Dear Sirs,

Please find the [redacted] comments to "Summary of Clinical Trial Results for Laypersons" in this mail.

General comments:

1. [redacted] welcomes the opportunity to comment on the consultation document “Summary of Clinical Trial Results for Laypersons”. We believe that lay summaries can be an important tool for disseminating clinical trial results. However, we do feel that the present document could be optimised, as outlined also in our comments below.

2. There is too much repetition of information in the guideline, and inconsistencies in several places. [redacted] suggests shortening the document and making it more focused. This will increase readability. We also are of the opinion that some sections are too detailed; see specific comments below.

3. [redacted] is of the opinion that mandatory use of the exact wording of the ten elements in Annex V of the EU Regulation in the headings of the summary is unnecessary restrictive and is by no means a guarantee that the content associated with the elements is addressed in an adequate way.

4. In light of the extensive list of references in the consultation document, [redacted] would favour numbering, to facilitate the use.

5. [redacted] would like a statement in the lay summary, expressing that the information provided is considered valid and correct at the time of submission, but that lay summaries are not kept up-to-date after submission.

Specific comments:

Line 48: “EU Portal and Database”. Once named consider replacing this term with the actual name of the Portal and the Database.

Line 49-52: Consider moving this paragraph to the general principles (chapter 4); consider furthermore to combine chapters 1 (introduction) and 2 (scope) in a single introductory paragraph.

Line 51-57: [redacted] suggests using one term for consistency: either clinical trial results or trial results or results from clinical trials.

Line 56-57: This duplicates line 50-51; [redacted] suggests avoiding such duplications as much as possible.

Line 57: [redacted] suggests to delete “and investigators”. Submission of the lay summary is a sponsor obligation according to Regulation (EU) 536/2014 (and also chapter 3 of the current consultation document).

Line 57: Change “These” to “These recommendations”.

Line 58: Change “summaries included” to “summaries <u>to be</u> included”, as the summaries must fulfill these requirements prior to upload in the database.

Line 58-63: [redacted] proposes the text to read as: ”The lay summary section of the EU database will be publicly available. Clinical trial participants and the general public are anticipated to be the primary audience for lay summaries. In view of this primary audience, the summaries will need to take

into account the average literacy level of the general population, provide simple explanations and apply other measures to support health literacy". Including a reference to healthcare professionals and academics in this paragraph is considered not necessarybecause they are not the primary audience for the lay summaries and the requirements/restrictions that need to be in place for the general population will not be relevant for healthcare professionals and academics.

Line 62: Please be aware of (and consider revision) the conflicting information on line 62 (average literacy level), line 97 (low to average literacy level) and line 148 (low level of literacy).

Line 66-67: [redacted] does not see a need to emphasize the sponsor's obligation in bold. Furthermore, "trial sponsor" is used instead of just "sponsor". Consider to use the same term for consistency.

Line 73: [redacted] suggests to add bullet point): "Make sure the 10 elements listed in Annex V of the Regulation are addressed (see Annex 1 for guidance on the content of each element/section; sponsors may deviate from the format given in Annex 1, with respect to headings and the order of elements, if the resulting lay summary meets the requirements for readability and understandability)". Note also that there is no reference to Annex 1 in the consultation document.

Line 73: [redacted] suggests to update the text to: "Develop the layout and content for each element/section in terms of style, language, *figures, illustrations, graphs,* and literacy…".

Line 75: [redacted] suggests specifying the length of a typical summary.

Line 79: "(see section ~~6~~ 5….

Line 83: [redacted] suggests to replace 'enhance' with 'improve the readability of' and, furthermore, to replace 'some studies' with 'all clinical trials'. Regarding studies vs. trials, it is considered important to use the same terms as in Regulation (EU) 536/2014 in the entire document.

Line 87-96: There seems to be inconsistency between this paragraph and chapter 6 (148-155). Consider rewriting, providing a single explanation of the principle with adequate literature reference(s): please note that in the consultation document, there is reference to OECD/PIAAC, but not to the International Adult Literacy Survey.

Line 89-94: [redacted] suggests moving this explanation to a footnote.

Line 95-135: [redacted] suggests an update of the section on directions for communication in simple everyday language. We appreciate the section content wise but suggest a slightly different presentation with more hands-on examples. Overall, the guidance could be clearer if recommendations/directions are presented as one-level bullets, followed by an example (where possible). Please also consider re-grouping, as an example, Line 108-114, which are in our opinion separate recommendations, not necessarily linked to the vocabulary.

Line 103: [redacted] suggests deleting, or adding another reference than "high school completion levels" as these may vary in EU.

Line 110: [redacted] suggests replacing "Remove unnecessary …" with "Avoid unnecessary…".

Line 124: Consider changing to '~~headlines and~~ Descriptive subheadings should be used to…'

Line 128: [redacted] recommends changing "for example, consider to separate topics by one or two empty lines ….".

Line 143-145: Consider changing to: “Sponsors should default to a minimum of size 12 sans serif fonts in the body text. Larger fonts may be appropriate for specific studies.

Line 150: The use of different scales (previously: IALS, here: OECD) is confusing and inconsistent. Consider rewriting – see also our comment regarding line 87-96.

Line 149 – 232: [redacted] strongly suggests moving this country-specific information to an appendix, to present the same level of detail for different countries and to add recommendations for the countries that are not yet included.

Line 152-155: [redacted] is of the opinion that the sentence on line 153 -155 that highlights EU countries with a larger proportion of adults with low literacy level should be removed, as this is considered not being critical information for developing EU lay summaries. The same applies for the sentence on line 152 -153, providing statistics on Level 3 performance

Line 249-262: It is noted that the language used in this chapter here is much more instructive than in the previous part of the document. [redacted] suggests having comparable levels of detail in the different parts of the document.

Line 261-262: Is this the example to follow? By making a reference this will most likely impact the layout of all future lay summaries. [redacted] suggests deleting, as this very easily could become a de facto standard used by sponsors. Note that this reference also appears in Appendix 1.

Line 271-276: [redacted] proposes to delete chapter 10. Providing direct feedback to clinical trial participants is outside the scope of this guidance and, moreover, a lay summary will most likely not cover the needs of participants.

Comments to Annex 1:

1. [redacted] is of the opinion that the layout of Annex 1 is not very user (or reader) friendly. Please consider adding a line, stating that – provided the requirements are taken into account – other formats may be used (see also general comment 3, and comment to line 73).

2. Comment on 6. Description of adverse drug reactions and their frequency: patients – and others will most likely compare what has been included in this summary and in other summaries. Thus, consider to include text to stress the difference of what may have been reported in different documents from the AE - ADR perspective; not only explaining what an ADR is.

3. Comment on 7. Overall all results of the clinical trial: [redacted] is of the opinion that the 1st bullet – information whether trial completed as planned etc. does not belong in a section on the results. Furthermore, in case a trial was closed early, this is already reported under 3.2, 2nd bullet.

4. Comment on 10. Indication where additional information could be found: There is a suggestion to include text like: *For general information about clinical trials, go to….* [redacted] is of the opinion that this should not be part of individual lay summaries. Instead, consider to add information on this on websites connected with the EU Database and Portal.

Yours sincerely,

[redacted]