Joint Statement on the Application of Good Clinical Practice to Training for Researchers

HRA, MHRA, Devolved Administrations for Northern Ireland, Scotland and Wales

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Summary

This joint statement advocates a proportionate approach to the application of GCP training to researchers.

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.

Researchers can sometimes be required, inappropriately and often disproportionately, to undertake GCP training when they do not conduct research in the field of clinical trials of investigational medicinal products (CTIMPs) or where their involvement in the trial is minimal and entirely within their professional expertise.

This document clarifies the requirements and expectations for researchers and staff involved in different types of research:

CTIMPs:

- For all CTIMPs it is the high level “conditions and principles” of GCP set out in the UK Clinical Trials Regulations that must be complied with and interpreted in proportion to the risks posed to the participants and to the integrity of the results.

- Sponsors of CTIMPs which are not to be included as part of a marketing authorisation application can choose to comply with ICH GCP as a standard in its entirety but may take a more proportionate approach depending on the nature of the trial.

- Staff involved in the conduct of clinical trials need to be appropriately trained but the specific training does not need to follow a generic syllabus, format or prescribed timing. It should be appropriate and proportionate to the activities undertaken by staff involved in the clinical trial.

Other types of research:

- There is no legal requirement for other types of research (i.e. studies which are not clinical trials of investigational medicinal products) to be conducted in accordance with the conditions and principles of GCP.

- Such research should be conducted in a manner that provides public assurance that the rights, safety and wellbeing of research participants are protected and that research data are reliable. Members of the research team in such studies are expected to be qualified by education, training or experience but should not be required or expected to undertake GCP training.

Introduction

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.

Clinical Trials of Investigational Medicinal products (CTIMPs) and GCP

The International Conference on Harmonisation GCP Guideline (ICH GCP) (as adopted by the Committee for Medicinal Products for Human Use (CHMP)) is part of European guidance, as an element of EudraLex Volume 10, and as such should be taken into consideration, where appropriate, as an established standard for GCP[1]. In particular, if a study is to be included as part of a marketing authorisation application then it is an expectation that ICH GCP should be complied with, and this is referred to in the annexes to the Notice to Applicants (Volume 2B) for the Common Technical Document.

Both the HRA and the MHRA advocate a **proportionate** approach to the application of GCP to the conduct of clinical trials and the appropriate training of staff involved, including those seeking consent from potential participants.

Sponsors of CTIMPs which are **not** to be included as part of a marketing authorisation application can choose to comply with ICH GCP as a standard in its entirety or they can take a more proportionate approach depending on the nature of the trial. Further information about this can be found in the MHRA guidance on risk adapted approaches in the management of CTIMPS.[2]

However, it is important to emphasise that for **all CTIMPs** it is the "***conditions and principles"*** of GCP set out in the UK Clinical Trials Regulations (SI 2004/1031, as amended) (see Annex A) that *must* be complied with. The *principles* of GCP are high level and may be interpreted in relation to the individual trial and *in proportion to the risks posed to the participants and to the integrity of the results*.

The UK Clinical Trials Regulations stipulate that:

> "*each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks*" (Schedule 1, Part 2, 2).

Staff involved in the conduct of clinical trials need to be appropriately trained so that all members of the investigating team know what is expected of them in relation to trial procedures, and in order to ensure that the conditions and principles of GCP can be applied to any trial in a proportionate manner.

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[1] Guideline for good clinical practice E6(R2) EMA/CHMP/ICH/135/1995 (Published: 15/12/2016 Effective from: 14/06/2017)

[2] MHRA - Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products, Oct 2011.

The training required does not need to follow a generic syllabus, format or prescribed timing, but should be appropriate and proportionate to the activities undertaken by staff involved in the clinical trial. It should be tailored to the specific roles and responsibilities being undertaken by an individual. For example, it may be appropriate that some staff only receive an overview of the clinical trial, which could be in the form of a written summary; or they could simply be made aware of the local trial team contacts and have an awareness of, rather than a detailed knowledge of, ICH GCP requirements.

In the case of pragmatic trials, involving only minimal risk related to the research, it may be appropriate for some members of the investigating team simply to have an awareness of GCP requirements (which could be achieved by self-directed learning/provision of written learning materials etc.). For example, a practice nurse taking a blood sample in a pragmatic trial for the purposes of research, might be considered to be undertaking an activity that the HCP is suitably qualified to undertake by virtue of their education, training and experience without undertaking detailed GCP training.

Training/awareness in the aspects of GCP relevant to that role would be considered acceptable (for example, recording of adverse events, documentation of activities in source notes or case report form (CRF), escalating any issues they identify as appropriate).

For certain trials it may be necessary for staff involved in trial activities to be aware of other regulatory requirements outside those of GCP. For example, healthcare professionals retaining tissue samples should be aware of relevant legislation such as the Human Tissue Act, The Blood Safety and Quality Regulations (BSQR, 2005) etc. or seek advice from others with appropriate knowledge and experience.

The MHRA also issued a statement in June 2012 to clarify the requirements for GCP training. The statement is on their website at 'What is the MHRA's position on Good Clinical Practice (GCP) training?' and is summarised below:

- The UK Clinical Trials Regulations (SI 2004/1031, as amended) state that no person shall conduct a clinical trial otherwise than in accordance with the conditions and principles of GCP (Regulation 28) and that each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks (Schedule 1, Part 2, 2).

- The frequency of GCP training is not defined in the regulations. How often this training is repeated is a business decision for the organisation concerned.

- Training needs may range from a detailed knowledge of GCP principles and associated UK Regulations and European guidance to an awareness of particular GCP principles, and training can be tailored accordingly.

- If an activity is part of a person's normal clinical role and all other protocol activities are undertaken by a member of the research team, then no GCP training may be required; however this should be reviewed as part of the risk assessment for a trial.

- The MHRA strongly recommends training in relevant aspects of GCP for anyone involved in conducting CTIMPs, even if the activities are part of an individual's routine job. - GCP training can be provided in a range of formats, including face-to-face, web-based and as self-directed reading.

- On inspection, MHRA GCP inspectors will look for evidence that individuals involved in the conduct of CTIMPs have received adequate training in GCP and appropriate legislative requirements commensurate with their roles and responsibilities.

Organisations involved in the conduct of CTIMPs are recommended to read the full MHRA statement and review their policies and procedures in light of this statement.

What happens with other types of research?

It should be noted that there is **no** legal requirement for other types of research (i.e. studies which are not clinical trials of investigational medicinal products) to be conducted in accordance with the conditions and principles of GCP. However, it is still important that such research is always conducted in a manner that provides public assurance that the rights, safety and wellbeing of research participants are protected and that research data are reliable. Members of the research team in such studies are expected to be qualified by education, training or experience but should **not** be required or expected to undertake GCP training.

The HRA has previously issued the following general statement[3] regarding GCP training:

- For research, training should be appropriate and proportionate to the type of research undertaken, and should cover the responsibilities of researchers set out in relevant legislation and standards.

- There is no set requirement for the frequency of such training. Researchers are expected to maintain awareness of current standards through reference to published guidance and relevant policies.

- Training may be updated when legislation has changed, new policies or practice have been implemented, different research activities are to be undertaken, or a significant period of time has elapsed since research activities have been conducted.

[3] Training requirements for researchers – progress update (v1.5 2012-07-27)

- For research involving CTIMPs, there is a requirement for GCP training. However, the timing of this training is not specified in legislation or guidance but should be appropriate and proportionate

Annex A

The Medicines for Human Use (Clinical Trials) Regulations (2004) [as amended[4]]

CONDITIONS AND PRINCIPLES WHICH APPLY TO ALL CLINICAL TRIALS

Principles based on Articles 2 to 5 of the GCP Directive[5]

1. The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.

2. Each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks.

3. Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.

4. The necessary procedures to secure the quality of every aspect of the trial shall be complied with.

5. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.

6. Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.

7. The protocol shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial, monitoring and publication policy.

8. The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.

9. All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.

Conditions based on Article 3 of the Directive

10. Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.

[4] Amended by S.I. 2006 No. 1928. The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
[5] Commission Directive 2005/28/EC

11. The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.

12. A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.

13. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded.

14. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial.

Organisations supporting this statement include:

The Academy of Medical Sciences

EMIG Ethical Medicines Industry Group

Faculty of Pharmaceutical Medicine
Advancing the science and practice of pharmaceutical medicine for the benefit of the public

Human Fertilisation & Embryology Authority

HTA Human Tissue Authority

independent cancer patients' voice
www.independentcancerpatientsvoice.org.uk

Public Health England
Protecting and improving the nation's health

RCGP Royal College of General Practitioners

RCR The Royal College of Radiologists

UK Clinical Research Collaboration
igniting our potential