ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

29 August 2016

Directorate General for Health and Food Safety DG SANTE
Unit B4 "Medical products – Quality, Safety and Innovation"
European Commission
F101 08/058
B-1049 Brussels

RE: Public consultation on "Summary of Clinical Trial Results for Laypersons"

Dear Sir/Madam:

The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through pivotal studies assessing the safety and effectiveness of new products – as well as post-approval and pharmacovigilance research. With over 33,000 employees engaged in research activities in Europe, and more than 120,000 worldwide, ACRO member companies advance clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants in 142 countries. On average, each of our member companies works with more than 500 pharmaceutical, biotech, and medical device sponsors of clinical trials each year.

ACRO's comments are organized into 3 sections:

- general comments
- suggested revisions to specific line numbers in the consultation document
- topics omitted from the consultation document and recommended for inclusion in the final document

I. General comments

ACRO welcomes and strongly supports the draft recommendations on the Summary of Clinical Trial Results for Lay Persons developed by the European Commission's expert group on clinical trials for the implementation of Regulation (EU) No 536/2014. ACRO congratulates the expert group on developing a well-considered document that provides helpful, practical guidance to ensure that summaries developed for lay persons will be understood by the target audience.

II. Suggested revisions to specific line numbers

Line Numbers	Current text	Issue/question	Suggested language
156 - 231	Inclusion of algorithms and formulas for proficiency assessments	In order to maintain the flow of the document for the reader, the Commission might consider omitting the complete algorithms and formulas for the proficiency assessments from the main text – and, instead, simply footnoting them or moving them to an appendix.	
233 - 241	"Other considerations"	The text (lines 161 – 231) immediately before this paragraph suggests recommended tests for assessing the readability of text in specific languages of the EU. However, this does not cover all official EU languages and the document does not provide specific guidance on readability assessment of the other languages, for which standard tests are not available.	Add the following sentence at the end of the "Other considerations" paragraph: "This is especially important for languages where a standardized, recognized test for readability is not available."
235-238	"Where feasible, sponsors should consider testing the readability of an initial version of the study results summary with a small number of people who represent the target population. Depending on the nature of the study, this could be patients with a particular disease or it	Whilst we accept the need for conducting readability testing, we are concerned about the practicality of conducting this for initial versions of the study results summary for all clinical trials. Might it be more efficient to consider an overall process for readability testing of the study results summary, which may not require testing for every clinical trial.	Add the following sentence: "Sponsors may consider implementing an overall process for readability testing of language used in study results summaries rather than testing for every clinical trial."

	could be members of the public."		
260	"Creative solutions to ensure understanding could include videos, cartoons and animation."	It is important that any language used in visual presentations should also be in compliance with the readability standards and use of plain language.	"Creative solutions to ensure understanding could include videos, cartoons and animation. Any language used should be in compliance with the standards as specified in section 6."
272 - 276	"The summary for lay persons in the EU database should not be regarded as the only way of communicating with trial participants. Whilst study participants may find the lay summary useful, sponsors should consider providing some direct feedback to patients who have taken part in their trials including an acknowledgement of their contribution and an expression of thanks for their time."	The phrase "sponsors should consider" is ambiguous, and it is not clear whether direct feedback to patients is considered to be a regulatory/ethical requirement or not. This lack of clarity could, for instance, lead to an adverse finding on inspection. Also, it is not clear what additional information to that contained in the lay summary sponsors would be expected to provide to study participants. Additionally, the term "patients" should be changed to "participants" as this statement is equally valid for clinical trials conducted in healthy volunteers.	"The summary for lay persons in the EU database should not be regarded as the only way of communicating with trial participants. Although not required by regulation, some sponsors may choose to provide the lay summary directly to participants who have taken part in their trials, together with an acknowledgement of their contribution and an expression of thanks for their time."
Annex 1, Templates	"It should be noted that the wording of the ten elements cannot be changed but that sponsors can, if they wish, combine categories where this makes sense. For example, some sponsors might wish to combine section 3.1 (where the trial was conducted) with 4.1 (the number of subjects	A comment should be included to make clear that, as the lay summary will be written in free text, no limit is placed on the size of the document.	Add the following sentences to this paragraph: "No limit is placed on the size of the document. However, it should be as succinct as possible while relaying the required information in a form that is readily understandable."

	included in the trial). Sponsors may also decide to change the order of the headings if they feel this is appropriate and add sub-headings as required."		
Annex 1, Section 2	"Name and contact of sponsor"	It is not clear how the situation in which a sponsor is located outside the EU should be addressed. ACRO recommends that this is clarified, and that, as in the current EU Clinical Trials Register, it should be possible for the contact point to be located outside the EU.	Add: "In the case of a non-EU sponsor, the sponsor contact point may be located outside the EU."
Annex 1, Section 3.2	"This trial started in December 2006 and ended in March 2010."	The terms "started" (e.g. first patient/first visit or screening) and "ended" (e.g. last patient/last data) should be defined.	"This trial started in December 2006 (which means that the first patient was screened/treated in December 2006) and ended in March 2010 (which means that last data of the last patient were observed in March 2010)."
Annex 1, section 4.3	If possible, sponsors should include references to age, gender, diagnosis, indication, disease stage or severity as this will help define the scope of the study (for example, 'stage IV chronic obstructive lung disease')	The example given in defining severity (stage IV chronic obstructive lung disease) is not very accessible to the general reader. Where medical terminology refers to defined stages of a condition, these can often be expressed (e.g., in the case of chronic obstructive lung disease) in terms of mild (stage I), moderate (stage II), severe (stage III) and very severe (stage IV). ACRO believes that these descriptors are more meaningful for the general reader.	"If possible, sponsors should include references to age, gender, diagnosis, indication, disease stage or severity as this will help define the scope of the study (for example, 'stage IV chronic obstructive lung disease' should be described as 'very severe chronic obstructive lung disease')."
Annex 1 Template	3. general information about the clinical trial	ACRO suggests that the Commission consider whether	Consider transferring information about use of

Section 3. and Section 5.	5. Investigational medical products used	information about use of placebo, explanation of the term placebo, randomization and blinding arrangements and all related explanations might be more useful to the reader in section 3, and should, therefore, be transferred from section 5 into section 3.	placebo, explanation of the term placebo, randomization and blinding arrangements and all related explanations from section 5 into section 3.

III. Omissions in consultation document recommended for inclusion in final document

There are several issues the Commission may wish to consider including in the final document.

Possible misinterpretation and inappropriate use of lay summaries

ACRO is concerned that people who are not familiar with clinical research might draw unwarranted conclusions from the information presented, and in extreme cases might even make decisions about their treatment on the basis of the results presented. ACRO therefore recommends that each lay summary should include a statement warning about misinterpretation of the trial results. Because of this, the Commission may wish to consider adding text to Annex 1 section 8 concerning the inclusion of a statement warning of misinterpretation of trial results by the reader. The following text is one suggestion: *"The results of this trial do not represent the full medical knowledge about the product. Therefore, patients should not make any change to their current treatment without seeking medical advice."*

Cross-referencing of related guidance documents

The European Commission has also issued a consultation document on ethical considerations for clinical trials on medicinal products conducted with minors, which states "The summary of the results should be accompanied by a summary of the results that is understandable by laypersons. In case of paediatric trials, the summary should be understandable by the children that have participated in the trial." This point is absent from the current consultation document. The Commission may wish to consider including a cross reference to the planned guidance on ethical considerations for clinical trials on medicinal products conducted with minors, and the following statement: *"In the case of paediatric clinical trials, the summary of the results that is understandable by laypersons should be understandable by the children that have participated in the trial."*

Data retention policy and timeframe

No information is given about how long the lay summary will be available in the data base. It should be stated if information will be available for a limited or unlimited time. The Commission may wish to consider adding the following text to the guidance document: *"The summary of clinical trial results for lay persons will usually be available within the data base for an <unlimited / limited> time.*

<If available for a limited duration: The information about clinical trial results will be available in the data base for XX weeks/months/years.>"

Background and context to aid in data interpretation

In Annex 1 section 7, the Commission may wish to consider including an additional section that provides a short description about study procedures to explain where data / information came from (e.g. blood sampling every 6 weeks, tumor assessment by CTs every 12 weeks, etc.) -- giving the layperson the chance to understand how the trial was performed and / or data compiled. For example, the Commission might begin the section with the following statement to Sponsors: *"Include a short description about study procedures to explain where data / information came from (e.g. blood sampling every 6 weeks, tumor assessment by CT scan every 12 weeks, etc.) giving the layperson the chance to understand how the trial was performed and / or data compiled."*

Additional guidance on literacy proficiency levels

The Commission might consider providing more specific examples of literacy proficiency levels. Although Annex 2 includes sample language for results, ACRO recommends inclusion of sample sentences for each proficiency level mentioned in the body of the document, with emphasis given to the most common levels (2-3). Examples should also be included for age-appropriate language to be used in lay summaries of paediatric clinical trials (or cross-referenced and included in the planned guidance on ethical considerations for clinical trials on medicinal products conducted with minors).

Additional guidance on suitable language and visuals

The Commission might consider providing examples of suitable language to describe clinical assessments, clinical laboratory results and pharmacokinetic assessments and also examples of Visuals. ACRO suggests the inclusion of an additional Annex that gives examples of suitable language to describe clinical assessments, clinical laboratory results and pharmacokinetic assessments and the inclusion of an additional Annex providing examples of suitable visuals.

ACRO thanks the Commission for the opportunity to comment on this public consultation on "Summary of Clinical Trial Results for Laypersons." Please contact ACRO if we can provide additional information or answer any questions (knoonan@acrohealth.org).

Respectfully submitted,

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EU Transparency Register information:
ACRO's public ID number in the Transparency Register is: **150920420956-26**