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DEPARTMENT OF
MEDICINAL PRODUCTS
FOR HUMAN USE

Annex IX

Minimum documentation necessary for requesting management of the contract to conduct clinical trials between the sponsor and the research sites. Date: 6th October 2016

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With the entry in force of Royal Decree 1090/2015, of 4 December, authorisation of a clinical trial [which is resolved by the Spanish Agency of Medicinal Products and Medical Devices (AEMPS) and a single Ethics Committee for Investigation with medicinal products (CEIm)] is separated from the conduct of this clinical trial in a specific site (a decision that is expressed by means of the contract between the sponsor and the site). This separation aims to adapt the procedures of Regulation (EU) No 536/2014 once it is fully applicable, to clarify the roles of the different agents involved and to promote competitiveness in this sector.

As a result of these changes, a large part of the documentation that previously reached the sites through the CEIm involved and which was used for signing contracts, must now reach these sites by another means. It is important to emphasise that negotiation and signing of the contract can be done at any time before or after authorisation of the trial (its entry in force being subject to authorisation of the trial by the AEMPS). Therefore, the site may require the necessary documentation before it has requested the opinion of the CEIm. Furthermore, as there will always be a single CEIm and one or several sites involved, document exchange flows should be established between the sponsor and the sites that are complementary and independent of the document flow between the sponsor, CEIm and AEMPS.

On the other hand, the CEIm involved were responsible for evaluation of local aspects of the participating sites, but now it will be necessary for the sponsor to obtain from the site a document accrediting its suitability by a CEIm that will no longer be in the site itself.

In this context, after the entry in force of Royal Decree 1090/2015, of 4 December, proposals have been made by sponsors, foundations and research sites to reach a consensus on the minimum information and documentation necessary for the sponsor to request signing of the control or to obtain the document on the suitability of facilities of each healthcare site participating in a trial. The AEMPS and representatives of the autonomous communities involved in aspects of clinical trial management have also noted this need and have agreed on the following proposal for the minimum documentation necessary to be submitted to start negotiation for signing of the contract to conduct clinical trials between the sponsor and the research sites.

1. Scope and documentation for obtaining the document on suitability of facilities (Annex IV of the instruction document of the Spanish Agency for Medicinal Products and Medical Devices for conducting clinical trials in Spain)

According to good clinical practice guidelines, both selection of the investigators and selection of the facilities where the clinical trial will be conducted are the responsibility of the sponsor. Therefore, the sponsor is responsible for accrediting before the CEIm evaluating the trial that the facilities chosen are suitable.

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Regulation (EU) No 536/2014 establishes that the document on the suitability of facilities submitted by the sponsor will be signed by the "director or designee of the healthcare site or institution where the clinical trial site is located". It is important to emphasise that this document only shows that the site chosen has adequate facilities for conducting the study and in no way implies a commitment to conduct the trial, which can only be expressed by means of the signing of a contract.

Therefore, it is recommended that each site have an established, agile and public procedure, indicating the email to request the document on suitability of facilities (submitting the documents in electronic format) and it is considered sufficient that the documentation submitted by the sponsor be limited to the ***protocol summary in Spanish or the protocol in Spanish and English in order to permit assessment of the suitability of the site for the trial****.*

2. Scope and documentation for signing the clinical trial contract

The legislation establishes that in order to start a clinical trial with medicinal products in a site it is necessary to have a) the favourable opinion issued by a CEIm in Spain, b) the decision to authorise the trial by the AEMPS, and c) the agreement of the management of the participating site expressed by the signing of the contract between the sponsor and the site. Only in clinical trials in which the sponsor/investigator belongs to the site and signing of the contract is not required will express agreement of the management of the participating site be required.

The contract can be formalised at any time but it will only be effective when the clinical trial is authorised by the AEMPS and hence it has the favourable opinion of the CEIm. This means that a contract signed before authorisation will be automatically suspended until such authorisation is obtained.

Therefore, it is the signing of the contract which establishes the link between the site and the sponsor of the clinical trial for its conduct once it is authorised. In this regard, the documentation that the sponsor must submit to the research sites is more extensive and it is considered that the common minimum would be:

1. ***Protocol*** *in English* ***or Spanish and protocol summary*** *in Spanish, to allow the sites to know the objectives, design, methods and organisation of the trial.*
2. ***Status of application for trial authorisation*** *(in preparation phase prior to submission of application, under evaluation, authorised).*
3. ***Insurance certificate*** *which should be contracted by the sponsor for all clinical trials, except those classified low-intervention clinical trials, provided that they are covered by the insurance of collective or individual professional civil liability or equivalent financial guarantee of the healthcare site where the clinical trial is conducted.*
4. ***Financial schedule of the site*** *which forms part of the contract and which should include the indirect costs that will be applied by the site and the extraordinary direct costs.*

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5. ***Identification of the principal investigator and staff of the site and department to which they belong.***

6. ***Pertinent documentation of sponsor delegation, if appropriate.***

In any case, whenever the initially established conditions of the contract are modified, these changes should be documented in terms that are acceptable for both parties, for instance, by the signing of an addendum, notifications with acknowledgement of receipt, etc.

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