Pharmaceutical Industries Ltd.

Date: August 30, 2016

To: European Commission
Unit B4 "Medical products – Quality, Safety and Innovation"
(by email to:) SANTE-B4-GL-results-laypersons@ec.europa.eu

From: Teva Pharmaceutical Industries Ltd

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

Dear Madams, Dear Sirs,

Please find below Teva comments on the European Commission on the public consultation on the Summary of Clinical Trial Results for Laypersons.

Teva Pharmaceutical Industries, duly represented by the private individual(s) indicated herein below, is a stakeholder company with affiliated companies incorporated and active in many Member States of the European Union ("EU"), manufacturing, marketing, distributing and selling Active Pharmaceutical Ingredients ("APIs") and/or Finished products.

Teva does not fall within the EU definition of a small or medium- sized enterprise.

General comments

General comments
In accordance with the Commission Guideline — Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006) the following is stated concerning the scientific results: Only one set of result-related data may be provided per planned analysis and trial. If the outcome is analysed on several occasions, each of these analyses should be posted. Thus in case of interim and final analyses (i.e 2 different reports) both reported results would be published. The more recent one would appear as "current". What would be the requirements for the lay summaries?

General comments
Please include that lay summaries should be mandated only for studies, for which technical results summaries will be published in the EU database.
There must be an easy way for a study participant to identify the layperson summary connected to their study, other than by title or sponsor's study number.
Please use either "trial" or "study" consistently.
Please use the term "sex" not "gender" consistently. The terms used in this document are not consistent with requirements in the Common Technical Document and with the Guideline on IMP and AMP (eg, "interventional drug", "Phase", "comparator product".
The general approach for early terminated studies should be addressed. In case where limited data is available, a letter justifying the lack of a summary / limited data should be acceptable. In case that a study was finally not conducted (e.g. no recruitment has taken place), no lay term summary in the language of the specific country should be mandated. A sentence explaining the situation should be included in the consultation paper.

Specific comments on text

Line number(s) of the relevant text	
56	Comment: We like to have clarified what the responsibility of the study investigators is. Proposed change (if any): Add section explaining this.
56-58	Comment: We propose a change in wording. Proposed change (if any): 'This document provides recommendations and templates for the production of summaries of clinical trial results for laypersons by sponsors and investigators ***for study summaries that are required to be*** included in the EU database ***only***.

Line number(s) of the relevant text	
62	Comment: Typo Proposed change (if any): …the summaries will need to ~~be~~ **take** into account the average literacy level of the general population…
63	Comment: Would it be possible to fully clarify and provide examples of "other measures to support health literacy"?
71-72	Comment: We propose to have this rephrased in a clearer way. Proposed change (if any): '~~Develop~~ ***T***he summary for a general public audience ***should be developed based*** on the assumption that there is no ~~and do not assume any~~ prior knowledge of the trial'
75	Comment: We like to ask to add a suggested length of the summary.
81-85	Comment: The regulation (No. 536/2014) is not mentioning involvement of patients, patient representatives or advocates in the development for review of the summary. We believe this sentence should be removed. If it cannot be removed, we like to have clarification of the proposed methods of "involving".
86	Comment: Please add another bullet stating that protected personal data and commercially-confidential information should not be included in a lay summary.
87-139	Comment: Within this section it would be helpful to add sub-headers for 'Principles' and 'Writing style'
97-98	Comment: This is more or less a repeat of lines 88-89. Duplication seems unnecessary, so in our opinion this could be deleted. All of the information on proficiency levels could be included in the first paragraph (lines 88-94) for ease of reading.

Line number(s) of the relevant text	
106	Comment: It is not clear how we should establish vocabulary that will be familiar to non-medical people. Guidance should be provided or just delete 'familiar to non-medical people'.
128-129	Comment: 'A minimum of 12-point font' should appear on a separate bullet since it does not really relate to adequate 'white space'.
144-145	Comment: The same approach for font size should be used irrespective of whether the trial relates to visual impairment or involves older people since the audience does not only include research participants but also the general public. Additionally a lot of trials will include a proportion of elderly.
146-147	Comment: We think this would be better phrased as 'The summary should be kept factual and the use of promotional language avoided' since some facts could be perceived as promotional.
148-155	Comment: A lot of this information seems to be a repeat of what it is in Section 5 (88-94 & 97-103) and could be better consolidated in one or the other section.
265	Comment: Requirement for local language versions is burdensome and there should not be any expectation that it is prepared in additional languages- this is not a requirement of the legislation. The English version only should be the requirement for multi-national trials.
271-276	Comment: Return of results to study participants may be a nice to have, however this is not a requirement of the regulation and has nothing to do with the lay summary. We propose to delete this section.

Line number(s) of the relevant text	
Pg. 13, Section 1, text on phase	Comment: It may not be helpful for lay persons, if the lay summary states whether a study was phase x or "outside the four phases". The purpose and objective seems more relevant (but this is to be stated in Section 3.3). If "outside the four phases" is to be kept, we like to have clarification what is considered to be "outside of the four phases".
Pg. 13, Section 1.1	Comment: Please explain what is meant by "linked" and how will the lay reader do this?
Pg. 14, Section 1.3	Comment: For clarity, we would like to have reference included of the EudraCT number Proposed change (if any): EU trial number **(EudraCT number)**
Pg. 15, Suggested wording for phases	Comment: It would be helpful, if general definitions, e.g. of the 4 phases, could be given on the EU portal next to individual lay summaries but not within each individual summary. Ideally, terms with an available general definition could be hyperlinked to the definition (or readers could read the definition by mousing over the term). This would avoid making the lay summaries long and general.
Pg. 15, Suggested wording for phase I	Comment: Each participant in a clinical study is a volunteer, according to the Declaration of Helsinki and the ICH E6. Therefore the "healthy volunteers" should be called "healthy people". Proposed change (if any): This study did not test if the drug helps to improve health. [Patients/healthy ~~volunteers~~**people**] took part in this study.
Pg. 15, Suggested wording for phase II	Comment: We suggest to use lay terms. Proposed change (if any): In this study, researchers were trying to find out if this new treatment could help patients with a particular ~~condition~~ **disease**.
Pg. 15, Section 4 about Population	Comment: We have the opinion that in some instances limited information should be acceptable, e.g. Orphan indication with only a few patients at one site in one country.

Line number(s) of the relevant text	
Pg. 16 Incl/Excl criteria	Comment: First bullet – It is confusing to highlight some bullets and not others. Surely it would be better to only include the most important inclusion/exclusion criteria to simplify this section
Pg. 17-22, example wording to explain randomisation in lay language	Comment: Putting people in groups by chance does not necessarily reduce differences between groups. The wording used in some examples in the consultation document is misleading rather than helpful ("to reduce **differences** … using two **different** groups") and should be modified. Proposed change (if any): We suggest rephrasing e.g. "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." to "… 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 ..."
Pg. 17, Section 6 on adverse reactions	Comment: The document states that it is intentional to require adverse reactions (i.e. drug-related adverse events) and not adverse events in the lay summary. Since knowledge about relatedness of AEs evolves with the (clinical) development of a substance, it could be misleading to limit the presentation to related AEs. It seems better to provide all AEs, irrespective of relatedness.
Pg. 17-18, Section 6 on adverse reactions	Comment: The document calls for very detailed information on adverse reactions, yet says at the same time that "very long lists" are not helpful. It is not clear how this can be achieved. Could this document provide examples of a section on adverse reactions, e.g. with example table(s) or graph(s)?
P19 on numerical concepts	Comment: Some examples of how to present statistical information in lay terms would be helpful since it could be difficult to avoid technical terms which describe certain analyses.
P22 patient reported outcomes	Comment: We assume it wasn't intended to include an actual drug name here i.e. tanezumab.

Line number(s) of the relevant text	
Pg. 24, Section 8 on outcome of trial	Comment: Unfortunately, example text is only given for the more straight-forward items, i.e. whether there will be further studies, whether there were differences between subgroups. No examples are given for statements about the outcome of a trial. Since such statements are especially challenging to make in lay language, examples would be particularly helpful.
P25 on Section 10	Comment: The amount of references etc seem to be excessive. The purpose of the lay summary is to inform not confuse so including a long list of sources of information which may not be written in a way that a lay person can understand is not necessarily very helpful.
Pg. 27, Annex 2 on neutral language	Comment: Due to it being more simplified, lay language may have a larger tendency for being perceived as promotional. Almost all example statements suggested as "neutral language" (right column) are longer and some are more difficult to understand than the "promotional language" statements (left column), e.g. if one refers to a specific endpoint rather than simply writing "works better". We suggest not putting the hurdle too high but rather accepting statements such as "works better" in lay summaries. (As an aside, the document itself uses "worked similarly" in recommended example sentences on pg. 24 about differences in subgroups)
Pg. 27, last example, left column	Comment: The example sentence on the left side is contradictory and should be corrected: "did not extend life… , people … lived longer"

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