

## FAQ: Principal Investigator, Investigator, Investigating Team, Trial Site

### 1. What are the consequences of the different terminology of investigating team, team of investigators?

The investigating team is composed of different groups of persons, including investigators and other persons involved in the trial. Investigators are responsible for the conduct of the clinical trial at a trial site (Art. 2 (2) No. 15 EU Regulation). They may delegate tasks to other members of the investigating team. The qualification requirements of the team members must be described in the trial site description. If a trial is carried out by several investigators at one trial site, one of the investigators must assume the function of the principal investigator. Having a team of investigators it is of practical importance as the organisational and management responsibility of the principal investigator must ensure that at least one investigator can actually perform the functions and tasks of the investigator during the conduct of the trial. In general, therefore at least one of the investigators should have the same qualification as the principal investigator.

### 2. What tasks can doctors who are neither principal investigator nor investigator take on in the context of a clinical trial?

In principle, the medical members of the investigating team can take on all tasks; however, the responsibility for organisation, management and supervision remains with the investigator or principal investigator.

For clinical trials involving minors or adults incapable of giving informed consent and in emergency situations, the regulation requires the involvement of the investigator for the following points (whereas, for example, delegation of informed consent to physicians of the trial team is explicitly allowed for the informed consent procedures for adults capable of giving consent):

- Art 31(1)(c): the explicit wish of an incapacitated subject who is capable of forming an opinion and assessing the information to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator.
- Art. 32 Para. 1 lit. c): the explicit wish of a minor who is capable of forming an opinion and assessing the information to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator
- Art. 35(1)(d): the investigator certifies that he or she is not aware of any objections to participate in the clinical trial previously expressed by the subject.
- Art. 35 Para. 2 lit a): For persons incapable of giving consent and minors, informed consent shall be sought by the investigator from his or her legally designated representative.
- Art. 35(2)(b): For other subjects, the informed consent shall be sought by the investigator without undue delay from the subject or his or her legally designated representative.

Note: The other members of the investigating team can, in principle, take on all tasks that can be delegated by a physician, but by no means the informed consent procedure.

### 3. Is the designation of one investigator sufficient?

It is unclear whether, on the basis of Article 73 of the EU Regulation, it is to be assumed that several investigators are active at a trial site or whether the emphasis on the function of the principal investigator is merely intended to ensure that, in the event that several investigators are present, one person assumes overall responsibility. This person should be as qualified as the principle investigator. The principle that several investigators should be present at an trial site is supported by the fact that, especially in the case of longer or more complex trials, it must be ensured that one person is always present and available to assume the responsibility of the investigator (also in connection with ICH/GCP), e.g. in guiding and monitoring the investigating team. This investigator should have the same qualification as the investigator.

Note: Only the change of a principal investigator (or single investigator) constitutes a change requiring approval as substantial modification (Art. 15 EU Regulation 536/2014).

### 4. What information on the staff of the investigating team should be submitted?

Pursuant to Art. 4 EU Regulation 536/2014, the Ethics Committee shall conduct an ethical review on Part I and Part II in accordance with the law of the Member State concerned. Pursuant to Section 40 (8) AMG, the ethics committee shall give its opinion on the aspects of the clinical trial relating to Part II.

According to Art. 7 Para. 1 lit. e) ("Compliance with Article 49"), the investigator and the persons working at the trial site must ensure that

- the investigator is being qualified for the role of investigator according to the law of the Member state concerned, and
- other persons involved in the clinical trial are adequately qualified by education, training and experience to perform their role.

If these requirements are not met, the approval shall be refused (cf. Art. 8 Para. 4 EU Regulation 536/2014 ("concludes, on duly justified grounds, that the aspects covered in Part II of the assessment report are not complied with").

For the investigator, an up-to-date curriculum vitae and other relevant documents shall be submitted in accordance with Annex M. No. 65. Previous education or training in the principles of good clinical practice or experience gained from work with clinical trials and patient care shall be described. To demonstrate sufficient knowledge of good clinical practice, confirmation of participation in training in accordance with the recommendations of the German Medical Association and the Working Group of Medical Ethics Committees is therefore required (cf. Announcement of the German Medical Association. Dtsch Arztebl.2022;119(19):A-888)). At least one member of the investigating team should have a training sufficient to act as proxy of the (principle) investigator. It is important that the necessary qualification of this member of the investigating team is sufficiently described in the site suitability form.

For all persons involved in the clinical trial, the necessary qualification have to be included in the site suitability form according to Annex N. No. 67. For this purpose, it must be described which qualification requirements exist for which study tasks (cf. requirements according to the applicable curricular advanced training as published by the German Medical Association in Deutsches Ärzteblatt and their website). The head of institution or as its delegate (principle) investigator has to sign the site suitability form. Please be reminded that the version of the site suitability form uploaded to the CTIS should not include the signature itself.

#### 5. Which training requirements arise for principle investigators, investigators and other members of the investigational team?

Sufficient regulatory knowledge, in particular on EU Regulation 536/2014, AMG and ICH/GCP, is required in the entire investigating team. For principal investigators and investigators, at least proof of a basic and advanced course is required (cf. requirements according to the applicable curricular advanced training as published by the German Medical Association in Deutsches Ärzteblatt and their website). Unlike, for example, in the MPDG, the investigator as a member of an investigational team has a management and supervisory function. For the other members of the investigational team, at least proof of a basic course appears to be sufficient. If necessary, an update course on the EU Regulation must also be demonstrated for the principal investigator, investigator and all medical members of the investigating team. Appropriate qualifications are also required for the non-medical members of the examination team, depending on the tasks to be performed. A formal requirement for regulatory and methodological knowledge has not yet been implemented.

#### 6. How can it be ensured that the level of quality at the time of application with regard to investigators is not undercut in the event of a change of investigators, which does not have to be applied for or notified?

The qualification requirements for the investigator are to be fixed in the trial site description (see answer to 4.).

#### 7. How is a trial site defined?

According to paragraph 1.59 ICH/GCP a trial site is defined as location(s) where trial-related activities are actually conducted. The (principle or single) investigator is responsible for the conduct of the clinical trial at a trial site. In general, a trial site will be located at a single location (one hospital or one doctor's office). The investigator must always be able to fulfil his guidance and monitoring function and remains responsible for the conduct of the trial. Thus, the investigator must be authorised to give instructions to the members of the investigating team.