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Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial

Page	Paragraph	Guideline text	Amendment proposal	Comments
7	After paragraph 2.1.1	---	**Add the followingnew paragraph:** **2.1.1.a Application for authorisation of a clinical trial** **The applicant submits to Competent Authorities and the Ethics Committee an application for the authorisation of a clinical trial.** **The Competent Authority and the Ethics Committee carry out an initial check of the documentation making up the application. The check consists of verifying that all documents required according to regulations have been submitted. This check will take no longer than 7 calendar days from receipt of the documentation and its outcome (including requests for missing**	In Chapter 2, paragraph 2.1 “Procedural aspects” provides some information on delay, follow up, withdrawal, amendments or applications which are not valid but a paragraph about the general rules for the initial submission of an application is not included. This would also allow better comprehension of the steps to follow in the management of an application. We feel that an initial verification of this type is essential up front to avoid delays later on in the process and is beneficial to both applicant and competent authorities etc. We consider a maximum of 7 days to be a reasonable period for this initial activity (you may wish to define a different time period here but this is optimal for Italy). The applicant must be made aware

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			documentation) will be communicated via e-mail to the applicant.	of the outcome at the end of this check period to aid internal planning and time-keeping for both the applicant and the authorities. To aid the authorities, the 7 days should not be part of the 60 days assessment period and day 0 must be day of receipt of complete documentation. Subsequent checks, if any, should not take more than 3 working days.
			In the case of an application which passes the initial check the communication will include "Day 0".. Day 0 is the day of submission of an application containing all documentation required by regulations. If any documentation is missing from the application, day 0 is the day of submission of the remaining missing documents and will also be communicated to applicant by the authorities. Checks of missing documentation should take no longer than 3 working days.	It is considered fundamental that the applicant be informed of the start date of the period of the assessment of an application;.This is especially important in the case of tacit authorisation that can be provided by a Competent Authority as foreseen in paragraph 2.1.2. subparagraph 3.

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7	2.1.2. First subparagraph; second sentence	The validation of the request for authorisation thus forms part of the delay of 60 days.	Delete the sentence.	As stated previously, for Italy, it is important that the validation of the request for authorisation does not form part of the delay of 60 days.
7	2.1.2. Second subparagraph; second sentence	Day 0 is the day of submission of the request.	Day 0 is the day of submission of a request containing all documentation required by regulations.	It is important that day 0 is the day of a submission containing all documentation required. In this way, any stops in the validation process will not be due to missing documentation. Stops will be only linked to requests for amendment of documentation or further supporting documents by Competent Authorities and Ethics Committee.
7	2.1.2. After subparagraph 3	----	**Add a subparagraph 4:** **If a national competent authority delegates, totally or partially, the assessment of an application to the Ethics Committee, the tacit authorisation of the application should also apply to the Ethics Committee for the delegated part**	For completeness.
11	2.5. After first subparagraph	----	**Add a sentence:** **A request for authorisation must be accompanied by a protocol.**	For completeness.

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18	2.8.3.Title	*Possibility to refer to* the Possibility to refer to the SmPC	Possibility to refer to the SmPC	Formal correction: remove duplication
21	2.10.	A list of national competent authorities to which the sponsor has already made the same application with details of their decisions.	A list of national competent authorities to which the sponsor has already made**/will make** the same application with details of their decisions**, if available.**	For completeness.
22	3.3.	-----	**Add a sentence.** **A change in the batch number should be considered a substantial amendment only if the change of the batch is required for safety or quality reasons.**	It is important to clarify this issue in order to provide a harmonized indication to Member States.
23	3.3.1. second bullet point	Introducing a new *monitoring* procedure.	Introducing a new **study** procedure.	It is important to specify that the sentence refers to a study procedure and not to a clinical monitoring procedure.
24	3.3.1. last bullet point	limited lengthening of the trial time	Delete the sentence.	As in the EUDRACT the expected end date of the trial should be indicated and as it is mandatory to communicate to the Competent Authority only the end date of the trial, a limited lengthening should not be considered as an amendment.
25	3.4. after last paragraph	---	**Add a sentence:** **If a Sponsor mistakenly notifies only one**	It is important to clarify this issue in order to provide a harmonized indication to Member States.

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			body instead of both Competent Authorities and Ethics Committee, or notifies the wrong authority or committee,, the Sponsor should be informed in writing of the mistake, and should submit the amendment to the correct body	
37	After attachment 3	----	**Add an attachment 4.** **INFORMATION REQUIRED BY MEMBER STATE COMPETENT AUTHORITIES**	Please, indicate a web link on the European Commission web site in which an applicant can find a list of the documentation required by the Competent Authority of the Member State. This visibility will aid standardisation across European countries without penalising individual countries and will also improve the compliance of the Applicant to national requirements. Each Competent Authority will be responsible to update the list with local requirements. Sponsor will be responsible to be compliant with national requirements. In order to allow a continuous update of the list, it would be more useful if the list is located on a web page instead of part of the guideline.

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General considerations:

This guidance will provide an important tool in order to strengthen and improve the harmonisation of the procedures, forms and format through Member States. It is important that all Member States make all efforts to put in place national regulation as close as possible to the indication contained in the guideline. It is considered also important a harmonisation of the definition of the amendments as substantial or not-substantial throughout the member states.