Break-out Session

Lay summary requirements – consequences for Phase I trials

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Structure of Session

- **Regulatory background and guidance documents**
- **Implementation strategies, challenges for early phase trials**
- **Example of a lay summary of a Phase I trial**
- **Discussion of questions from the audience**
- **Take home messages**

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Dr. Kerstin Breithaupt-Grögler acts as an independent consultant in clinical pharmacology and has no conflicts of interest to declare

Recommendations for EU Guidelines on Lay Summaries

- **EU Clinical Trials Regulation 536/2014 calls for summary of clinical trials results in a format understandable for laypersons**
- **Annex V of CT Regulation sets out 10 elements that must be addressed in a Lay Summary**
- **EU Expert Group developed recommendations provided to the EC Ad Hoc Working Group**

Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, 2018

Whom do lay summaries address?

- **General public**
- **Patients**
- **Trial participants**
- **Others**
- **People without prior knowledge of the trial, medical terminology or clinical research**

Meet the needs of the general public - What should be covered? (1)

1. **Clinical trial identification** (study name)
2. **Name and contact details of the sponsor**
   (Who sponsored this study?)
3. **General information about the clinical trial**
   (When and where was this study done? What was the main objective?)
4. **Population of subjects**
   (What patients/people were included in this study)

Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, 2018

Meet the needs of the general public - What should be covered? (2)

5. **Investigational medicinal products used**
   (Which medicines (or vaccines) were studied?)
6. **Description of adverse reactions and their frequency**
   (What were the side effects?)
7. **Overall results of the clinical trial**
   (What were the overall results of the study?)
8. **Comments on the outcome of the clinical trial**
   (How has this study helped patients and researchers?)

Meet the needs of the general public - What should be covered? (3)

9. **Indication if follow up clinical trials are foreseen**
   (Are there plans for further studies?)
10. **Indication where additional information could be found**
    (Where can I find more information about this study?)

Timelines for Lay Summaries

- **In general, Lay Summaries need to be provided within 12 months after end of the trial** (last patient/last visit?, data base closure?, ??)
- **For Phase I trials with non-therapeutic intent this is prolonged up to 30 months**
- **Shorter timelines apply for paediatric trials (6 months)**

Appendix, on disclosure rules, to the 'Functional specifications for the EU portal and EU database to be audited EMA/42176/2014'

Overview on guidance documents

EU and Draft FDA Guidelines

- EU CTR 536/2014 Article 37
- EU Guideline on Summaries of Clinical Trial Results for Laypersons, (February 2018) (Expert group recommendations)
- FDA Guidelines on Lay Summaries

Overview on guidance documents

Guidance on writing:

- Multi-Regional Clinical Trials Version 3.0 March 20, 2017
- EFPIA: PhRMA Principles for Responsible Data Sharing
- Reflection Paper – EFPIA Guiding Principles on Layperson Summary
- TransCelerate: Lay Summaries of Clinical Trials: An Implementation Guide
- TransCelerate: Recommendations for drafting non-promotional lay summaries of clinical trial results
- Federal Plain Language Guidelines:

https://www.plainlanguage.gov/guidelines/

Overview on guidance documents

Guidance on writing:

- Health Literacy Principles: Guidance for Making Information Understandable, Useful, and Navigable
https://nam.edu/wp-content/uploads/2015/06/HealthLiteracyGuidance.pdf

- The eConsent: Health Literacy, TransCelerate (section 3 is relevant principles for lay language)
www.transceleratebiopharmainc.com/wp-content/uploads/2017/11/eConsent-Health-Literacy.pdf

Recommendations of EU Expert Group

- **Health literacy level and readability**
- **Numeracy principles**
- **Use of visuals (figures, graphs, animation)**
- **Non-promotional language**
- **English mandatory plus languages of trial participants**
- **As short as possible but explain all medical and research basics**
- **Establish clinical trial term glossary**

Health literacy level and readability

- **Health literacy includes numeracy skills**
- **Health literacy requires knowledge of health topics**
- **Health information can overwhelm even persons with advanced literacy skills**
- **Literacy is the ability to read, write, speak, and compute and solve problems**
- **Plain language is a strategy for making written and oral information easier to understand to improve health literacy**

https://health.gov/communication/literacy/quickguide/factsbasic.htm

Communicate science in plain language

Enable users to understand plain language the first time they read or hear it

https://health.gov/communication/literacy/quickguide/factsbasic.htm

Communicate science in plain language

- **Key elements of plain language include**
  - ✓ Organizing information so that the important points come first
  - ✓ Breaking complex information into understandable pieces
  - ✓ Using simple language and defining technical terms
  - ✓ Using active voice
  - ✓ Know your audience and have them test your materials before, during, and after they are developed

https://health.gov/communication/literacy/quickguide/factsbasic.htm

Recommendations of EU Expert Group

- **Readability and plain language**
  - Keep sentences short and concise
  - Remain factual and objective, avoid promotional language
  - Use a language-specific reading test to assess the literacy level
  - Text should be assessable from the age of 12 years upwards
  - Test readability with a small number of people of the target population

Recommendations of EU Expert Group

- **Numeracy principles**
  - Present absolute numbers and percentages rather than relative risks or odd's ratios
  - Use whole numbers rather than decimals
  - Less is more
  - Do the math for the reader, provide examples
  - Explain what the numbers mean
  - Combine numbers with text or visuals

MRCT Return of Results Guidance Document July 13, 2016

Transcelerate Recommendations

RECOMMENDATIONS FOR DRAFTING NON-PROMOTIONAL LAY SUMMARIES OF CLINICAL TRIAL RESULTS

TransCelerate Background

TransCelerate BioPharma Inc. is a non-profit organization dedicated to improving the health of people around the world by accelerating and simplifying the research and development (R&D) of innovative new therapies. The organization's mission is to collaborate across the global R&D community to identify, prioritize, design and facilitate implementation of solutions designed to drive the efficient, effective and high quality delivery of medicines. The biopharmaceutical members of TransCelerate are committed to enhancing public health and medical and scientific knowledge through the sharing and transparency of clinical trial information.

Background

A lay summary (plain language summary) of a single clinical trial is written to be understandable to the general public and may be posted to public websites and/or provided to trial participants after the trial has concluded. The European Medicines Agency (EMA) intends to post these summaries to the European Union (EU) database according to the EU Clinical Trial Regulation (EU Regulation) where the public may view the summaries.[1] At this time, there are no regulatory requirements for lay summaries to be posted outside of the EU nor are there regulatory requirements world-wide for disseminating lay summaries more directly to clinical trial participants. However, sponsors may decide at their discretion to provide them to clinical trial participants.

These recommendations are intended to provide general principles to help sponsors prepare lay summaries in a manner that reduces the risk that the summaries could be perceived as promotional, which would raise regulatory concerns. Adjustments may need to be made for local laws and regulations and any sponsor-specific policies and processes.

TransCelerate BIOPHARMA INC

Recommendations for Using Non-Promotional Language for Lay Summaries

- The overall tone and content should be factual and objective.
- Care should be taken that comments on the outcome of the clinical trial are factual in nature and do not make inferences or assessments. The Neutral Language Guidance section of the MRCT Return of Results Toolkit provides examples of recommended language.[2]
- Materials should not have a commercial or marketing appearance related to the investigational medicine (e.g., do not use brand colors, brand logos orimagery; however the same concern may not apply to sponsor logos or colors).
- Information should be accurate and not misleading in any way.
- Materials should be fair and balanced (i.e., include information on the efficacy and the safety data from the trial). Materials should also be fair and balanced in terms of formatting (e.g., appropriate detail and prominence of the safety data).
- Care should be taken to ensure that the lay summary is made available in a non-promotional context (e.g. where posted to a sponsor's website, there should not be links from webpages that are promotional).
- A statement should be added that further information on the trial can be found on ClinicalTrials.gov & the EU Clinical Trial Register so that additional information is readily available.
- A statement should be included stating that results are from a single trial and new information or different results may be obtained from other studies
- A statement should be included that therapeutic changes should not be made based on the results of a single trial without consulting a healthcare professional.
- Approval status should not be provided in the lay summary. Specific indications and countries where approved should not be provided as indications may vary in different countries which could lead to a promotional concern if stated too broadly.
- If an organization elects to provide translations they should be cautious to ensure that the translated text doesn't contain promotional language.

Roadmap Initiative (EFGCP / EFPIA) on Good Lay Summary Practices

Multiple stakeholders across various institutions are joining forces

- To find a systematic approach to impact the infrastructure required for successful Lay Summaries
- To ensure that Lay Summary development and dissemination can be reliably handled by commercial and academic sponsors and involved patients
- To discuss and find solutions for areas of particular complexity like ‘implementation processes beyond existing guidances’, ‘competencies required for writing and translation’, ‘dissemination within an beyond the EU portal’, ‘funding’, ‘suitable technology to reach public and patients’, ‘communication of safety results’

EFGCP, European Forum for Good Clinical Practice
EFPIA , European Federation of Pharmaceutical Industries and Associations

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Points of discussion

- **What makes Phase I Lay Summaries attractive for the general public?**
- **Does the transparency associated with Lay Summaries affect the planning of a Phase I trial with respect to commercially confidential information?**
- **How to generate the additional means that are required to engage in Lay Summary Writing?**
- **How may sponsors and investigators profit from engaging in Lay Summaries?**
- **How may the use of modern technologies facilitate visibility of your research?**

Take home messages

- **Lay Summaries are required for Phase I trials in healthy subjects as well as in patients**
- **Familiarise yourselves with the available guidances**
- **Start preparing the Lay Summary process now**
- **Analyse and adapt to your institution‘s needs**
- **Turn Lay Summaries into an important tool to increase your visibility in the general public**