

Summary of the Proposed Amendments to Implement EU Directive 2005/28/EC on Good Clinical Practice

The UK Clinical Trials Regulations in 2004 implemented the original EU Clinical Trials Directive of 2001. This 2001 Directive has now also been added to the 2005 GCP Directive, and a revised set of Clinical Trials Regulations will be needed in order to reflect the provisions of the new 2005 GCP Directive. The UK Government has therefore proposed to amend the existing Regulations; both to align them with the 2005 GCP Directive, and to implement some other detailed requirements. The summary of proposed changes/amendments to existing Regulations and ICH-GCP are given below:

Scope of the GCP Directive

The EU Directive 2005/28/EC applies to clinical trials of “investigational medicinal products”, in other words, medicines which are being developed for human use. The Directive has 6 Chapters and proposed amendments are:

Chapter 1 Specific Provisions for Non-commercial Trials

The Directive has proposed “Specific modalities” or the “specific ways of working” which will be applicable to certain non-commercial trials. The Commission is currently preparing guidance on these ways of working. The UK Government/MHRA will consider how best to take advantage of the flexibilities offered in these specific modalities. It is possible that the UK Government/MHRA may have to further introduce amendments to the Regulations.

Chapter 2 Principles of Good Clinical Practice

Good Clinical Practice: The principles set out in the existing Regulations (2004) are very similar to those in the new GCP Directive. The MHRA is proposing to make the wording consistent.

Ethics Committee: The IRB/IEC will be required to retain documents for at least 3 years and must have systems for exchange of information with the UK competent authority – the MHRA.

Sponsors: The Regulations will be amended to clarify the current position, which is that a sponsor may delegate aspects of a clinical trial whilst still retaining overall responsibility.

Investigator’s Brochure: The proposed amendment would require that the brochure is prepared in a concise, simple, objective, balanced, non-promotional form. For a marketed product, the Summary of Product Characteristics could be substitute for it. The amendment would also require that IB should be updated at least annually or for new safety concerns.

Chapter 3 Manufacturing or Import Authorisation

Exemption for Hospital & Health Centres and Reconstitution: The current Regulations state that a hospital or health centre does not need to hold a manufacturing authorisation for the packaging and labelling of medicines for use in a clinical trial. For this exemption to apply, the activity must be carried out by specified people and the repackaged or labelled medicinal product must be used exclusively on site for a clinical trial. Reconstitution of a medicinal product for use in a clinical trial does not fall within the scope of manufacturing. The MHRA is not proposing any amendment to this aspect of the Regulations.

Conditions of Holding a Manufacturing Licence: Minor amendments are proposed to implement other provisions relating to the manufacturing of investigational medicinal products. Applicants would have to specify the form a medicine will take and details of the manufacturing process in their application where relevant. Holders of manufacturing authorisations will have to comply with requirements relating to staff, standards of good manufacturing practice (GMP), quality control, and communication with the MHRA.

Chapter 4 Trial Master File and Archiving

Format of Trial Master File: The GCP Directive sets out new requirements regarding the documents which are to be included in the master file, reporting on clinical trials, and how these documents are to be archived. Regulations will be amended to reflect these new requirements. The Commission is preparing guidance on the content of the documents which are to be included in the Trial Master File.

Retention of Essential and Medical Records: The GCP directive requires that essential documents be retained for at least 5 years after the completion of the trial. A trial subject's medical files are retained in accordance with national legislation. The amendment would specify a minimum of 5 years after the end of the trial.

Chapter 5 & 6 GCP and GMP Inspectors' Qualifications, Training and Procedures

The provisions of these chapters are directed to the Licensing Authority and the MHRA. The Regulations will be amended to require the MHRA to adopt appropriate new rules and procedures for GCP and GMP inspectors, and to ensure that inspections are conducted in accordance with the new rules.

Additional Amendments: The MHRA is proposing minor changes to the following aspects of the current regulations of clinical trials to improve patient safety and administrative requirements:

Serious Breaches of GCP: The amendment would require the sponsor of a clinical trial to notify the MHRA whenever the sponsor becomes aware of serious breaches of GCP, for example when investigators or team members at a site put patients' safety at risk, or persistently fail to comply with the protocol or GCP, or falsify data.

Requirement to hold a Clinical Trial Authorisation: The current Regulations do not provide for the MHRA to issue an infringement notice when inspections, checking for compliance with GCP and GMP, find that a sponsor does not in fact hold a Clinical Trial Authorisation (CTA) at all. The amendment would allow this.

Arrangements for Paying MHRA Application Fee: Currently a sponsor must submit the fee with the application to the MHRA for a CTA. The amendment would allow a valid application without the applicable fee, provided a sponsor had made arrangements to pay the fee.