Consultation document

Detailed arrangements for clinical trials inspection procedures including the qualifications and training requirements for inspectors, pursuant to Article 78(7) of Regulation (EU) No 536/2014

The sole purpose of this consultation is to collect views, relevant evidence and information from stakeholders as regard clinical trial inspections to help the Commission develop its thinking in this area with a view of preparing the required implementing legislation.

This document does not necessarily reflect the views of the European Commission and should not be interpreted as a commitment by the Commission to any official initiative in this area.

Table of Contents

1. INTRODUCTION

Pursuant to Article 47 of Regulation (EU) No 536/2014[1] the sponsor and investigator of the clinical trial shall ensure that the clinical trial is conducted in accordance with the protocol and with the principles of good clinical practice.

Article 78(1) of Regulation (EU) No 536/2014 puts an obligation on Member States to perform inspections in order to supervise compliance with that Regulation. Member States should also ensure that inspectors are adequately qualified and trained.

Inspectors should verify that principles on good clinical practice and requirements of Regulation (EU) No 536/2014 are implemented effectively. For this reason Article 78(7) of Regulation (EU) No 536/2014 requires that the Commission adopts implementing acts on the detailed arrangements for inspection procedures including the qualification and training requirements for inspectors.

With a view of preparing an implementing act, this consultation document is intended to seek the views of stakeholders regarding:

- the rules on clinical trials inspection procedures, in particular for the preparation, conduct, reporting, follow up, communication and record keeping and archiving of the inspections,
- the coordination of the cooperation of the various Member States, and the follow up of the inspections,
- minimum standards of qualification of inspectors, in particular regarding their education and training.

This consultation document carries over to the extent possible the principles and guidance set out in Chapter 5 and 6 of Directive 2005/28/EC[2], having in mind the scope of Article 78(7) of Regulation (EU) No 536/2014 which is the legal basis for the implementing act. Additional provisions are introduced to include more detailed arrangements.

Once Regulation (EU) No 536/2014 becomes applicable inspections of clinical trials of medicinal products for human use authorised under that Regulation will follow the detailed arrangements of clinical trials inspection procedures laid down by the implementing act provided for in Article 78(7) of Regulation (EU) No 536/2014.

The legal text is expected to take the form of an implementing regulation.

---

[1] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158, 27.05.2014, p.1)

[2] Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (OJ L 91, 09.04.2005, p. 13)

2. GENERAL PRINCIPLES

The implementing act shall apply to inspections of:
- clinical trials conducted in the EU, including clinical trial sites related to these trials but located outside the EU;
- clinical trials conducted in third countries and referred to in marketing authorisation applications in the Union.

Clinical trials inspections may take place on any of the following occasions:

(a) before, during or after the conduct of the clinical trial;

(b) as part of the verification of applications for marketing authorisation;

(c) as a follow-up to the granting of authorisation.

3. INSPECTORS

3.1. Qualifications, training and experience

Inspectors shall have completed education at university level, or have equivalent experience, in medicine, pharmacy, pharmacology, toxicology or other fields relevant to Good Clinical Practice principles.

Inspectors shall receive appropriate training, including participation in inspections, and their training needs shall be assessed regularly. Appropriate action shall be taken to maintain and improve their skills.

Inspectors shall have knowledge of principles and processes that apply to the development of medicinal products and clinical research and have knowledge of applicable Union and national legislation and guidelines applicable to the conduct of clinical trials and the granting of marketing authorisations.

Inspectors shall be familiar with the procedures and systems for the recording and management of clinical data, and with the organisation and regulation of the healthcare system in the relevant Member States and, where appropriate, in third countries.

Inspectors shall also be able to apply an appropriate degree of risk assessment.

Inspectors shall have the ability to make professional judgements in relation to the compliance of the inspected party with the requirements of Regulation (EU) No 536/2014, guidelines on Good Clinical Practice, and the relevant national legislation.

The qualifications, training and experience of each inspector should be documented and Member States should maintain these records up-to-date.

Each inspector shall have access to standard operating procedures and details of their duties, responsibilities and ongoing training requirements. Member States shall maintain those procedures up to date.

Member States shall provide inspectors with suitable means of identification.

3.2. Conflict of interest and confidentiality

Inspectors shall not have conflicts of interest. They shall be independent of all of the following parties:

a. the sponsor,
b. the clinical trial site,
c. the investigators taking part in the clinical trial;
d. persons financing the clinical trial;
e. any other party involved in the conduct of the clinical trial.

Each inspector shall sign a statement declaring any financial or other links to the parties to be inspected. That statement shall be taken into consideration when inspectors are to be assigned to a specific inspection.

Inspectors shall be free from commercial, financial or other constraints or undue influence which could improperly affect their impartiality and their judgement.

The inspectors appointed by the Member States pursuant to Article 78(1) of Regulation (EU) No 536/2014 shall be made aware of confidentiality rules and maintain confidentiality whenever they gain access to confidential information as a result of good clinical practice inspections in accordance with applicable Union requirements, national laws or international agreements.

4. INSPECTION PROCEDURES

4.1. General principles

Inspectors shall verify the compliance of the inspected party with principles of good clinical practice and with the requirements of Regulation (EU) No 536/2014, and with relevant national legislation.

Inspectors shall follow the inspection procedures presented in this consultation document to be laid down in the implementing act in combination with any detailed national procedures drawn up in line with Commission guidelines.

Member States shall establish national procedures for at least the following actions:
(a) appointing experts to accompany inspectors in case of need, and who will be bound by the same rules of confidentiality and conflict of interest as inspectors;
(b) arranging inspections in third countries.

Member States shall make those procedures publicly available.

Inspectors shall carry out inspections on behalf of the Union. The results of those inspections shall be recognised by all Member States.

4.2. Right of access of inspectors to premises and documents

To verify compliance with the principles of good clinical practice, the inspectors shall be entitled to inspect the sites, documents, facilities, records, quality assurance arrangements, data and any other resources that are deemed by the competent authority to be related to the clinical trial. This includes the trial site or sites, any laboratory used for analysis in the clinical trial, any contract research organisation's facilities, the sponsor premises, or other establishments deemed appropriate by the regulatory authority.

Member States shall set up a legal and administrative framework with regards to the powers of inspectors, including inspectors from other MS, for entry into sites and access to data, as set out in the above paragraph.

4.3. Resources

Member States shall provide sufficient resources for the achievement of the objectives of Regulation (EU) No 536/2014. In particular an adequate number of inspectors shall be appointed to ensure effective verification of compliance with good clinical practice and with the requirements of Regulation (EU) No 536/2014.

In order to ensure the availability of necessary skills for specific inspections, Member States may appoint teams of inspectors and experts with appropriate qualifications and experience to fulfil collectively the requirements necessary for conducting inspections.

4.4. Collaboration between Member States

National competent authorities shall collaborate with each other, with the Commission and with the European Medicines Agency to improve the commonly-recognised Union standards for the conduct of inspections. This collaboration may take the form of joint inspections, agreed processes and procedures and sharing of experience and training.

A national competent authority may request assistance from another national competent authority in the matter of inspection.

4.5. Coordination of cooperation of Member States by EMA

In accordance with Article 78(5) of Regulation (EU) No 536/2014 the European Medicines Agency shall coordinate the cooperation of the Member States in conducting inspections. This shall consist of processing of information on inspections that are envisaged, scheduled, or conducted, in order to assist national competent authorities to ensure the most efficient use of inspection resources.

4.6. Inspection reports and records

Without prejudice to the obligation to submit the inspection reports via the EU Portal in accordance with Article 78(6) of Regulation (EU) No 536/2014, the national competent authority shall keep relevant records of national and, if applicable, international inspections including good clinical practice compliance status and their follow up, for at least 25 years.

4.7. Confidentiality

Inspectors and other experts involved in inspections shall respect confidentiality according to national rules.

When processing personal data inspectors and other experts involved in inspections shall comply with the requirements of Directive 95/46/EC[3] and national legislation.

[3] Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data (OJ L 281, 23.11.2015, p. 31)