GOOD CLINICAL (RESEARCH) PRACTICE

All persons involved in the conduct of clinical research, from whatever discipline, need to be familiar with the principles of Good Clinical (Research) Practice. In the UK these were first set out formally in guidelines published by the ABPI in 1988, and adopted, voluntarily, as a policy. These were followed by a directive (91/507/EC) from the European Commission which effectively requires clinical trials, in all four phases, to be conducted in accordance with principles of good clinical practice. Guidelines were also drafted by the Committee on Proprietary Medicinal Products (CPMP) on Good Clinical Practice for Trials on Medicinal Products in the European Community which was adopted by the Commission in July 1990, and operative from 1 July 1991. Most recently, the International Conference on Harmonisation (ICH) process has, in May 1996, signed off as a Step 4 document a Consolidated Guideline on Good Clinical Practice which effectively means that this document will become the definitive international GCP Guidelines with which all clinical trials conducted for regulatory purposes should comply.

These guidelines clearly set out the responsibilities of investigators taking part in sponsored clinical trials as follows:

The investigator must:

- submit an up-to-date curriculum vitae to the sponsor, and, if necessary, to the research ethics committee and to the relevant authorities.
- ensure that he/she is fully familiar with the properties of the investigational medicinal product(s), as described in the Investigators' Brochure.
- ensure that he/she has sufficient time to conduct and complete the trial, nominating if appropriate a local study co-ordinator to assist in the administration of the trial.
- ensure that he/she has adequate support staff and appropriate facilities (including laboratories and archive space) which are available for the duration of the trial.
- ensure that other trials do not divert essential subjects or facilities away from the trial in hand.
- agree a publication policy with the sponsor before the start of the study.
- obtain local research ethics committee approval, and, if necessary, approval of the unit management, and provide details of the ethics committee membership and working procedures to the sponsor, before the study commences.
- provide retrospective data on numbers of patients who would have satisfied the proposed entry criteria during preceding time periods, in order to assure a realistic but adequate recruitment rate for the trial.
- agree and sign the protocol submitted to the research ethics committee.
- agree to work to this protocol, and accept that no changes should be made to the protocol without agreeing them with the sponsor, except if necessary to eliminate an apparent immediate hazard to a subject; such changes should form a protocol amendment to be signed by the investigator and the sponsor, and resubmitted by the investigator to obtain further research ethics committee approval.
- obtain informed consent from trial subjects in accordance with the Declaration of Helsinki before including them in the trial, in writing, otherwise witnessed indicating the date, and provide a specimen copy of the consent form to be used, if this has not been provided by the sponsor.
- with the subject's consent inform the family doctor preferably prior to starting the trial.
- ensure that subjects enrolled in a trial are provided with an information sheet giving details about the trial, which should include contact addresses and telephone numbers where further information can be obtained in case of action needed at another place.

- provide relevant information about the subject, in addition to other details provided by the sponsor, to all staff members involved with the trial or with other elements of the management of the subject, whilst ensuring that the confidentiality of all identifiable information about the subject is respected by all persons involved.
- ensure that deliveries of investigational medicinal products from the sponsor are correctly received by a responsible person, such as a pharmacist, and are recorded.
- ensure that investigational products are handled and stored safely and properly and are only dispensed to trial subjects in accordance with the protocol.
- ensure that any unused products are returned to the sponsor, or other disposal as agreed in the protocol.
- conduct the trial properly so that it is possible to reconcile the medication delivery records with records of usage and of return of unused stock when the trial is completed, giving account for any discrepancies, and signing certificates of delivery and of returns, and/or destruction.
- ensure that the trial code randomisation code envelopes are kept safely, and that they are returned intact to the sponsor, if not used, at the end of the study; the treatment code should only be broken in accordance with the protocol, and the sponsor should be consulted or informed whenever this is done, with reasons.
- ensure that the data and case record forms (CRFs) are complete and accurate, and are completed in accordance with the protocol, with any corrections to data (which must be dated and initialled) made in such a way so as not to obscure the original entry.
- make available the data (CRFs) results and interpretations of the trial to the sponsor.
- maintain for as long as required all patient files and other source data relating to the study, including copies of case record forms. For example, patient identification codes are required by the EC directive to be kept for 15 years.
- ensure that subjects are told about any information which becomes available during the trial which may be of relevance for them.
- notify the sponsor (and if applicable the local research ethics committee, and the relevant authorities) immediately of any serious adverse events, irrespective of (apparent) causality, with appropriate documentation.
- agree with, and sign, the final report of the trial; for multi-centre trials the signature of the co-ordinating investigator may suffice if this is stated in the protocol.
- maintain an accurate set of clinical records, which should clearly and prominently indicate that the subject is taking part in a clinical trial; this is to provide essential source material for auditing purposes, making these available (whilst still maintaining requisite confidentiality of personal subject details) at any stage during the trial to the monitor or quality assurance personnel from the sponsor company and/or relevant authorities for verification/audit inspection purposes.
- maintain confidentiality of the information provided by the sponsor.
- ensure appropriate medical care/follow-up of trial subjects after the trial.

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