and Research on Human Subjects: International Guidelines

Z. Bankowski & R.J. Levine, Eds.

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International Ethical Guidelines for Biomedical Research Involving Human Subjects

Translations only available in Ch/Fr/Port//Sp/Viet

International Ethical Guidelines for Epidemiological Studies

(Updated Edition)

2009. ISBN 92 9036 081 X. Sw.fr. 45.

### DRUG DEVELOPMENT AND USE

Definition and Application of Terms for Vaccine Pharmacovigilance

(Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance)

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Safety Requirements for the First Use of New Drugs and Diagnostic Agents in Man

C.D. Dollery & Z. Bankowski, Eds.

1983. ISBN 92 9036 012 5. Sw.fr. 15.

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Diseases of the Female Genital System, Volume VIII  
1992. ISBN 92 9036 044 5  
Out of print

### SERIES OF PAPERS ON BASIC REQUIREMENTS FOR THE USE OF TERMS FOR REPORTING ADVERSE DRUG REACTIONS

1. International Reporting on Adverse Drug Reactions: the CIOMS Project. *International Journal of Clinical Pharmacology, Therapy and Toxicology*, 1990;28(4): 133-138
2. Standardization of definitions and criteria of causality assessment of adverse drug reactions. Drug-induced liver disorders: Report of an International Consensus Meeting. *International Journal of Clinical Pharmacology, Therapy and Toxicology*, 1990;(28(8): 317-322
3. Standardization of definitions and criteria of causality assessment of adverse drug reactions. Drug-induced cytopenia. *International Journal of Clinical Pharmacology, Therapy and Toxicology*, 1991;29(2): 75-81
4. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions. Key words: Anaphylactic shock, arrhythmia, cardiac failure, hypertension, thrombosis and embolism. *Pharmacoepidemiology and Drug Safety*, 1992; 1: 39-45
5. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (II). Key words: Colitis, gastrointestinal haemorrhage, hepatocellular damage, peptic ulcer, pancreatitis. *Pharmacoepidemiology and Drug Safety*, 1992; 1: 133-137
6. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (III). Key words: Aplastic anaemia, bone marrow depression, coagulation disorders, agranulocytosis, thrombophlebitis. *Pharmacoepidemiology and Drug Safety*, 1992; 1: 191-196
7. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (IV). Key words: Dyskinesia, depression, myopathy, neuropathy, paralysis, convulsions. *Pharmacoepidemiology and Drug Safety*, 1993; 2: 149-153
8. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (V). Key words: Vision abnormal, keratitis, cataract, retinal disorder acidosis. *Pharmacoepidemiology and Drug Safety*, 1994; 2: 189-193
9. Definition of Adverse Drug Reactions and Minimum Requirements for Their Use - Cardiovascular Disease Terms. Key words: Heart malformation, artery malformation, aortic coarctation, atrial septal defect, pulmonic stenosis congenital, aortic stenosis, mitral insufficiency, pericarditis, pericardial effusion, haemopericardium, endocarditis, myocarditis, arteriosclerosis, atherosclerosis, angina pectoris, myocardial ischaemia, myocardial infarction, coronary artery disorder, thrombosis coronary, cardiac aneurysm, myocardial rupture (post infarct), cardiomyopathy, fibrosis endomyocardial. *Pharmacoepidemiology and Drug Safety*, 1993; 2: 591-602
10. Harmonizing the Use of Adverse Drug Reaction Terms. Definitions of Terms and Minimum Requirements for Their Use: Respiratory Disorders and Skin Disorders. Key words: Apnoea, asphyxia, asthma, bradypnoea,

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bronchoconstriction, chronic obstructive pulmonary disease, dyspnoea, hypercapnia, hypoventilation, hypoxia, interstitial lung disease, pneumonitis, pulmonary fibrosis, pulmonary oedema, respiratory arrest, respiratory depression, respiratory distress syndrome acute (ARDS), respiratory paralysis. *Pharmacoepidemiology and Drug Safety*, 1997;6: 115-127

11. Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (VIII): Renal and Urinary System Disorders. Key words: glomerular vasomotor disorder, glomerulonephritis, nephritis interstitial: acute and chronic, nephropathy toxic, nephrotic syndrome, renal failure, renal failure (intrinsic) acute, renal tubular disorder, renal vasculitis, urinary retention. *Pharmacoepidemiology and Drug Safty*, 1997; 6: 203-211

12. Definitions and Terms for Reporting Adverse Drug Reactions (IX): Nervous System and Psychiatric Disorders. Key words: Central and peripheral nervous system terms: anticholinergic syndrome, choreoathetosis, dysphonia, dystonia, encephalopathy, extrapyramidal disorder, gait abnormal, hypertonia, hypotonia, neuroleptic malignant syndrome, oculogyric crisis, serotonin syndrome, speech disorder. Psychiatric disorder terms: anorexia, apathy, delirium, depersonalization, personality disorder, psychosis, thinking abnormal. *Pharmacoepidemiology and Drug Safety*, 1998; 7: 39-49

13. Definitions and Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (X): Gastrointestinal System Disorders. Key words: Abdominal pain, colitis collagenous, constipation, diarrhoea, dyspepsia, gastritis, gastrointestinal infarction/necrosis/gangrene, haematemesis, haematochezia, ileus, intestinal ischaemia, intestinal obstruction, intestinal perforation, intestinal stenosis, melena, oesophageal ulcer, peritonitis, stomatitis, stomatitis ulcerative, ulcer oesophago-gastro-intestinal, or ulcer of the alimentary tract. *Pharmacoepidemiology and Drug Safety*, 1998; 7: 281-287

14. Definitions and Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (XI): Cardiovascular System Disorders. Key words: Arterial occlusive disease, hypotension, hypotension postural, hypertension pulmonary, syncope, circulatory failure, shock, arrhythmia ventricular, fibrillation atrial, fibrillation ventricular, AV block, cardiac arrest, palpitation, torsade de pointes, cerebral infarction, cerebral haemorrhage, cerebrovascular disorders, haemorrhage intracranial. *Pharmacoepidemiology and Drug Safety*, 1998; 7: 351-357

15. Definitions and Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (XII): Collogen Disorders and Musculo-Skeletal Disorders. Key words: Fracture pathological; lupus erythematosus syndrome: myositis; osteoporosis; retroperitoneal fibrosis; vasculitis. *Pharmacoepidemiology and Drug Safety*, 1999; 8: 141-145

16. Definitions and Basic Requirements for the Use of Terms for Reporting Adverse Drug Reactions (XIII): Clinical Pathology and General Disorders. Key words: Aggravated/exacerbated; anaemia aplastic: anaemia haemolytic: anaemia hypochromic mycrocytic; anaphylactic reaction; anaphylactic shock; anaphylactoid reaction; asthenia; dehydration; gout; hypovolaemia; malaise; ototoxicity; pancytopenia; rigors; withdrawal syndrome. *Pharmacoepidemiology and Drug Safety*, 1999; 8: 217-224

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