Response to EU Consultation | Summary of Clinical Trial results for Lay Persons | August 2016

General Comments
Dear Committee Thank you for the invitation to comment on your document. By way of introduction – I have performed paediatric clinical trials for 17 years. My writing experience includes 4 years training about how to write for children (evening classes). I have written scientific/pharmaceutical lay language communications for the clinical trial public of all ages – and children in particular - since 1999. This easy-to-understand information has been widely translated for global clinical trials and improved recruitment and compliance. Please feel free to get in touch if you have any questions or I have misunderstood anything. General comments: • Literacy levels vary with education, disease severity, age, cognitive ability and visual impairment. • Therefore it would be good if the lay language summary is as easy to read as possible. • However, could it be argued that this draft guidance makes the lay summary more complex than originally intended by the Clinical Trials Regulation? • To make it easier for the lay public a lay language abstract at the beginning would be helpful. • Then add an index after the lay abstract with internal hyperlinks to each section (similar to PIL index) • MHRA published a "PIL of the month" to assist best practice. Perhaps EMA could publish "Lay summary of the month" to likewise encourage best practice? • Suggest back-translations are essential to ensure the original sense and neutrality of the original is retained. • Suggested alternative text examples are in blue Best regards *Jane Lamprill* Jane Lamprill RN RSCN FICR Owner and director **Please Read Carefully™** Specialist medical writing for children & lay public

Line	Text	Specific comments/suggested text
61	....may also be accessed by others such as healthcare professionals and academics.	Lay summaries may also be read by the press, social media so care needs to be observed for • transparency – especially in adverse event reporting • contact details for further information should not refer to individuals

62	Average literacy level of general population	• Impossible to assess especially if person is reading in a second language • People who are unwell have a shorter attention span • Suggest writing to a reading level similar to an in-flight magazine but with shorter sentences
75	Keep the document as short as possible	• This is a problem. When writing clear English, it is necessary to explain technical terms which requires more words • It may not be possible to have a short lay summary for a complex study • Suggest a lay language abstract at the beginning with index for easy reading
89-94	Repetition of 97-103	Could you delete one of these sections?
114	Avoid ambiguous words and phrases	Especially the words • "study" as this is what you do for exams and is a room in a house • "trial" is also something that happens to criminals Clear explanations need to be given throughout the document not just in a glossary. It is confusing for readers to keep switching between glossary and text.
118	Active voice: "Researchers studied the effect of tamoxifen on breast cancer"	Suggest this is still not clear to a lay person. Scientists studied the effect of tamoxifen, a medicine that can help stop breast cancer
124	Headlines	As per line 134 – headlines in bold, slightly bigger font than following text
125	Presentation of the "big picture" before the details	• Agree but should be at top of document • As for line 75 - suggest lay language abstract of no more than ¼ page A4 double spaced.

164	Readability testing	• Best to **print out text** before reviewing as eye and brain coordinate differently when reading paper to screen • Gunning Fog Index is best tool in my experience • Does not give measure of comprehension, just how easy it could be to read
257	Graphs	• Suggest short explanation of graph with easy legends as general public may not be educated to read graphs
264	Language translation	• Requirement for a translation in every country that the drug was tested in seems overly onerous on companies • Care needed when translating into different language regions e.g. Spanish Spanish or Mexican Spanish etc • American English and English English are not the same
P13	**Annex 1 – templates** …..the wording of the ten elements cannot be changed …The use of suggested wording is not mandatory	Start of paragraphs 2 and 3 appear contradictory – what wording are your talking about? Do you mean the titles of the ten elements? Please clarify thank you
P13	#1- Phase	• Suggest short paragraph on drug development saying briefly what happens at each stage so that patients can put the study into context • Very important if drug has early promise signals but may be 10 years away from market • Important not to raise false hopes and state that this trial is part of the big picture of many other studies

	1.1 Title **If the full title is lengthy and/or complicated then also provide a shorter and/or simpler lay title upfront followed by the full title. A short title alone may lead to confusion with other similar studies. Avoid technical terms and explain them further down in the document if necessary. The title should focus on the basic aim of the study.**	• Always provide a shorter and simpler lay title followed alongside or very near the full title. • Clearly identify titles to avoid confusion e.g. Scientific and Everyday titles • Explain technical terms as near as possible to the title text.
	1.2-1.4 Identifiers	• Suggest have ID numbers at the top of the document with the summary date in large font for clear identification • Especially important if similar studies published at same time
14	**Contact**	Suggest never give names of individuals for security reasons
	3.1 Trial location	No need to bullet list of countries as wastes space & you want document as short as possible
		Bullets are used to separate out different points – a country list is the same point
14	**3.2 When the trial was conducted**	• Suggest you have consistency of terminology in this guideline and for the lay summaries • Trial or study? Both confusing as trials happen to criminals
15	**Suggested wording for Phase 1 trials:** **In this study, researchers looked at how this drug works in the body. The researchers are able to get information on the effect that the drug has including side effects. This study did not test if the drug helps to improve health.** **[Patients/healthy volunteers] took part in this study.**	• Try to avoid "the body" as this could mean a corpse in back translation • Grammar: be careful to use the same tense in the same paragraph The aim of this research was to test the new drug xyz with healthy men at a research clinic. Researchers did medical tests before and after the men had taken the medicine to find out • If there were any chemical changes in their blood or urine that showed how they used up or reacted to drug xyz • If there were any benefits or unwanted side effects

15	**Suggested wording for Phase 2 trials:** **In this study, researchers were trying to find out if this new treatment could help patients with a particular condition.**	• The word "could" is passive and not easy to translate as has different nuances in different languages: • Be specific – what is the main objective of the study? Researchers gave new medicine xyz to volunteer diabetic patients to find out if it lowered the amount of sugar in their blood
15	**Suggested wording for Phase 3 trials: In this study, researchers compared the new treatment to the standard treatment used for [disease/condition] or placebo.**	This study wanted to know how patients with diabetes reacted to tablets that were • Their usual treatment OR • The new research treatment OR • Placebo (no treatment in the identical looking tablets)
15	**Suggested wording for Phase 4 trials:** **This study was carried out after the new treatment had been approved for use. Researchers looked at**	• What does "approved for use" mean for the lay public who know nothing about drug development?
	the effect of new treatments in a larger number of people.	After medicine xyz was licensed and allowed to be prescribed by doctors, a large number of volunteer patients helped researchers find out even more about the drug
	Population of subjects	• Subjects are those who are ruled by someone. Research is voluntary. All these people are volunteers or participants
	4.1 the number of subjects included in the trial: **in each of the Member States concerned,** in the EU and in countries outside the EU **This study included [specific population to whom this study applies, including healthy volunteers and patients as appropriate]** **The study was run in following [list country (ies) that enrolled patients]. In each country [name the country] [#] individuals were enrolled in this study. If there are a lot of countries involved, it may be easier to present this data in a table.**	• This does not make sense – do you mean Member States in which case they are in the EU? • Can you just list the countries in Alphabetical order? This study included 2000 volunteer patients with diabetes. The research was done in 7 countries: Brazil, Chile, Denmark, Finland, Germany, Hungary and the United States.

16	**4.2 Age group and gender breakdown**	Could you combine this with 4.1 to save words and say e.g. This study included 2000 volunteer patients aged between 18 and 64 years who had diabetes. 800 were women and 1200 were men. The research was done in 7 countries: Brazil, Chile, Denmark, Finland, Germany, Hungary and the United States.
16	**4.3 Inclusion and exclusion criteria** **#2 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')**	• **Please could the EMA give guidance here – presumably only the main criteria are required otherwise the document will be too long?** • Example language too technical • What is the difference between diagnosis and indication in practical terms? (e.g. Paediatric Investigation Plan discussions around this) **Here are the main rules for taking part in the study:** **Patients who were allowed** • Men or women between 18-64 • Men or women with severe lung problems for over ten years. The air passages in their lungs were too narrow. (obstructive lung disease) • Were using their blue medicine puffers (inhalers) more than three times a day **Patients who were not able to take part in the research** • Smokers • Those pregnant or breast feeding • Having steroid injections • Had problems with their heart, liver or kidneys

17	**"People with diabetes were put into 3 groups by chance (randomised) to reduce differences between the groups.** **[If the study was double blinded, also add the following wording] This study was also "double blinded" – this means that neither patients nor doctors knew who was given which treatment/drug. This was done to make sure that the study results were not influenced in any way.** **[If the study was single blinded, use the following words]This study was single blinded, this means the patient did not know who was given which treatment/drug but the doctor did know. A single blinded trial may mean that the results may be biased by knowing who received each treatment.** **[If not randomised, list how many patients/people were in each group, and how this was determined.]**	• Avoid words like biased • Patients/people – patients are people! The study was 'double blinded'. This means only the medicines company, not the doctor or patients knew which identical looking research drug was which. This was to stop anyone wrongly guessing if the medicine worked as this might give the wrong research results.
17	**Description of adverse reactions and their frequency**	• The most important and most controversial section • There may be side effects that are not yet known about • Please advise regarding **consistent terminology**. Do you want adverse reactions, side effects or adverse events? Using different terminology is confusing for writers, companies and public. • You ask for this document to be as short as possible, but a large amount of detail is required in this section – the document will not therefore be short • Will you include the Euralex recommendations for partially sighted people? • It would be helpful if companies use clear colours e.g. not white writing on a green background etc.

18	**Side effects [in Group A] included:** ***[List the most serious and/or most prevalent adverse reactions. Apply numeracy and health literacy principles.]***	• The word "included" is misleading here. It implies that they were included amongst other things which have been missed out. Is this because the EMA only wants the main side effects listed? • Do you mean The most important side effects experienced by Group A patients were:
20	**Results – Composite** **These events were measured together (combined) because each one is quite rare. Researchers also wanted to see if the drug worked in patients who had all 3 conditions.**	• Suggest **not** using the word "event" – it has many meanings and is confusing for the lay public who normally pay to see events!
20	**Dose escalators** **"This study was carried out to find the highest [dose/amount] of treatment that people could take without having too many side effects."**	• Again, ambiguous language. "Carried out" can mean being physically carried • Also you have not graded this for severity – "too many side effects" – one side effect can be catastrophic! The reason for the research was to find the highest dose of xyz medicine that healthy volunteers can safely take without having serious side effects.
21	**Morbidity** **"People with diabetes were put into 2 groups by chance (randomised) to reduce differences between the groups. This was done because no one knew if one treatment was better than another.**	• Is this correct? What sort of differences do you mean for the general public?

22	**"Women who had a bone fracture after they stopped having their monthly periods (menopause) were put into 2 groups by chance (randomised) to reduce differences between groups. The study was carried out using two different groups because no one knew if one treatment was better than another.**	• Periods may not be monthly when nearing menopause Women who had broken a bone after their periods had finished (menopause), took part in a research project. A computer randomly divided the women into two groups. Each group received either drug A or drug B to find out which was the better treatment.
24	**#8 Comments on the outcome of the clinical trial** **Write a general high level statement summarising the overall results and their implications without using promotional language (See neutral language guidance in Annex 2).**	• Suggest you also describe any benefits if demonstrated, in non-promotional language. These are requested by (1) ethics committees /IRBs to help elucidate the benefit/risk ratio (2) help patients decide whether or not to participate in a future study
	Describe the most important limitations of the study. If required, sponsors can refer to further detailed information in the technical summary.	• Also good to balance limitations with **positive attributes** of the study or the public will wonder if you know what you are doing • The general public will not understand the technical summary. Perhaps a link for further information can be given. • Where patients are interested in participating in future trials, they could be referred to the relevant patient organisations for their country
25	**Were there any differences in side effects?** **Sex: Treatment A had a similar side effect profile in men and women.**	• Too technical e.g. profile • "Sex" on its own here could have very confusing interpretations **Men and women** – there was no difference in the type of side effects that either sex experienced when taking Drug A
	Suggested wording might be: **To learn more about this study, you can find more detailed information about this study on this website.**	• Too wordy and repetitive. Please click here for more detailed information on the XYZ website (mention name of website in case of change to URL)

	More information may also be available by looking up the official number or title, or by going to	• Not clear Each research study has a unique ID number. More information is available if you go to XYZ clinical research results website and type in the ID number in the "search" box.
26	**References**	• Needs title • I assume all links have been checked • Could you also give names of websites in case URLs change?
27	**Annex 2: Neutral language**	• Agree. Suggest you ask patient organisations to check language for neutrality and user friendliness? • Suggest getting a **back-translation** to ensure that the translated lay summary also uses neutral language.