Agence française de sécurité sanitaire des produits de santé
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Comments on draft
revision 3 of Detailed guidance for the request for autorisation 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

We agree with the new version of the CTA guidance, whose objective is to simplify the CTA process and to avoid further national requirements.

However, it should go further in the context of an administrative simplification and should propose not only a common CTA dossier but also:
- a single repository and an electronic submission of the dossier into Eudract;
- the possibility to accept English language (note that section 2.1.6 expresses the disharmony of National Competent Authorities/NCAs on that topic).

In order to improve harmonisation, the document could also discuss the distribution of responsibilities between NCAs and Ethics Committees (ECs). As a matter of fact, ECs' missions are detailed in the directive; should NCAs responsibilities be described in that guidance ? We propose that NCA is responsible to ensure the quality and the safety of IMPs and the safety of the trial subjects in the protocol.

As said in the section relating to the scope of this guideline, only clinical trials (CTs) with Medicinal Products (MP) defined in Directive 2001/83/EC are concerned. It should be clarified whether or not CTs with IMPs which are manufactured by hospital pharmacists (which is often the case for paediatrics) are included.

As regard the assessment of unexpectedness of adverse reactions, the reference document should be called the "reference safety information," in order to be in accordance with the next DSUR guidance (ICH).

In the table 1, regarding reduced information for certain IMPs, particularly where they have a marketing authorisation in any EU Member or in an ICH country or in a previous CTA, the 1st and 4th lines should highlight the fact that they only concern cases where the IMP is not modified. Otherwise, there is a need to have further data.

Other documents to be submitted in the CTA dossier include scientific advice's report "or" peer reviews (section 2.10). We strongly support the idea to have scientific advices in the dossier but we do not accept that peer reviews can replace the scientific advice report: "or" should be replaced by "and".

Finally, we, as a NCA, need to have the synopsis of the protocol in the CTA dossier. The text should use the terms “protocol, including its synopsis”.

I take the opportunity of this consultation to ask for a modification of the substantial amendment form: replace “B TRIAL IDENTIFICATION (When the amendment concerns more than one trial, repeat this form as necessary.)” by “When the amendment concerns more than on trial, repeat **the concerned sections of this form** as necessary”. It would avoid the multiple submissions of several forms instead of only one.