Commission Implementing Regulation (EU) 2017/556 of 24 March 2017 on the detailed arrangements for the good clinical practice inspection procedures pursuant to Regulation (EU) No 536/2014 of the European Parliament and of the Council (Text with EEA relevance)

COMMISSION IMPLEMENTING REGULATION (EU) 2017/556

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(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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[1], and in particular Article 78(7) thereof,

Whereas:

(1) Regulation (EU) No 536/2014 lays down the legal framework for the conduct of clinical trials on medicinal products for human use in the Union to ensure that the rights, safety and well-being of the subjects are protected, and the data generated in clinical trials are robust and reliable. In particular, the sponsor of a clinical trial and the investigator are to ensure that the clinical trial is conducted in accordance with the relevant protocol and the principles of good clinical practice. Compliance with the applicable legal requirements, the protocol and the principles of good clinical practice, including with standards relating to data integrity and ethical conduct of the clinical trial, is to be verified by means of inspections conducted under the responsibility of the Member State where the inspection takes place.

(2) The inspection in the context of clinical trials may concern good manufacturing practices as regards the manufacturing of the investigational medicinal products or good clinical practice as regards the conduct of clinical trials. Article 63 of Regulation (EU) No 536/2014 empowers the Commission to adopt delegated acts specifying the detailed arrangements for good manufacturing practice inspections as regards investigational medicinal products. Therefore, this Regulation should only lay down detailed arrangements for good clinical practice inspections procedures and requirements regarding training and qualifications of good clinical practice inspectors.

(3) Member States may conduct inspections of clinical trials performed in third countries, either because a clinical trial is related to a clinical trial authorised in the Union or because the data of the clinical trial is being referred to in a clinical trial authorisation application in the Union. Those inspections should allow verifying whether such

clinical trials were conducted in accordance with standards equivalent to Union standards. Inspections of clinical trials in third countries may also be conducted in order to verify whether the clinical trials, whose results are referred to in marketing authorisation applications in the Union, meet the ethical requirements set out in Regulation (EU) No 536/2014. Therefore, provisions on detailed arrangements for the inspection procedures should apply also to inspections conducted outside the Union in accordance with Regulation (EU) No 536/2014.

(4) The International Conference on Harmonisation (‘ICH’) reached a consensus in 1995 to provide a harmonised approach for good clinical practice. Pursuant to Article 47 of Regulation (EU) No 536/2014, the ICH guidelines should be appropriately taken into account by the sponsor when drafting the clinical trial protocol and conducting the clinical trial. To the extent that those guidelines are compatible with the relevant Union law and EU guidelines, inspectors should refer to the ICH guidelines, taking into account the characteristics of each trial.

(5) Member States should be required to set up quality systems to ensure that the inspection procedures are observed and consistently monitored. A well-functioning quality system should comprise an organisational structure, clear processes and procedures, including the standard operating procedures to be followed by inspectors when performing their tasks, clearly defined details of the inspectors' duties and responsibilities and ongoing training requirements, as well as adequate resources and mechanisms which aim at eliminating non-compliance.

(6) It is necessary to enable inspectors to ensure the practical effectiveness of provisions on good clinical practice. That objective should be reflected in the minimum requirements for the qualification of inspectors, in particular as regards their education and training. For the same reasons, detailed rules on inspection procedures should be laid down.

(7) In order to safeguard the effectiveness of inspection, the inspectors should be granted the necessary powers of access to the premises and data. This includes in particular any laboratory used for analysis in the clinical trial, any contract research organisation's facilities or the sponsor's premises. They should also be empowered to contact the trial subjects in justified cases.

(8) In order to ensure the compliance with arrangements for good clinical practice inspections and in accordance with Article 77 of Regulation (EU) No 536/2014 Member States should take corrective measures if necessary. When during an inspection a major non-compliance or breach is identified, or the inspectors' investigatory powers are not recognised by the sponsors, Member States should have recourse to penalties.

(9) In order to ensure the protection of confidential information, in particular personal data of clinical trial subjects related to their health as well as commercially confidential information, the inspectors and experts involved in inspections should be bound by the highest standards of confidentiality and the applicable requirements of the Union law, national laws and international agreements. The inspectors and experts involved in inspections should comply with the requirements of Directive 95/46/EC of the European Parliament and of the Council[(2)] when processing personal data.

***Changes to legislation:** There are currently no known outstanding effects for the Commission Implementing Regulation (EU) 2017/556. (See end of Document for details)*

(10) Commission Directive 2005/28/EC[(3)] should be repealed in order to ensure that only one set of rules applies to the conduct of good clinical practice inspections of clinical trials, including clinical trials governed by Directive 2001/20/EC of the European Parliament and of the Council[(4)]. However, in order to ensure consistency with Article 98 of Regulation (EU) No 536/2014 setting up a transitional period maintaining, as regards certain requests for authorisation of a clinical trial, the applicability of Directive 2001/20/EC, Directive 2005/28/EC should, with the exception of its Chapters 5 and 6 referring to good clinical practice inspection procedures and inspectors, remain applicable during that transitional period to all clinical trials authorised on the basis of Directive 2001/20/EC.

(11) This Regulation should become applicable at the same time as Regulation (EU) No 536/2014.

(12) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Medicinal Products for Human Use,

HAS ADOPTED THIS REGULATION:

CHAPTER I

GENERAL PROVISIONS

Article 1

Scope

This Regulation applies to inspections of:

(a) clinical trials conducted in the Union, including clinical trial sites related to those trials but located outside the Union;

(b) clinical trials referred to in the applications for clinical trial authorisations pursuant to Article 25(5) of Regulation (EU) No 536/2014;

(c) clinical trials conducted in third countries and referred to in marketing authorisation applications in the Union.

Article 2

Time frame for inspections

Inspections may take place in any of the following circumstances:

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

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

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

Changes to legislation: There are currently no known outstanding effects for the Commission Implementing Regulation (EU) 2017/556. (See end of Document for details)

Article 3

Quality system

1 Each Member State shall set up a properly designed quality system ensuring that the inspection procedures are observed and consistently monitored.

Member States shall maintain those quality systems up to date.

2 Each inspector shall have access to and comply with standard operating procedures, details of their duties, responsibilities and training requirements.

CHAPTER II

INSPECTORS

Article 4

Qualifications, training and experience

1 Inspectors shall have completed education at university level, or have equivalent experience, in medicine, pharmacy, pharmacology, toxicology or other fields relevant to the principles of good clinical practice.

2 Inspectors shall receive appropriate training, including participation in inspections. Their training needs, necessary to maintain or improve their skills, shall be assessed regularly by a person appointed for that task.

3 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 on the conduct of clinical trials and the granting of marketing authorisations.

4 Inspectors shall have the ability to make professional judgments in relation to the compliance with applicable Union and national legislation and guidelines. They shall be able to assess data integrity as well as aspects related to ethical conduct of clinical trials.

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

6 Inspectors shall be able to assess the degree of risk as regards the safety of the subjects enrolled in the clinical trial as well as the data integrity.

7 Inspectors shall be aware of the applicable rules as regards confidentiality and protection of personal data.

8 Member States shall keep records of the qualifications, training and experience of each inspector and maintain those records up-to-date for as long as inspector is in active duty.

***Changes to legislation:** There are currently no known outstanding effects for the Commission Implementing Regulation (EU) 2017/556. (See end of Document for details)*

Article 5

Conflict of interest and impartiality

1 Inspectors shall be free from any influence which could affect their impartiality or their judgement.

2 Inspectors shall not have conflicts of interest. In particular, they shall be independent of all of the following parties:

a the sponsor;

b the investigators involved in the clinical trial;

c persons financing the clinical trial;

d any other party involved in the conduct of the clinical trial.

3 Each inspector shall make an annual declaration of their financial interests and other links to the parties to be potentially inspected. That declaration shall be taken into consideration for the purposes of assigning an inspector to a specific inspection.

CHAPTER III

INSPECTION PROCEDURES

Article 6

Subject matter of inspections

Inspectors shall verify the compliance with the requirements of Regulation (EU) No 536/2014, including protection of the rights and well-being of the clinical trial subjects, the quality and integrity of data generated in clinical trial, the compliance with principles of good clinical practice, including the ethical aspects and the relevant national legislation.

Article 7

Procedures to be established by Member States

1 Member States shall establish the relevant procedures for at least the following:

a appointing experts to accompany inspectors, if additional expertise is required for an inspection;

b arranging inspections outside the Union;

c verification of good clinical practice compliance, including the modalities for examining the study management procedures and the conditions under which the clinical trial is planned, performed, monitored and recorded, as well as follow-up measures, such as a review of an analysis of the root cause of a significant non-compliance and verification of corrective and preventive actions implemented by the sponsor.

Member States shall make those procedures and rules publicly available.