General comments

We are generally supportive of the proposed revisions and acknowledge the Commission's effort to further harmonise clinical trial requirements throughout the European Union and reduce administrative burden. We do, however, feel it would still be useful to have a clear and comprehensive listing or tabulation of the harmonised requirements. The guidance would also benefit from greater consistency in the referencing convention. For example, some of the reference document titles are in italic and others are not. Also, when referencing EudraLex Volume 10, it would be useful to refer to a specific chapter rather than just referencing the Volume.

Specific comments

In addition to the general comments above, Gilead Sciences International Limited would like to kindly ask the European Commission to consider the following specific comments.

Page 4: 1.1. "…*Directive 2001/20/EC is exhaustive, i.e. the harmonisation is not based on minimum requirements, and Member States are not allowed to "add on" the Community rules*."
Based on this statement, will the Italian Competent Authority and its Ethics Committees accept EudraCT Annex 1 forms, instead of the Osservatorio upload?

Page 8: 2.1.4.2. "*At the initiative of the sponsor, for example following the opinion of the Ethics Committee or in view of new relevant safety information: In this case the timeframe set out in Article 9(4) of Directive 2001/20/EC re-starts, i.e. the amended request for authorisation shall be considered as rapidly as possible and may not exceed 60 days*."
Please clarify if Competent Authorities will restart the 60-day review period even though the request for submission of documentation is not an initiative of the sponsor; for example, where the Ethics Committee opinion has been submitted to the Spanish Agency (AEMPS) prior to Competent Authority approval.

Page 18: 2.8.3. *"Possibility to refer ~~to the Possibility to refer~~ to the SmPC"*
Phrase repeated in subsection title.
This subsection also states: **"*The sponsor may submit the current version of the SmPC as the IMPD if an IMP has a marketing authorisation in any Member State or in an ICH country and is being used in the same form, for the same indications and with a dosing regimen covered by the SmPC.*"**
We suggest the final guideline includes confirmation that the US Product Information from a US approved product would be sufficient as the IMPD for a CTA.

Page 23: 3.3.1. *"With regard to the protocol, the following is a non-exhaustive list of amendments which are typically "substantial": […] Change in principal or co-ordinating investigator (this could significantly impact on the conduct or management of the trial); Addition of clinical trial sites."*
Change of principal or co-ordinating investigator or addition of clinical trial site are both listed as substantial amendments but some EU countries do not require notification of such changes. How is the Commission planning to address the inconsistency between different Competent Authorities?

Page 25: 3.5. *"Substantial amendments to the information supporting the initial authorisation of the trial or to the protocol should be reported using the Amendment Notification Form as published in volume 10 of EudraLex – the Rules Governing Medicinal Products in the European Union".*
Will the Italian authorities be required to accept the Amendment Notification Form?

Page 31: 4.3. *"The clinical trial summary report is indicated as part of the end of trial notification. However, the clinical trial summary report can be submitted subsequently to the end of trials notification."*

As the clinical trial summary report and end of trial notification are two separate submissions it would be clearer if these were presented separately in the guidance. The Commission should also clarify the expected timeframe for submission of clinical trial summary reports because *"subsequently to the end of trials notification"* can be considered subjective.