

CURRENT PROGRAMME AND PLANNED ACTIVITIES

(Working Groups and other projects active as of February 2008)

1. CIOMS/WHO Working Group on Vaccine Pharmacovigilance

The Working Group was created in November 2005 at the request of WHO to:

1. Develop general definitions strictly focused on Vaccine Pharmacovigilance
2. Contribute to the development review evaluation and approval of definitions on adverse events following immunisation as developed by the Brighton Collaboration process and to their dissemination:
 - In endorsing already existing definitions
 - In participating in the review of definitions under development
 - In proposing priorities for the development of new definitions
 - Facilitating the translation and dissemination of the definitions
3. Collaborate with other CIOMS working groups especially that on Standardised MedDRA Queries (SMQs) and CIOMS VIII on Application of Signal Detection in Pharmacovigilance.

The Working Group is currently composed of 23 members from pharmaceutical industry, regulatory agencies, governmental institutions, and academia both from industrialised and developing countries as well as from international organisations

Five meetings have been held since the establishment of the Working Group:

November 22-23, 2005, in Geneva (Switzerland)
May 30-31, 2006, in Langen (Germany)
November 6-7, 2006, in Brussels (Belgium)
May 30-June 1 2007 in Geneva (Switzerland)
October 29-30, 2007 in Bethesda, MD (USA)

Planned meetings: May 27-28, 2008 at EMEA, London. and
October 27-28 at Public Health Agency of Canada, Ottawa, Canada

The Working Group has been developing or will be developing 43 definitions. Of these 24 have been finalized and published as seen in the table below.

DEFINITIONS LIST (As of February 2008)

DEVELOPED	IN PROGRESS	PLANNED
Fever Hypotonic-Hyporesponsive Episode (HHE) Intussusception Nodule at injection site Persistent crying Seizure Abscess, Cellulitis Pruritus, Swelling Induration at or near Injection Site Allergic reaction, Anaphylaxis Rash SIDS, USID Aseptic Meningitis, Encephalitis Fatigue Thrombocytopenia Smallpox AEFI: <ul style="list-style-type: none"> • Generalized Vaccinia • Inadvertent inoculation • Eczema vaccinatum • Robust take • Progressive vaccinia 	CFS GBS	Myalgia Arthralgia Diarrhea Paresthesia Urticaria Bell's palsy ORS Flu like syndrome Apnea Syncope Conjunctivitis Rhinitis Dizziness Vasculitis <u>Proposed</u> Viscerotropic syndrome (YF) Auto immune pathologies Kawasaki disease (KD)

The first internationally developed definition of *Vaccine Pharmacovigilance* has been developed and agreed within the Working Group and was posted in November 2007 on this website for general use.

2. CIOMS Working Group on Standardised MedDRA Queries (SMQs)

Historically, the project began in 2003 as a CIOMS initiative, in response to indications received from some drug regulatory authorities and pharmaceutical companies that they had concerns about the parallel development of special drug safety search programmes based on the Medical Dictionary for Regulatory Activities (MedDRA). This would cause an unavoidable duplication of effort and uncertainty within pharmaceutical companies about the utility of these searches on the part of drug regulatory authorities.

The drug regulatory authorities and pharmaceutical companies identified a need to harmonize and standardize their adverse drug reaction database search queries based on MedDRA in order to use the terminology in a rational way and to allow comparisons of

drug safety findings between different databases. However, at an early stage it became clear that such an activity would benefit from cooperation among all stakeholders, i.e. the CIOMS Working Group, MedDRA/MSSO, the ICH MedDRA Management Board and the ICH Secretariat

Since 2003 the CIOMS Working Group on Standardised MedDRA Queries (SMQs) has developed search queries for some 95 selected adverse drug reactions. The WG met 12 times in 2003-2005, and four times in both 2006 and 2007.

To date it has published 63 SMQs and will finalize an additional 12-15 SMQs in 2008. Thereafter, the WG will meet once or twice a year in order to maintain, review and update as required the existing SMQs and consider newly suggested candidate SMQs.

Between CIOMS and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), a Memorandum of Understanding was drafted in 2003 regarding the SMQ projects. This will be reviewed in 2008 to cope with the future activities of the CIOMS SMQ WG.. The agreement is also a link with ICH for which IFPMA functions as a Secretariat.

Planned meetings: 5-6 February 2008 in Basel, Switzerland, and
7-8 May 2008 in Geneva, Switzerland.

3. Drug Development Research and Pharmacovigilance in Resource-Poor Countries - a joint CIOMS/WHO Working Group

Many endemic diseases appear only in developing countries and the development of safe and effective treatments requires clinical trials to be conducted in these countries. There is also a need to develop responsible and operative systems for pharmacovigilance in resource-poor countries to address the efficient collection and assessment of drug safety data from clinical trials during drug development and to assure the reporting and surveillance of drug safety in the post-authorization phase when the product is used in local treatment settings. Many obstacles and barriers to clinical trials need special consideration and appropriate solutions in resource-poor countries.

CIOMS established a Working Group on this topic in 2004 and members included scientists from WHO, national/academic research institutions in resource-poor countries and the pharmaceutical industry. The core group published the results of its work in 2005 as a draft document which was posted on the CIOMS website for comment. WHO is collecting comments from its Members States via its Regional Offices. Based on the comments the final document will be developed.

4. CIOMS Working Group VIII on Application of Signal Detection in Pharmacovigilance (CIOMS VIII)

An important objective of pharmacovigilance activities is to rapidly and accurately detect previously unrecognised drug-related adverse events that are novel with respect to clinical nature, severity, or frequency. This requires collection and classification of adverse event data in database(s) and searches of the data that reveal preliminary high-value signals for further workup.

Based on requests from some drug regulatory authorities and a number of pharmaceutical companies, in 2006 CIOMS set up a working group of senior scientists (from drug regulatory authorities, the pharmaceutical industry, and academia) *to develop consensus Points to Consider in the development and application of quantitative methods for signal detection using pharmacovigilance databases*. The guidance document would define the preferred approaches to evaluating and validating the utility and limitations of various quantitative approaches to signal detection, as well as when and how to use preferred methods and interpret results of their application across different databases. The Points to Consider document is to be used by industry and regulators to guide development and selection of quantitative methods to detect previously unrecognised safety signals. It is anticipated that the working group will contemplate application of data mining and signal detection methods to databases that include drugs, vaccines, and therapeutic biological products, both before and after they are marketed.

Issues to be Resolved

The recent implementation of disparate, non-validated signal detection methods has accelerated the need for global harmonisation in this important pharmacovigilance speciality. . The following issues require resolution:

- Design and validation methodology;
- The theoretical underpinning of each signal detection method;
- Technical distinction between the various methods;
- Strengths, limitations, pitfalls, and outstanding unresolved issues for each method;
- Generalisability across databases;
- Distinction between utility of spontaneous databases and observational epidemiological databases, including inherent biases;
- Impact of database design, coding principles and practices, and conventions;
- How to use and when to use various methods; and
- How to interpret, report, and follow up results of data mining and signal detection exercises.

Further, it will be important for the CIOMS Working Group VIII to make a recommendation on the balance between use of automated signal detection methods and the need to engage the prepared mind.

The working Group held two meetings in both 2006 and 2007 and the draft report will be compiled and finalized in future meetings for printing during 2008.

Planned meetings: 10-11 March, 2008 at Afssaps, Paris, France, and
30-31 October, 2008 at MHRA, London, UK.

5. CIOMS Organizes a session at the Drug Information Association (DIA) Annual Meeting, June 2008, Boston, USA

China is an increasingly popular location for clinical trials because many leading multinational pharmaceutical companies have moved their clinical research there. National legislation, Good Clinical Practice (GCP) and ethical principles guiding clinical research are under development in that country. The session will review progress made, detail challenges and provide suggested solutions for investigators and sponsors of research.

In 2007, the DIA Secretariat requested that CIOMS organize a session on “Legislation, GCP and Ethical Principles Guiding Clinical Trials in China” at the DIA Annual Meeting on 22-26 June 2008 in Boston, USA. The speaker will be Professor Qiu Renzong, President, Ethics Committee (CASS), China Ministry of Health and Dr David Lepay (USFDA). The session will be chaired by Professor Juhana E. Idänpään-Heikkilä, Senior Adviser, CIOMS.

6. CIOMS Working Group VII on Development Safety Update Report (DSUR) - (CIOMS VII)

The Working Group was established in 2005 and meeting reports are posted in the WHAT'S NEW section of this website.

The Working Group published its report “The Development Safety Update Report (DSUR): Harmonising the Format and Content for Periodic Safety Reporting During Clinical Trials in December 2006.

7. CIOMS Working Group on Pharmacogenetics

The reports of the meetings are available in the WHAT'S NEW section of this website.

The Report of the CIOMS Working Group on Pharmacogenetics entitled: Pharmacogenetics - Towards improving treatment with medicines, was published in February 2005.

8. Revision of the CIOMS 1991 International Guidelines for Ethical Review of Epidemiological Studies

The revision of these CIOMS 1991 Guidelines was initiated in June 2003. The Secretariat requested comments on the 1991 Guidelines regarding the need for revision from some 20 experts worldwide, some of whom had been involved in the development of the 1991 Guidelines. In September 2003, a Core Group for the revision process met at WHO Headquarters, in Geneva, to consider the comments and to plan the next steps in the revision process. The Core Group met again in Geneva on 28 January 2004, on 3 June 2004, on 11-12 October 2004 and on 10-11 February 2005. Details of how the revision process was selected and updates on the progress made can be found in the reports of the Core Group meetings which are available in the WHAT'S NEW section of this website.

The updated version of the guidelines were posted as Provisional International Guidelines for Ethical Review of Epidemiological Studies on this website in February 2008

9. The CIOMS 2002 International Ethical Guidelines for Biomedical Research Involving Human Subjects

The revised CIOMS 2002 Guidelines were published in October 2002 and were already made available on the CIOMS website in September 2002.

The Guidelines have been translated into French (Lignes directrices internationales d'éthique pour la recherche biomédicale impliquant des sujets humains) and are posted on this website under "Texts of Guidelines and Other Normative Documents". The publication can be ordered from CIOMS.

The Spanish translation (Pautas Éticas Internacionales para la Investigación Biomédica en Seres Humanos) was prepared and published by the Pan American Health Organization/World Health Organization in collaboration with CIOMS in August 2003 and is available on this website under "Texts of Guidelines and Other Normative Documents."

Translations into Chinese, Portuguese, Japanese, Farsi, Korean and Vietnamese have been completed. A partial translation into Italian is completed and a second translation of the full text is in process.

CIOMS Meeting Schedule 2008

21 - 26 January 08	WHO EB, Geneva	
22-24 January 08	WHO ARV Pharmacovigilance programme	
5 - 6 February 08	SMQ WG (MedDRA), Novartis, Basle	
5 - 7 March 08	DIA EuroMeeting, Barcelona	
10 March 08	World Medical Association (WMA) Workshop on Review of Declaration of Helsinki, Helsinki, Finland	
10-11 March 08	WG VIII on Signal Detection, Afssaps, Paris	
9 - 12 April 08	ECCEO 8 th Conference, Istanbul	
28 & 29 April 08	6th CIOMS/WHO Vaccine WG, EMEA, London	
7 & 8 May 08	SMQ WG (MedDRA), IFPMA, Geneva	
19 -24 May 08	WHA, Geneva	
29 - 30 May 08	Geneva Conference on Person-Centered Medicine	
22-26 June 08	DIA Annual Meeting, Boston, USA - Session	
20 - 25 September 08	XIV World Congress on Psychiatry, Prague - presentation	
16-17 or 24-25 Sept	1st SMQ Core Group Meeting (MedDRA),	
27 & 28 Oct 08	7th CIOMS/WHO Vaccine WG, Ottawa, Canada	
30 & 31 Oct 08	WG VIII on Signal Detection, MHRA, London	
02 Dec 08	CIOMS Executive Committee Meeting	