What are the safety reporting requirements for Medicinal Clinical Trials?
The UK Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 is the legislation which regulates all Clinical Trials involving medicines. This leaflet provides guidance on the safety reporting requirements under the regulations. This leaflet therefore aims to firstly define the types of events and then to describe what should be reported to whom and how.

Definition of Terms

**Investigational Medicinal Product (IMP)**
A pharmaceutical form of an active substance or placebo being used in a clinical trial.

**Adverse event (AE)**
Is an untoward and unexpected occurrence.

**Adverse reaction (AR)**
Is any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject.

**Serious Adverse events and Reactions (SAR/SAE)**
For both adverse events and reactions to be classed as serious one of the following criteria needs to be met:

- Results in death
- Is life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect.

**Suspected Unexpected Serious Adverse Reaction (SUSAR)**
Is an Adverse Reaction that is deemed to be Serious (as defined above) which is ‘unexpected’. This is when its nature and severity are not consistent with the information about the medicinal product such as given below:

- In the case of a product with marketing authorisation, in the summary of the product characteristics for that product
- In the case of any other investigational medicinal product, in the investigator’s brochure relating to the trial in question.

**Reporting Requirements**

**AE/AR**
The reporting mechanisms for both AEs and AR should be outlined in the trial protocol.

**SAR/SAE**
All expected adverse drug reactions (as indicated in the Summary of Product Characteristics, SmPC, or the Investigators Brochure) and expected serious adverse event (related to the nature of the study population and unrelated to the Investigative Medicinal Product, IMP) should be detailed in the trial protocol. The safety reporting arrangements and responsibilities should also be set out in the protocol; the Clinical Trials Regulations allow the Sponsor/Chief Investigator to specify in the protocol SAEs that do not need to be notified immediately, for example if the event is one of the main outcomes in the trial.

For SAEs not specified in the protocol the trial Sponsor must be notified of SAEs immediately and have systems in place to ensure that they are assessed for causality (is it a reaction to a trial medicine or not?) and expectedness (is the reaction a recognised adverse effect of the medication or is it unexpected?).

**SUSARs**
Sponsors have to make sure that SUSARs are reported promptly to both the regulatory authorities (MHRA) and the relevant Ethics Committee. It is often the case that the sponsor will delegate responsibility to the Chief Investigator. The Regulations set time limits:

- Fatal or life threatening SUSARs: not later than 7 days after the sponsor for pharmacovigilance had information that the case fulfilled the criteria for a fatal or life threatening SUSAR, and any follow up information within a further 8 days.
- All other SUSARs: not later than 15 days after the sponsor for pharmacovigilance had information that the case fulfilled the criteria for a SUSAR.

An annual safety report on all Serious Adverse Reactions (including SUSARs) must also be sent to the MHRA and relevant Ethics Committee.

Safety reports may be submitted by the Sponsor, or by the Sponsor’s representative, or by the Chief Investigator.
Reports of SUSARs in double-blind trials should normally be unblinded.

Further information about safety reporting for both medicinal and non-medicinal research can be found on the NRES website http://www.nres.npsa.nhs.uk/applications/after-ethical-review/safetyreports/ as well as detailed guidance on adverse reaction reporting on the MHRA website http://www.mhra.gov.uk/Safetyinformation/Reportingssafetyproblems/index.htm

For more information, please contact:-
IoP/SLaM R&D Office, Room W1.08, Institute of Psychiatry, De Crespigny Park, London, SE5 8AF.
Tel: 020 7848 0251 Fax: 020 7848 0147
R&D website: www.iop.kcl.ac.uk/RandD

For KCL/SLaM sponsored studies: Joint Clinical Trials Office (JCTO) http://www.jcto.co.uk/

Pharmacovigilance and reporting requirements in Medicinal Clinical Trials

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