

The lay summary – remember the reader

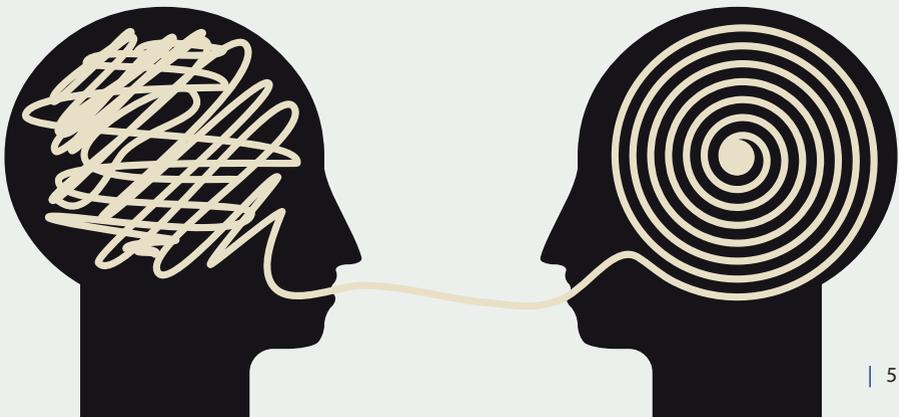
Founded in 2002, Trilogy Writing & Consulting specialises in high-end medical writing. Senior partners Lisa Chamberlain James and Barry Drees examine the 10 suggested headings in the EMA regulation CTR EU No 536/2014, and outline potential issues and oversights that could potentially lead to misinterpretation.

In 2014, as part of its Clinical Trial Transparency initiative, the EMA mandated a requirement (CTREU No 536/2014) for clinical trial sponsors to prepare a summary of the results of every clinical trial written in language understandable to lay persons (plain language) no later than one year after the end of the trial in the EU. These CTR lay summaries will be made available in a new EU database; it was planned for 2018, but it is likely that it will not now be implemented before 2020.

Overall, the regulation is a very positive development and chance to deliver clinical study results to the general public in a form that can be understood by anyone. However, there is a danger that this opportunity will be missed; either through lack of clarity in the requirements, or because writing for the layperson is notoriously difficult and so often poorly executed. The lay summary also describes a single study – there is no context of wider clinical development to enable proper evaluation of the benefit-risk of the drug, and there is a danger that ambiguity in the regulation may result in misinterpretation.

The regulation gives 10 suggested headings, some of which are open to interpretation:

1. **Clinical trial identification (including title, protocol number, EU trial number, other identifiers):** how helpful this section will be for lay audiences is questionable. If the title is complex, a simpler title should also be added, but when simplified, titles can become misleading.
2. **Name and contact of sponsor:** self-explanatory.
3. **General information about the clinical trial (including where and when the trial was conducted, the main objectives of the trial, an explanation of the reasons for conducting it):** the methods section should be straightforward, but if the results for every parameter are mentioned, these ‘summary sections’ can mushroom into long lists of numbers and multi-page tables.
4. **Population of subjects (including information on the number of subjects included in the trial; age group, gender breakdown, inclusion and exclusion criteria):** there can be huge numbers of inclusion and exclusion criteria and complex terms that can be very difficult to understand.



Which criteria should be included, if the lists are too long?

5. **Investigational medicinal products used:** the lay audience is unlikely to be familiar with generic names, and brand names can differ in different countries.
6. **Description of adverse reactions and their frequency:** discussing adverse reactions can be very challenging. Even the term 'adverse reaction' can cause confusion, and the seriousness and frequency of each reaction should be explained and described. Most reactions are described in MedDRA terms and so these must be explained in lay language. The general challenge is to communicate benefit-risk information.
7. **Overall results of the clinical trial:** describing results can be very difficult considering that it is much harder for lay audiences to understand and interpret numbers related to health information. Technical terms such as number needed to treat, confidence interval and so on are particularly difficult to explain, and even more difficult to interpret. How confident can we be that patients will be able to correctly interpret a Forest Plot, or Kaplan-Meier survival analysis? Using statistical terms to explain how much 'trust' the reader can place in a result can also increase the perception of risk. Presenting only the top level or main results can also be interpreted as cherry picking, so a balanced representation of the results must be given. For efficacy results, discussing the difference between the interpretation of primary, secondary, and exploratory analyses is extremely challenging. Giving the lay audience complex information does not help them to make decisions, and this calls into question the value of disclosing complex clinical trial results without context and explanation (neither of which is currently mandated by the regulation). How can we communicate that studies are designed with statistical power such that statistically significant results for the primary analysis indicate a clinically relevant effect, whereas for secondary analyses the interpretation is weaker and more complex? This is a challenge even for a scientifically literate audience. Safety results might appear at first glance to be easier to communicate, but most adverse reaction results are given with a frequency.

The accuracy of these frequencies, however, is strongly dependent on the sample size, and drops sharply in small studies. How much it drops and the relative importance of different events can be very difficult to explain.

8. **Comments on the outcome of the clinical trial:** this should be unbiased and not sound promotional in any way. It is difficult to describe positive results so that they are not interpreted as promotional, but this is an excellent opportunity for companies to describe how clinically meaningful the results are.
9. **Indication if follow-up clinical trials are foreseen:** self-explanatory.
10. **Indication where additional information could be found:** links could be given in this section to more general sites, such as plain language dictionaries.

These challenges are not insurmountable and have not been ignored. The EMA has ongoing consultations with industry and patient groups to try to improve the guidance for industry in communicating with the lay audience. The continued dialogue between regulators and industry around the issues of transparency and communicating with the lay audience offers the chance to develop guidelines that can lead to documents that truly aid the public's understanding of clinical research, and improve their trust and perception of the pharmaceutical industry.

It would be a tragic waste of an opportunity if these new regulations simply lead to the addition of another overly long and hard to understand summary of clinical study results. Instead, everyone involved in writing or designing templates and procedures for lay summaries should invest time and resources in making sure that the resulting documents facilitate rather than hinder communication with the lay audience. The pharmaceutical industry has few opportunities to communicate directly with patients in Europe, and so it would be good to remember the reader when producing this document, and see the CTR lay summary not as yet another regulatory hurdle to be mechanically created, but rather as a unique chance to expand the science-public interface and improve the general understanding and acceptance of science. ●

References available on request.

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