

***International Guidance and Suggestions on Reporting of  
Adverse Events from Clinical Trials to IRBs/IECs***

by

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**(ABSTRACT)**

**This abstract summarises how some major international guidance documents address the reporting of adverse events (AEs) and adverse drug reactions (ADRs) from clinical trials (CTs) to Institutional Review Boards (IRBs) or Independent Ethics Committees (IECs). The documents reviewed are the WMA Declaration of Helsinki, the EU Clinical Trial Directive – 2001/20/EC (EU CT Directive), and the CIOMS International Ethical Guidelines on Biomedical Research Involving Human Subjects (2002). Moreover, the suggestions made by the CIOMS Working Group on "Management of Safety Information from Clinical Trials" (also called CIOMS VI) will be summarised. All the above documents are in agreement that IRBs/IECs are responsible for protecting the safety and wellbeing of subjects in CTs and that IRBs/IECs are required to monitor CTs. Furthermore, researcher(s) are to provide information on serious adverse events/reactions to IRBs/IECs.**

**The EU CT Directive and the Guidance Document (April 2004) for its implementation prescribe that the investigator must report all serious AEs immediately to the sponsor who is responsible for their prompt notification to the Ethics Committee. The documents define "Suspected Unexpected Serious Adverse Reactions" (SUSARs). The sponsor has to report fatal or life-threatening SUSARs to IRBs/IECs as soon as possible but not later than within seven calendar days and the follow-up information has to be submitted within eight calendar days. Non-fatal and non-life-threatening SUSARs have to be reported by the sponsor as soon as possible to IRBs/IECs but not later than within 15 calendar days. Use of the CIOMS-I form or the equivalent for reporting is recommended.**

**How are ethics committees informed about SUSARs in the EU countries? The EU CT Directive and its Guidance Document prescribe that IECs may only receive expedited individual reports of SUSARs as follows: (1) all SUSARs from Member States and from third countries should be reported at least quarterly as a line listing, accompanied by a brief report by the sponsor highlighting the main points for concern and (2) any changes increasing the risk to subjects and any new issues adversely affecting the safety of subjects should be reported within 15 days. The sponsor should send a safety report to ethics committees once a year or on request with global analysis taking into account all new available safety information received during the reporting period.**

**At the request of some drug regulatory authorities and pharmaceutical companies, CIOMS established in 2001 a working group on the "Management of Safety Information from Clinical Trials" The members included senior scientists from nine drug regulatory authorities (EMEA, BfArM/Germany, Health Canada, FDA, MHLW/Japan, MCA/MHRA/UK, MPA/Sweden, TGA/Australia and ANMAT/Argentina). Eleven senior scientists from the following companies also participated: Aventis, AstraZeneca, Bayer, Eisai/Japan, GSK, Lilly, Merck & Co., Novartis, Pfizer, Roche and Wyeth. Other members included WHO, University of Zagreb/Croatia, Pasteur Institute/Morocco and CIOMS Secretariat. After a number of meetings and discussions the 28 senior scientists making up the CIOMS WG VI decided to make the following recommendations regarding safety reporting to IRBs/IECs:**

***1. Replace the current practice of sending large numbers of individual case reports to IRBs/IECs with a more reasonable approach, namely periodic and ad hoc communications to investigators and ethics committees that include regular updates of important safety information as well as the evolving benefit-risk profile and highlights of important new safety information; and***

***2. Significant new safety information, occasionally a single case report, that has implications for the conduct of the clinical trial or that warrants an immediate revision to the informed consent, would be communicated on an expedited basis.***