# Good Lay Summary Practice

**This guidance was developed in cooperation with the Roadmap Initiative to Good Lay Summary Practice and adopted by the Clinical Trials Expert Group (CTEG, a working group of the European Commission representing Ethics Committees and National Competent Authorities (NCA)).**

**Version 1**

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# Good Lay Summary Practice

This “Good Lay Summary Practice” (“GLSP”) provides recommendations on how to prepare, write, translate, and disseminate summaries of clinical trial results in lay language. This is a mandatory requirement laid out in Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use[1] (“EU CTR”) and a transparency obligation to all trial participants and the interested public.

### How to Use This Document

The GLSP is organised in two parts. Part 1 is a GLSP Quick Guide and Part 2 is the full GLSP Handbook. The GLSP Quick Guide contains core extracts from the GLSP Handbook and may serve as an overview of the recommendations offered in the Handbook. Since the intention of the GLSP is to provide practical recommendations and strive for good lay summary practices, professionals directly involved in lay summary projects are encouraged to read the full handbook to benefit from the detailed recommendations.

The GLSP recommends clinical trial sponsors to organise the lay summary process (“LS process”) in four steps: planning, development, translation, and dissemination. A stepwise approach will help sponsors with their proactive planning and execution and will ensure a high quality of the lay summary (“LS”). However, unless otherwise stated, the order in which information is presented in the GLSP does not necessarily drive a linear process with a set order of priorities. Company or research institutional standard operating procedures (SOPs) and other considerations may require activities to be performed in another sequence.

The four steps and related core activities are depicted in the flowchart below with further defined input and output. It is recommended that the trial sponsor determines which output or deliverables may be desired before a next step is initiated. For easy navigation, both the Quick Guide and the Handbook are organized in the same way.

Throughout the GLSP, the use of the word “must” refers to legal requirements, as laid out in the EU CTR, whereas the use of the word “should” refers to optional recommendations (anchored in ethical obligations and best practices). To further aid this distinction, mandatory requirements under the EU CTR are marked with a “§” icon throughout the GLSP. In addition, to easily identify recommendations on paediatric LS, a paediatric icon is added to relevant text sections.

The Appendices offer supplemental information. Appendix 1 contains additional useful considerations and information related to each step of the LS process. A list of glossaries is included in Appendix 2 and a number of additional guidance references are presented in Appendix 3.

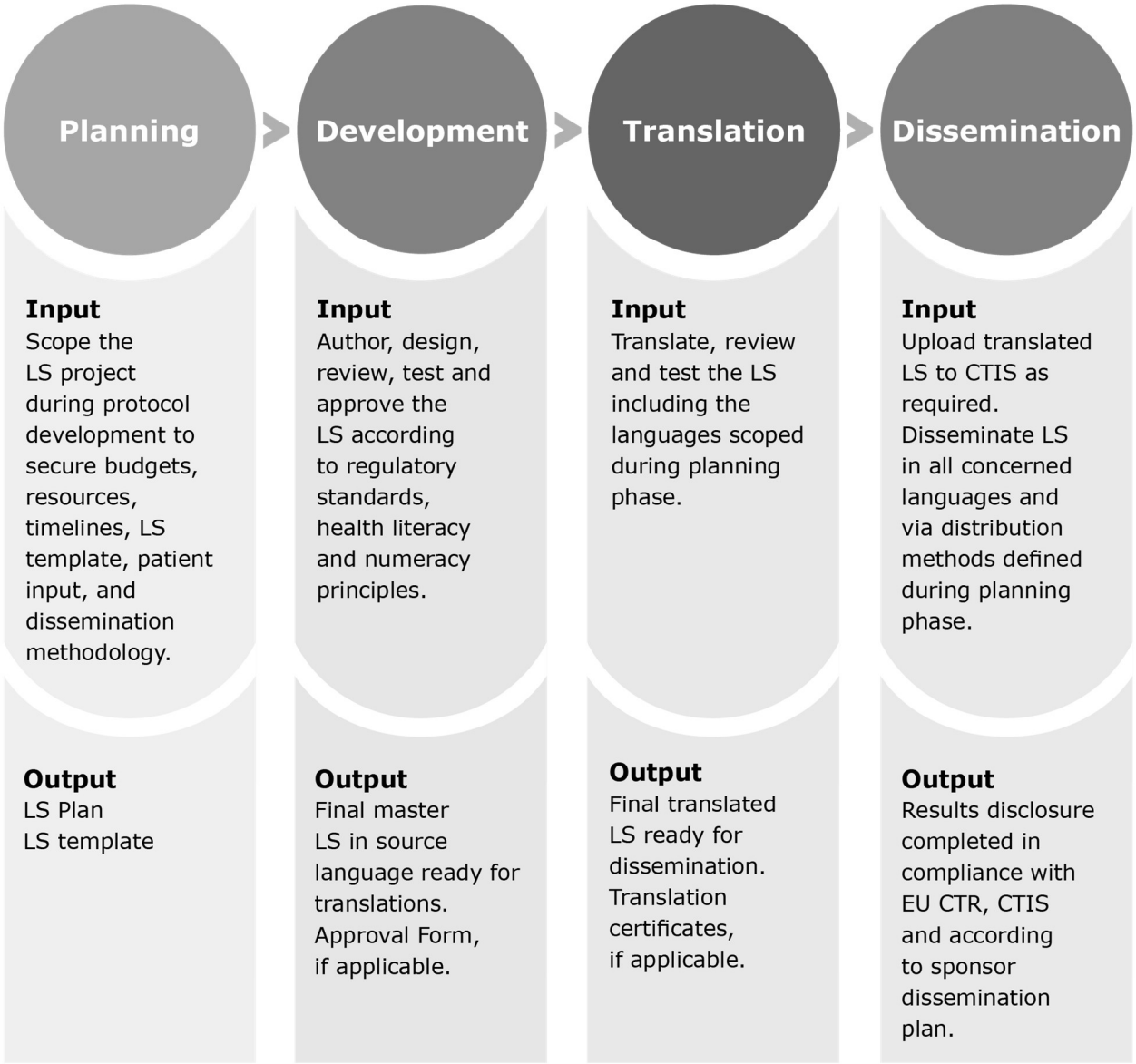


Figure 1: Flowchart of the Lay Summary Process

| Document Icon Key | |
|---|---|
| § | Mandatory requirements under the EU CTR |
| | Recommendations on paediatric LS |

# Abbreviation List

| | |
|---|---|
| ADR | Adverse Drug Reaction |
| AE | Adverse Event |
| AESI | Adverse Event of Special Interest |
| CDC | Centers for Disease Control and Prevention |
| CSR | Clinical Study Report |
| CTCAE | Common Terminology Criteria for Adverse Event Reporting |
| CTIS | Clinical Trials Information System |
| CTR | Clinical Trial Regulation |
| EEA | European Economic Area |
| EFGCP | European Forum for Good Clinical Practice |
| EFPIA | European Federation of Pharmaceutical Industries and Associations |
| EMA | European Medicines Agency |
| EPF | European Patients' Forum |
| EU | European Union |
| EUPATI | European Patients' Academy on Therapeutic Innovation |
| FDA | Food and Drug Administration |
| GLSP | Good Lay Summary Practice |
| ICF | Informed Consent Form |
| ICH | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| IMI | Innovative Medicines Initiative |
| IPPOSI | Irish Platform for Patient Organisations, Science and Industry |
| IRB/IEC | Institutional Review Board/Independent Ethics Committee |
| LS | Lay Summary |
| LPLV | Last Participant/Patient Last Visit |
| MDR | Medical Device Regulation EU 2017/745 |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MRCT | Multi-Regional Clinical Trials |
| NAP | National Academies Press |
| PhRMA | Pharmaceutical Research and Manufacturers of America |
| PIS | Patient Information Sheet |
| QA | Quality Assurance |
| QC | Quality Control |
| R&D | Research and Development |
| SAE | Serious Adverse Event |
| SAR | Serious Adverse Reaction |
| SME | Small and Medium-sized Enterprise |
| SOP | Standard Operating Procedure |
| US | United States |
| WAI | Web Accessibility Initiative |
| WHO | World Health Organization |

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# GLSP Quick Guide

## 1. Introduction

The Regulation (EU) No. 536/2014, Article 37[1] (”EU CTR”), requires trial sponsors to submit a summary (“lay summary” or “LS”) that is understandable to laypersons for each clinical trial with pharmaceuticals into the EU Database, a core element of the EU “Clinical Trials Information System”[2] (“CTIS”). The LS must be submitted to the CTIS via the EU Portal no later than 12 months from the protocol-defined end of the clinical trial, 6 months for paediatric studies, and up to 30 months for non-therapeutic Phase 1 trials. More detailed rules about the publication of clinical trial results can be found in “Functional specifications for the EU Portal and EU database to be audited - EMA/42176/2014”[3]. If the lay summary cannot be reported within these timelines for scientific reasons, it shall be submitted as soon as possible. In that case the protocol shall specify when the results are going to be submitted. Deferral of the publication timelines can be requested for approval by the Member States concerned either in the initial trial application or as a substantial modification.

The content required in the lay summary is listed in Annex V of the EU CTR and will accompany a ”Summary of Clinical Trial Results”, the content of which is laid out in Annex IV. Suggestions for structure and presentation of the content of lay summaries are provided in the “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: ”Summaries of Clinical Trial Results for Laypersons”[4] (“EU CT Expert Group Recommendations”).

Trial participants must be informed about the LS availability and, to the extent possible, its timing within the Informed Consent process.

This “Good Lay Summary Practice” (“GLSP”) is presented in two parts, Part 1, a GLSP Quick Guide, and Part 2, a GLSP Handbook. It provides the key aspects, respectively detailed recommendations for best practices of planning, preparation, translation, and dissemination of high-quality lay language summaries of results from clinical trials with medicinal products:

- The GLSP provides recommendations on building LS processes with the aim to enable all sponsors to generate and disseminate objective and understandable information on clinical trial results.
- The GLSP contains recommendations on how to enable patient engagement all through the LS process although it is acknowledged that sponsors’ resource and infrastructure constraints can limit a routine involvement of patients in the different steps.
- The GLSP gives recommendations for LS dissemination aiming to inform trial participants and the general public to ensure fair access to information for all.
- The GLSP recognises and addresses the need for specific skills and strategies for LS on paediatric trials and highlights the limited experience available so far.

- LS recommendations in this document apply to aggregate clinical trial results only; therefore, return of individual patient-level data to a given trial participant is out of scope.
- Although some shared principles may apply, other types of result information to lay audiences, such as plain language summaries of journal publications and conference abstracts, are out of scope.

Considering the terms “plain language” and “lay language” as synonyms, the GSLP has adopted the definition of plain language from the Plain Language Association International: “A communication is in plain language if its wording, structure, and design are so clear that the audience can easily find what they need, understand what they find, and use that information"[5].

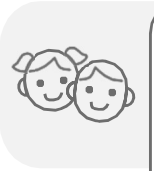
The GLSP is the result of a roadmap and consultation process integrating the experience and recommendations from more than 60 industry, academia, patient and not for profit organisations from within and outside of the EU in collaboration with Competent Authority and Ethics Committee representatives of the EU Commission Expert Group on Clinical Trials, which are committed to clinical trial result transparency and the development and dissemination of factual, non-promotional, and reader-friendly lay summaries. In addition to the EU CT Expert Group Recommendations (entitled “Summaries of Clinical Trial Results for Laypersons. 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”[4]), the GLSP takes into consideration the recommendations from TransCelerate BioPharma on “Layperson Summaries of Clinical Trials”[6] and from the Multi-Regional Clinical Trials (MRCT) Draft FDA Guidance on Provision of Plain Language[7].

## 2. Planning of the Lay Summary

**Timing of the Lay Summary**

Planning of the LS should start at the time of protocol preparation.

LS planning including translations (where applicable) should be aligned with the preparation of the Patient Information Sheet (PIS) and the Informed Consent Form (ICF), since these documents partly share content and readership. A coordinated approach across these documents can reduce duplication of effort or discrepant use of plain language terminology.



In line with the EU CT Expert Group’s Recommendations, a well written LS should normally be accessible by young people from the age of 12 years upwards[4]. Sponsors of paediatric studies are encouraged to consider developing a child-focused version of the LS for younger trial participants in addition to the version for the parents or legal representatives, particularly where they have already developed an Assent for the paediatric patient’s information about trial participation.

When planning the LS, its dissemination should be coordinated with the publication plans for the clinical trial results in general but also with the regulatory requirements for posting trial results on databases such as EU Clinical Trials Register[8], the EU Portal (mandatory upon implementation of the EU CTR), or on others such as ClinicalTrials.gov. For multinational and multicentre trials, LS dissemination should be coordinated across all trial sites, and if distribution is planned via investigational sites, access to

information for all participating patients should be considered in the interest of fairness. For additional recommendations on the timing of the LS, refer to Section 2.1 in the GLSP Handbook.

**Lay Summary Production Planning**

LS development and dissemination approaches may differ, e.g., according to the type of clinical trial or resource capacity of the sponsor. Sponsors should develop a standard operating procedure (SOP) for their LS approach.

Use of a LS template (e.g., in line with the EU CT Expert Group's Recommendation) can aid efficient and consistent preparation of LS. It may be helpful to pre-fill the template with general information on the trial and the endpoint presentation structure, and hence create an outline 'shell' document, in advance of trial results availability. However, once available, the sponsor must present the main objectives and overall results of the clinical trial[1].

The EU Portal provides an option for uploading of interim scientific summary of trial results but does not anticipate this option for a LS of interim results. Should the protocol foresee an interim analysis with uploading of the results to the publicly available EU Portal, and the sponsor plan the preparation of a LS, such LS availability and planned dissemination should be presented in the Patient Information Sheet/Informed Consent Form. Potentially available local restrictions to such dissemination should be respected.

Complex clinical trials (e.g., basket, umbrella, or platform trials) can contain separate parts that constitute individual clinical trials, or they can be characterised by extensive prospective adaptations. For these complex designs, the end of trial definition(s) applicable to individual parts and the results-sharing strategy should be carefully planned. Planning should foresee that the chosen approach will be addressed in the Patient Information Sheet/Informed Consent Form and reviewed during amendments.

To enable adherence to the LS finalisation timelines, the LS review process needs to be efficiently planned. According to the sponsor's SOP other stakeholders may be involved in the LS review process, e.g., scientific/statistical experts, patient representatives, legal and medical communication experts and/or investigators. Their involvement and tasks should be well defined and logistically structured.

At the time of LS finalisation, it is recommended that the sponsor's content owners document their approval of the LS. Having finalised and "locked" the LS content in source language, the document can then be entered into the EU Portal, and potentially further translated and disseminated. When trial sites are located outside the EU, the sponsor will need to track local LS requirements to ensure regulatory compliance. For additional recommendations on Production Planning for the LS, refer to Section 2.2 in the GLSP Handbook.

**Cost Implications**

Generally, but especially for resource-limited sponsors from academia, charities, or Small Medium-sized Enterprises (SME), planning of the process and resources required for production and dissemination of a LS should begin with budgeting at the time when a research proposal for a clinical trial is submitted to a funding source. Budget implications such as patient involvement in the LS process, costs of standard or special patient population communication tools, and for translations and/or dissemination beyond the CTIS need to be factored in at the proposal stage. For additional recommendations on Cost Implications, refer to Section 2.3 in the GLSP Handbook.

**Stakeholder Communication**

If direct dissemination of the LS to trial participants is planned, investigators should be made aware of their roles pertaining to the LS as early as possible and the contractual conditions agreed.

EU legislation does not foresee ethics committee review of communication to patients after the notification of the end of trial. However, through upload of the LS to the EU Portal, ethics committees concerned will be made aware of the availability of the LS and thus of its content.

According to EU CTR Article 29.6, the trial participant must be informed during the Informed Consent process that a LS will be made available in the EU Database and, to the extent planned, when the LS will become available, potentially also through other distribution channels. For additional recommendations on stakeholder communication, refer to the GLSP Handbook, Section 2.4.

**Patient Involvement in the LS Process**
The contributions from patients should be regarded as valuable input into LS planning, review and dissemination, ensuring the suitability of the LS for patients, trial participants and the general public. Patients can contribute by providing perspectives that may be different than those of researchers and healthcare providers. Patients may also be able to inject important considerations and insights into issues or terminology used in the patient community.

Depending on the input desired from a comprehensive spectrum of the concerned patient population and the availability of resources, the sponsor should consider the most suitable approach to involving one or several patients with different disease stages, ages, and knowledge of clinical research methodology in the process of LS development, review/user testing, translation and/or dissemination. Planning and preparation of this involvement should start as early as possible and well before the end of the trial.

The GLSP recommends that patient experts are invited during LS planning. Development and review of the LS and its dissemination plan can benefit from support from patient experts, patient advocates or patient organisation representatives, while patients or representatives of the public without any familiarity with clinical trials should be selected for the potentially planned user testing of the master LS, where possible. For definition of patient types and additional recommendations on patient involvement in the LS process, refer to Section 2.5 in the GLSP Handbook.

## 3. Development of the Lay Summary

**General Principles**
GLSP supports the suggestion of the EU CT Expert Group on Clinical Trials to provide a short summary as a starting point in the LS and to thank the participants. The LS should be dated.

**Content as Laid Out by the EU CT Expert Group on Clinical Trials**
The EU CTR Annex V lists 10 elements that must be included in the LS. The EU CT Expert Group's Recommendations provide examples of reader-friendly headings, covering the content of all 10 elements. Sponsors must cover all 10 elements listed below but may combine them or change their order.

**Element 1: Clinical trial identification.**

The trial title (as given in the PIS/ICF), protocol number, the EudraCT number, and other identifiers. A simple lay title could be provided[9].

**Element 2: Name and contact details of the sponsor.**

Sponsors may need to establish procedures, specifying how to handle public contacts based on the information provided in the LS. National regulatory guidance and local law may need to be consulted regarding the provision of topics concerning medical information.

**Element 3: General information about the clinical trial.**

In addition to the information recommended by the EU CT Expert Group (including trial rationale, objectives, location, timing), an explanation of the trial design may be helpful. This may include information on the type of randomisation, treatment arms, use of placebo, titration of medication, wash-out periods, and long-term follow up (where appropriate). Simple diagrams may be a helpful way to communicate trial design, particularly where multiple treatment groups/phases are concerned.

**Element 4: Population of subjects (trial participants).**

This should include main demographics and selection criteria. Care should be taken not to inadvertently identify specific individuals, particularly in trials involving rare diseases. Where there are differences in the numbers of randomised and treated trial participants, information should be presented clearly to avoid confusion. As far as possible, the numbers should align with the number of trial participants referred in the results section. Any differences should be explained in a simple way in the relevant section.

**Element 5: Investigational medicinal products used.**

The trial treatments should be named as in the protocol and trial registration. When describing investigational products and comparators, sponsors should not provide promotional information. Repetitive use of compound code names may impair readability. The route of administration should be stated together with the treatment regimen.

**Element 6: Description of adverse reactions and their frequency.**

Adverse reactions must be clearly defined and presented with their frequency. The EU CT Expert Group Recommendations specify that serious adverse reactions should be listed first, followed by other common adverse reactions listed by frequency given in numerical terms and percentages. It should be made clear that these are the results of a single clinical trial. A detailed discussion of safety information in the LS is provided in Section 3.5 of the GLSP Handbook.

**Element 7: Overall results of the clinical trial.**

The LS must include the overall results of the trial. The sponsor must present the main objectives and overall results of the clinical trial[1]. According to the "Clinical Trials Regulation (EU) No 536/2014 DRAFT Questions & Answers" document, this means that the LS should reflect at a minimum the results of the primary

endpoint(s) and potentially also patient-relevant secondary endpoints[10]. Since no broadly accepted definition for "patient-relevant" exists, sponsors may prefer to limit results presentation to the primary endpoint(s). However, if sponsors plan to select and include patient-relevant secondary endpoints, it is recommended that these endpoints are defined according to an established, documented framework for endpoint selection across all the sponsor's trials, ideally as early as trial finalisation but prior to availability of interim results, and no later than database look.

Secondary endpoints may lack statistical power and presenting such endpoints should therefore aim to avoid lay readers placing undue emphasis on these results[6].

Independent of the sponsor's choice on endpoint presentation a reference link to the complete list of outcomes in the scientific Summary of the Clinical Trial Results (Annex IV) in the EU Database should be included in the LS[4].

Additional safety data important to the overall results of the trial should complete the presentation of overall results.

**Element 8: Comments on the outcome of the clinical trial.**

This section should state whether the results are applicable to a specific population and should describe the most important limitations. Sponsors should reinforce that the LS reflects the outcome of one single trial and that other trials may show other results or other outcomes.

**Element 9: Indication if follow-up clinical trials are foreseen.**

Publicly available information about related trials should be provided and sponsors should ensure that the information disclosed is non-promotional. Reference literature should be chosen with caution, providing general sources of information only such as public databases or clinical trial registries. Sponsors may decide to combine the information given on this element with another element, e.g., "comments on outcome."

**Element 10: Indication where additional information could be found.**

This section may provide links to other websites deemed helpful (including industry-based websites and academic websites) or public trial registries. Sponsors need to make sure readers will not unintentionally be exposed to promotional content, or selective presentation of data, via such links.

**Competencies to Enable Good Lay Summary Development**

Depending on available resources, the LS can be prepared by a team or an individual, however, a variety of competencies (knowledge, skills, and attitudes) are helpful to prepare a suitable LS. These are:

- Scientific knowledge
- Familiarity with the reference and source documents (e.g., PIS/ICF, scientific Summary of the Results, CSR, or full set of structured trial results)
- Disease and patient/trial participant population characteristics
- Clinical research methodology
- Terminology and judgement on safety results

- Statistical knowledge
- Lay language communication skills
- Skills for quality control and accuracy checks
- Legal and regulatory knowledge
- Visual and design skills
- Skills to integrate stakeholder validation
- Attitude of willingness to work in a team and dedication to lay communication

For additional recommendations on competencies to enable good lay summary development, refer to Section 3.3 in the GLSP Handbook.

**Writing and Presentation of the LS**

The need to translate complicated messages related to clinical trial results into a language understandable to people with low to average levels of health literacy is a challenge and requires different writing skills than for scientific or regulatory purposes. A fundamental principle when addressing a lay audience is using conversational language. In practice, this means to "write the way you talk" for a given audience.

To attract the attention and comprehension of a heterogeneous lay audience, using everyday conversational language is a pre-requisite. The GLSP recommends helpful principles to apply, e.g.,

- Use short words, sentences, and paragraphs
- Use active rather than passive voice
- Do not use technical or scientific language
- Present medical terms in brackets
- Use neutral, non-promotional language
- Do not use statistical terms
- Apply numeracy principles
- Use words and terms consistently
- Be respectful in your language and apply cultural sensitivity
- Do not use Latin expressions

Practical wording examples are provided in Table **3.2**.

Although LS should be as short as possible, it should be acknowledged that explanations in lay language may make a text longer.

As trial results are mostly presented in numbers, a lay-friendly presentation of numbers is essential in a LS. Health numeracy principles include the use of visuals for interpretation of numbers, whole numbers, and consistency in denominators and units. Percentages should be presented with caution and calculations not left to the reader. Health numeracy principles and practical examples are provided in Table 3.3.

To maximise the chance for preparation of an accessible LS, the following aspects should be taken into consideration:

- Awareness of available guidance and application of practical experience with health numeracy attributes[1,4,6,7]
- Consistent non-promotional language
- Application of available recommendations on text presentation in LS, e.g.,

- Use headings and descriptive sub-headings
- Use adequate white space and black text
- Limit the use of logos and icons but use simple graphs
- Use bold text to add emphasis but do not use underlining, italics, fancy fonts, all CAPS

- Use of suitable graphics: bar graphs for comparison across groups and pie charts for numerical proportions. Infographics and pictorial representation can also be useful.

Paediatric patients focused LS may differ in terms of presentation and style (more illustrations or graphics) to assist children in understanding trial results. Differences in the development of cognitive capabilities in three age groups (≤8, 9-11, 12-17 years) and potential disabilities should be taken into account when preparing the messaging methodology. Narratives, e.g., are often associated with increased recall, ease of comprehension, and shorter reading times. For more information on paediatric LS, refer to the GLSP Handbook Section 3.4 and Appendix 1.

To be readable by people with visual impairment, electronic copies of the LS in PDF format are the most accessible; however, it should be ensured that any security settings of the PDF file do not interfere with the screen reader's ability to convert the on-screen text to speech or Braille. HTML or XML formats may also be used and should be accessible to this population as well. Partially sighted readers benefit from larger fonts and enhanced contrasts. Charts or graphs are not always legible with screen readers and LS should encompass colour-blind peoples' needs. Therefore, a short summary of charts or graphs might be provided.

For additional recommendations on writing and presentation of the Lay Summary, refer to Section 3.4 in the GLSP Handbook.

**Presentation of Safety Information**

The LS author needs to be aware of the differences in presenting safety information in the LS (adverse reactions) and in the Summary of Clinical Trial Results (adverse events). To avoid readers' confusion with side effects presented in the package leaflet (when applicable), the LS should clearly explain the relevance of "side effects" described in the clinical trial. According to EU CTR Annex II 2.1.3; "In determining whether an adverse event is an adverse reaction, consideration shall be given to whether there is a reasonable possibility of establishing a causal relationship between the event and the investigational medicinal product based on an analysis of available evidence".

If the trial has safety information investigation as the primary objective, this result should be presented in the overall trial results section, and adverse reactions should be presented in a separate, dedicated section. For additional recommendations on presentation of safety information, refer to Section 3.5 in the GLSP Handbook.

In paediatric trials, explanatory and graphic efforts should be made to explain the safety results to patients as of the age of 12 years and the content should be adapted to their cognitive capabilities.

**Layout and Design of Lay Summaries**

Layout and design are as important as the wording in a LS. Appearance and attractiveness of the LS have a strong impact on whether it may be read at all. The use of headings and descriptive sub-headings, of adequate white space and reduction of unnecessary imagery like logos can help the lay summary appear reader-friendly and accessible. Choice of columns, page breaks and colours can help provide a more attractive structure of the pages in a LS. Further points to consider are presented in Table 3.6 in the GLSP Handbook.

Well-chosen and clearly designed graphics or visuals can enhance comprehension of the text[4]. Graphics designed with the audience in mind can be powerful in supporting and facilitating the processing of numbers in the text. In general, bar graphs are recommended for comparison across groups and pie charts for numerical proportions. Infographics or pictorial representation can also be useful. Figure 3.2 offers examples of how numbers can be presented graphically. Section 3.6 in the GLSP Handbook provides further recommendations.

**Review and User Testing of the LS**

A LS review by different stakeholders involved in the clinical trial (patient(s), medical monitor, statistician, etc.) is recommended to ensure completeness and accuracy of the LS in all aspects. In resource-limited settings this should at least be envisaged for the LS template.

While not mandatory, it is good practice to user test the LS with individuals who are not involved in the trial and unfamiliar with clinical research methodology. Clear instructions on tasks expected from the test persons and a well-prepared feedback process are essential. For additional recommendations on review and user testing of the LS, refer to Section 3.7 in the GLSP Handbook.

## 4. Translation of the Lay Summary

Availability of a LS in patients' native language is an important element of fair access to information. While the EU CTR does not request translations, the EU CT Expert Group Recommendations suggest that as a minimum, the LS should be provided in the local official language(s) of each of the countries where the trial took place, matching the languages employed in the Patient Information Sheet/Informed Consent Form[4] ("PIS/ICF"). Where resources allow, sponsors should consider preparing an English version if the trial did not include the Republic of Ireland or Malta to allow greater accessibility across the EU and globally.

Thorough review of the LS before translation, a well-managed translation process, and use of glossaries and pre-defined terminology are helpful for achieving successful translation of LS. Technology and linguistic skills could be leveraged. Even with limited resources or budget, proactive planning and management will facilitate the quality, timeliness, and adequacy of LS to the target audience.

The translated LS versions should be made available as soon as possible, ideally in parallel to the release of the source version, to ensure fair availability of information to all patients and the public.

For additional recommendations on translation of the lay summary and a step-by-step translation process, refer to Section 4 in the GLSP Handbook and Table 7.7 in Appendix 1.

## 5. Dissemination of the Lay Summary

Sponsors must upload the LS to the EU Database via the EU Portal as required by EU CTR. The EU Expert Group on Clinical Trials' preferred additional option to the EU Portal is direct dissemination to trial participants. In the interest of transparency, sponsors may wish to disseminate the LS further.

Delivery of the LS outside of the EU mandate needs to be done in compliance with local laws, restrictions, and standards.

The sponsor's LS dissemination strategy can consist of a direct approach that for example involves sharing of printed LS with trial participants by the investigator and/or an indirect, approach through unrestricted, open communication channels such as publicly available websites.

Whichever suitable dissemination approach is selected, the sponsor policy should ensure dissemination of all sponsor's LS, regardless of outcome and in a non-promotional manner. Such LS dissemination policy should describe the principles, planning, strategies, and communication of the LS dissemination process and apply across all trials covered under the policy, regardless of outcome. In addition, such policy should respect local laws, standards, and restrictions. The respective strategy should be decided, ideally as early as the initial trial approval application but not later than before database lock.

In cases where dissemination pathways other than the EU Portal and Database are planned, sponsors should consider including a general statement in the PIS/ICF that a LS will be prepared and disseminated per internal policy standards and local laws. In addition, the PIS/ICF should contain sufficient details to properly inform trial participants of where and when to expect the LS.

Irrespective of the strategy implemented, sponsors should weigh the benefits against the risks of the various dissemination methods and consider partnering with the investigator to ensure a proper results communication. The best fit should be based on a proactive assessment of aspects such as logistics, timing, technology, costs, privacy, risk of miscommunication and vulnerability of the trial population.

Dissemination of LS beyond the EU Portal and Database requires consideration of the ethical, legal, and regulatory obligations with regard to results communication, as well as a profound understanding of advantages and concerns of different dissemination strategies. Detailed considerations and recommendations on dissemination of LS are provided in Section 5 in the GLSP Handbook.

# GLSP Handbook

## 1. Introduction

The importance of consistently and reliably presenting the results of all clinical trials in easily understandable language to the public and in particular to trial participants, has also been recognised by global stakeholders involved in patient engagement[11,12].

The EU Clinical Trial Regulation ("EU CTR") 536/2014, Article 37 requires the public dissemination of trial results presented in lay language through the EU Database, a core element of the EU "Clinical Trials Information System" ("CTIS"), at the time of availability of the scientific Summary of Clinical Trial Results[1].

Lay summaries ("LS") can serve multiple purposes ensuring transparency, knowledge sharing and trust building towards clinical research benefiting current and future clinical trial participants. However, the practice of patient involvement in the lay summary process with the purpose of supporting sponsors' efforts to better meet patients' and the public's needs has not yet been consistently established. Sharing and presenting best practices among different stakeholders should facilitate patient engagement as well as the development and dissemination of LS.

### 1.1 Purpose & Scope of the Good Lay Summary Practice

Article 37 of the EU Clinical Trial Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use requests the sponsor to prepare a summary of clinical trial results written in a manner that is understandable to laypersons for interventionalclinical trials with medicinal products in adult and paediatric populations conducted in the EU/EEA[1]. The content required in such lay summary is listed in Annex V of the EU CTR.

The EU CTR does not call for LS on non-interventional studies or medical device trials. However, the recommendations provided in the GLSP can be useful in the preparation of LS for such studies, albeit considering that some EU CTR-defined elements may not apply, e.g., the required timelines for preparation of LS.

- **The EU CTR defines a clinical trial as a "clinical study which fulfils any of the following conditions:**

| | | |
|---|---|---|
| **(a)** the assignment of the subject to a particular therapeutic strategy is decided in advance and does not fall within normal clinical practice of the Member State concerned, | **(b)** the decision to prescribe the investigational medicinal product is taken together with the decision to include the subject in the clinical study, or | **(c)** diagnostic or monitoring procedures in addition to normal clinical practice are applied to the subjects." |

Suggestions for structure and presentation of the content of lay summaries are provided in the "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: "Summaries of Clinical Trial Results for Laypersons"[4] ("EU CT Expert Group Recommendations").

This Good Lay Summary practice ("GLSP") expands on these recommendations and takes into consideration the recommendations from TransCelerate BioPharma on "Layperson Summaries of Clinical Trials"[6] and from the Multi-Regional Clinical Trials (MRCT) "Draft FDA Guidance on Provision of Plain Language Summaries"[7].

The GLSP Handbook provides detailed recommendations for best practice in terms of planning, preparation, translation, and dissemination of high-quality lay language summaries of results from clinical trials with medicinal products:

- The GLSP provides recommendations for building an LS infrastructure and processes with the aim to enable all sponsors to generate and disseminate objective and understandable information on clinical trial results.
- The GLSP contains recommendations on how to enable patient engagement throughout the LS process although it is acknowledged that sponsors' resource and infrastructure constraints can limit a routine involvement of patients in the different steps.
- The GLSP gives recommendations for LS dissemination aiming to inform trial participants and the general public to ensure fair access to information for all.
- The GLSP recognises and addresses the need for specific skills and strategies for LS on paediatric trials and highlights the limited experience available so far.
- LS recommendations in this document apply to aggregate clinical trial results only; therefore, return of individual patient-level data to a given trial participant is out of scope.
- Although some shared principles may apply, other types of result information to the lay audience, such as plain language summaries of journal publications and conference abstracts, are out of scope.

**1.2 Target Audience for the Good Lay Summary Practice**

The target audience for the GLSP constitutes professionals who have been assigned the responsibility to plan, develop, review, translate, disseminate and/or upload LS to the EU Database, as well as stakeholders who wish to offer LS outside of the mandatory EU CTR requirements.

### 1.3 Target Audience for the Lay Summary

The target audience for Lay Summaries are "laypersons," which is the term referenced in the EU CTR, Article 37. The EU CT Expert Group also indicates that a primary audience for the LS is expected to be the general public[4]. It is a common conception that the actual audience of LS concentrates on people affected by disease, living with a condition or otherwise with an interest in clinical research results.

**Target audiences may therefore primarily include:**

- Participants/people who took part in the clinical trial or care for a trial participant.
- People from patient organisations who communicate with patients within specific disease areas, potentially with limited access to the Internet.
- Individual patients, their caregivers, relatives, friends or generally people who are interested in research results on treatments.

> **!** Although the EU CTR does not define the term "layperson", a definition is offered in the new EU regulation on medical devices "Regulation (EU) 2017/745 of the European Parliament and of the Council" (commonly referred to as the EU MDR). The EU MDR defines a layperson as "an individual who does not have formal education in a relevant field of healthcare or medical discipline".

### 1.4 Terminology and Language

Different terms are used for LS in different countries and among organisations, research institutions and sponsors. The GLSP acknowledges that the EU CTR also refers to "layperson summary" but for consistency, the terms "lay summary" and "LS" are adopted and applied throughout this document. Other terms applied include, but are not limited to, "Plain Language Summary", "Trial Results Summary" and "Simple Language Summaries".

To avoid confusion, sponsors need to distinguish between the different types of "summaries" of clinical trial results to be prepared:

- A scientific "Summary of the Results of the Clinical Trial" to be uploaded to the CTIS according to Article 37 of the EU CTR (specified in Annex IV).
- A "Summary of the Results of the Clinical Trial for Laypersons" ("lay summary") in a language understandable for laypersons according to Article 37 of the EU CTR (specified in Annex V).
- A summary of the Clinical Study Report according to the ICH E3 guideline ("Synopsis")[13].
- A summary of the clinical trial's publication ("Abstract"). This may be accompanied by a "Plain Language Summary".

As for the term "lay language", no globally agreed definition exists, however, the following definition is offered for the term "plain language" and is adopted in the GLSP:

"A communication is in plain language if its wording, structure, and design are so clear that the audience can easily find what they need, understand what they find, and use that information"[5].

It should become clear from the recommendations in this GLSP that plain or lay language is not only about how written content is understood by non-scientists or lay persons but also about the structure, organisation and visual means applied in the LS communication process.

## 2. Planning of the Lay Summary

Planning of the LS should commence during protocol development or even at preparation of a research proposal and related budget. Careful and proactive planning is strongly encouraged to ensure timely delivery of a high-quality and compliant LS.

### 2.1 Timing of the Lay Summary

According to EU CTR, Article 37, the LS must be submitted to the EU Database no later than 12 months from the protocol-defined end of the clinical trial in adults,6 months in paediatric studies, and up to 30 months for non-therapeutic Phase 1 trials. More detailed rules about the publication of clinical trial results can be found in "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"[3]. If the summary of results cannot be reported within these timelines for scientific reasons, the summary of results shall be submitted as soon as possible. In that case the approved protocol shall specify when the results are going to be submitted. Deferral of the publication timelines can be requested for approval by the EU Member States concerned either in the initial trial application or as a substantial modification.

This requirement applies in all concerned EU Member States irrespective of the trial outcome and is consistent with the timing of the Summary of the Clinical Trial Results submission.

Early in the trial, LS planning should be aligned with the preparation of the Patient Information Sheet (PIS) and the Informed Consent Form (ICF) since these documents partly share content and readership. A coordinated approach across these documents can reduce duplication of effort or discrepant use of lay language terminology. If the documents are prepared by different writing teams, planning and collaboration between these teams should be enabled.

In line with the EU Expert Group on Clinical Trials Recommendations, a well written LS would normally be accessible by young people from the age of 12 years upwards[4]. Sponsors of paediatric studies are encouraged to consider developing a child-focused version of the LS for younger trial participants in addition to the obligatory version for the parents or legal representatives[14], particularly where they have already developed an Assent for the paediatric patient's information about trial participation.

The dissemination of LS should be coordinated with the publication plans for the clinical trial in general but also with the regulatory requirements for posting trial results on databases such as the EU Clinical Trials Register[8], the EU Portal and Database (mandatory upon implementation of the EU CTR), or others such as ClinicalTrials.gov. For multinational and multicentre trials, LS dissemination should be

coordinated across all trial sites, and if distribution is planned via investigational sites access to information for all participating patients should be considered in the interest of fairness.

Finally, proactive planning of translations is important for successful results communication in the local languages of patients participating in global, regional and local trials matching the languages employed in the PIS and ICF.

**2.2 Lay Summary Production Planning**

The LS production process requires early and efficient planning to enable all required contributions from different stakeholders in time for meeting the LS completion and submission in line with the respective legal obligations.

LS development and dissemination approaches may differ, e.g., according to the type of clinical trial or resource capacity of the sponsor. Sponsors should develop a Standard Operating Procedure ("SOP") on their organisation's LS planning, development, review, translation, and dissemination process.

The EU Portal will accept LS to be uploaded in a PDF file format. This entails materials suitable for print which include text and figures as well as cartoons but excludes videos and animations at the current stage of the technical system. Recommendations in this GLSP are focused mainly on written content and cartoons, e.g., for paediatric trial result LS, to convey storytelling that would be compliant under the EU CTR. However, sponsors are free to develop videos and animations in their LS for separate dissemination.

In line with the EU Expert Group on Clinical Trials Recommendations[4], use of a LS template can aid efficient and consistent preparation of LS. It may be helpful to pre-fill the template with general information on the trial and the endpoint presentation structure, and hence create an outline 'shell' document, in advance of database upload and trial results availability. Once final trial data are available, a person experienced in clinical trial result presentation and lay language should prepare the LS draft. This draft should be reviewed by the sponsor's trial team which is familiar with both the trial conduct and the results and which will also review the Summary of Clinical Trial Results, the Clinical Study Report (CSR) or full set of structured study results and/or publication. According to the sponsor's SOP, other process stakeholders may be involved in the review process, e.g., scientific/statistical experts, patient representatives, legal and medical communication experts and/or investigators. Quality control on the final LS should be carried out by other stakeholder(s) than the LS author to ensure the accuracy of the content against the source data. At any review step, tailored checklists and review instructions will provide helpful guidance to reviewers. Should the final version of the CSR not yet be available at the time the LS writing starts, advanced draft versions may be used. However, in such cases the content of the final LS should be checked against the final version of the CSR or full set of structured study results. In addition, final consistency checks between the scientific Summary of the Results of the Clinical Trial and the LS need to be ensured.

Some countries may have national requirements for local posting of LS, and – if outside the EU - also may have different specifications for LS content and format. Thus, sponsors need to track local requirements to ensure regulatory compliance. This will also apply to new sites from additional countries joining after trial initiation. It will generally be the intention to generate a single master version of the LS for all countries. In cases in which country-specific requirements cannot be

accommodated in a single version of the LS, sponsors will need to decide on the most appropriate approach.

At the time of LS finalisation, it is recommended that the sponsor's content owner (e.g., the responsible physician/medical officer for the trial) document their approval of the LS. Having finalised and "locked" the LS content in source language, the document can then be translated and disseminated as described in Sections 4 and 5, respectively.

### 2.2.1 Endpoint Presentation

The EU CTR requires the LS to include the main objectives and overall results of the trial[1]. The LS should therefore reflect at a minimum the results of the primary endpoint(s) and potentially patient-relevant secondary endpoints[4]. As no broadly accepted definition for "patient-relevant" endpoints exists and in order to keep the LS short, sponsors may prefer to limit result presentation to the primary endpoint(s).

Independent of the sponsor's choice on endpoint presentation, a reference link to the complete list of outcomes in the scientific Summary of the Clinical Trial Results in the EU Database should be included in the LS.

Presenting tertiary/exploratory endpoint results in the LS is generally discouraged.

### 2.2.2 Secondary Endpoint Inclusion

For most trials, a comprehensive discussion of all results would neither be feasible within a concise LS nor helpful to a non-scientific audience due to the volume and complexity of the information. The EU Expert Group on Clinical Trials Recommendations propose to limit results presentation to the primary endpoint(s) and results by trial arm which were pre-specified by the statistical analysis plan. However, secondary endpoints may be of interest to the general public, particularly to trial participants or patients represented in the trial population. For some studies, secondary endpoints may be confirmatory for efficacy claims for product indications. Additionally, certain secondary endpoints involve invasive or time-consuming or otherwise burdensome procedures for trial participants who may want to know the results. Since relevance is subjective, patient-relevant secondary endpoint inclusion inevitably involves a selective process. In the absence of a broadly accepted definition of the term "patient-relevant", selectively presenting secondary endpoint information could put sponsors at risk of being perceived as intentionally promoting or "cherry-picking". Consequently, an influence of trial results on the selection of secondary endpoints should be avoided. To demonstrate the absence of promotional intent, a sponsor policy or SOP that defines the sponsor's strategy on outcomes and endpoint selection and presentation across all trials' LS should be implemented before interim or final trial results are available[15].

Secondary endpoints may lack statistical power, and thus could be misleading to non-scientists and result in readers placing undue emphasis on certain results[6]. In such instances, the LS should help the reader understand the uncertainties in the results of statistically non-significant secondary endpoints.

Further considerations are presented in Appendix 1, Section 7.1.2.

### 2.2.3 Interim Results

The EU Portal enables upload of one LS, namely at the end of the trial. It allows for uploading interim results as pre-specified in the protocol but does not foresee this option for a related LS.

Should the protocol foresee an interim analysis with upload of the results to the publicly available EU Portal and the sponsor plan the preparation of a LS, such LS availability and planned dissemination should be presented in the PIS/ICF. Potentially available local restrictions to such dissemination should be respected.

### 2.2.4 Complex Clinical Trials

For the purposes of this document, trials are defined as complex if they contain separate parts that could constitute individual clinical trials, or if they are characterised by extensive prospective adaptations[16]. For these complex designs, careful planning of the results-sharing strategy is imperative. This should be addressed during protocol development and reviewed during amendments.

Complex trials can be submitted as a single trial, which may have a master protocol and multiple sub-protocols, or as separate linked trials. As such, complex trials, including basket, umbrella and platform designs, present challenges for data transparency planning[15]. From a trial participant's or public perspective, timely availability of information on sub-protocol results is needed.

The EU Expert Group on Clinical Trials recognises that some arms in multi-arm trials may close and publish results long before the overall trial closes. Where there are extended follow-up periods, with different completion times between cohorts, life expectancy of participants may be a consideration. For these complex trial designs, the end of trial definition(s) applicable to individual parts if they were submitted as a single protocol/CTA and the result-sharing strategy should be carefully planned. Planning should foresee that the chosen approach will be addressed in the PIS/ICF and reviewed during amendments. Considerations on planning the timing of individual LS within a complex design are provided in Section 7.1.3 in Appendix 1.

## 2.3 Cost Implications

Generally, but especially for resource-limited sponsors from academia, charity, or Small and Medium-sized Enterprises (SME), planning of the process and resources required for production and dissemination of a LS should begin with budgeting at the time when a research proposal for a clinical trial is submitted to a funding source.

The major costs will account for staff or contractors for the production and translation of the lay summary. Sponsors who decide to provide LS beyond dissemination through the EU Database will need to plan for additional translation and/or dissemination costs.

Additionally, remuneration for the functions involved in LS generation, including patient advisors and reviewers should be taken into account during planning. If appropriate, representative patient involvement in relation to the development of the LS may require additional funding. For additional information, see also Appendix 1.

It should be noted that most funding bodies do not foresee budget allocation for LS preparation. Moreover, most funding bodies require eligible costs to have been incurred during the funding period. As the LS may only be due after the end of the project and thus the funding period, it may be impossible to secure funds for LS simultaneously with the main part of the trial. It may be prudent to check the policy of the funding body in advance.

### 2.4 Stakeholder Communication

#### 2.4.1 Investigators

If direct LS dissemination to the trial participants through investigators is planned, the investigators should be made aware of this additional task as early as possible. The timing, relevance, and planned process of their communication with the participant on the trial results should be explained during the site preparation period. Potential logistical challenges of access to the trial participants for LS dissemination months or years after the end of his/her trial participation should be identified and mitigated. In case investigators are actively involved in the dissemination, it should be considered to include such responsibilities in the investigator agreement[6].

#### 2.4.2 Ethics Committees

EU legislation does not mandate ethics committee review of communication to trial participants after the end-of-trial notification. However, through upload of the LS to the EU Portal, the ethics committees concerned will be made aware of the availability of the LS and thus of its content. The GLSP recommends that sponsors generally mention their planned LS dissemination approach in the PIS/ICF.

In cases where sponsors choose to disseminate LS beyond the EU/EEA territories, it should be noted that different IECs/IRBs may have varying requirements. Compliance with local restrictions and standards in such cases is the responsibility of the sponsor.

#### 2.4.3. Trial Participants

According to EU CTR Article 29.6 the trial participant must be informed that a LS will be made available in the EU Database and, to the extent planned, when the LS will become available, potentially also through other distribution channels. This information must be provided as part of the Informed Consent process. Including information in the PIS/ICF[1,6] on how and when trial participants can access the trial results is good practice and therefore encouraged. In a short trial, it may suffice to make trial participants aware of the forthcoming LS via information contained in the PIS/ICF. However, with a longer trial, it may be necessary to remind the trial participants before the end of the overall trial about the availability of a LS and further information in the EU Database; e.g., at the individual participant's last treatment visit (for mortality trials) and/or last visit.

### 2.5 Patient Involvement in the LS Process

Contributions from patients should be regarded as valuable input into LS planning, review and dissemination ensuring the suitability of the LS for patients, trial participants and the general public. Patients can contribute by providing perspectives that may be different than those of researchers and healthcare providers. Patients may also be able to inject important considerations and insights into issues or terminology used in the patient community.

Depending on the patient input desired from a comprehensive spectrum of the intended patient population and the availability of resources, the sponsor should consider involving one or several patients with different disease stages, age and knowledge of the clinical research methodology in the process of LS planning, development, translation and/or dissemination. Also, the EU Expert Group on Clinical Trials Recommendations encourage sponsors to "involve patients, patient representatives/experts in the development and/or review of the summary to assess comprehension and the value of the information provided"[4]. It is important to bear in mind that involving individual patients in LS activities does not ensure patient representativeness.

In order to clarify terminology applied for potential patient interaction presented in the GLSP, the following distinctions are made, as defined in the Innovative Medicines Initiative (IMI) EUPATI project[12].

| | |
|---|---|
| **Individual patients** | Individual patients are persons with personal experience of living with a disease. They may or may not have technical knowledge in research and development (R&D) or regulatory processes, but their main role is to contribute with their subjective disease and treatment experience. |
| **Carers** | Carers include persons supporting individual patients, such as family members, paid- or volunteer helpers. |
| **Patient advocates** | Patient advocates are persons who have the insight and experience in supporting a larger population of patients living with a specific disease. They may or may not be affiliated with an organisation. |
| **Patient organisation representatives** | Patient organisation representatives are persons who are mandated to represent and express the collective views of a patient organisation on a specific issue or disease area. |
| **Patient experts** | Patient experts, in addition to disease-specific expertise, have the technical knowledge in R&D and/or regulatory affairs through training or experience, for example EUPATI Fellows who have been trained by EUPATI on the full spectrum of medicines R&D. |

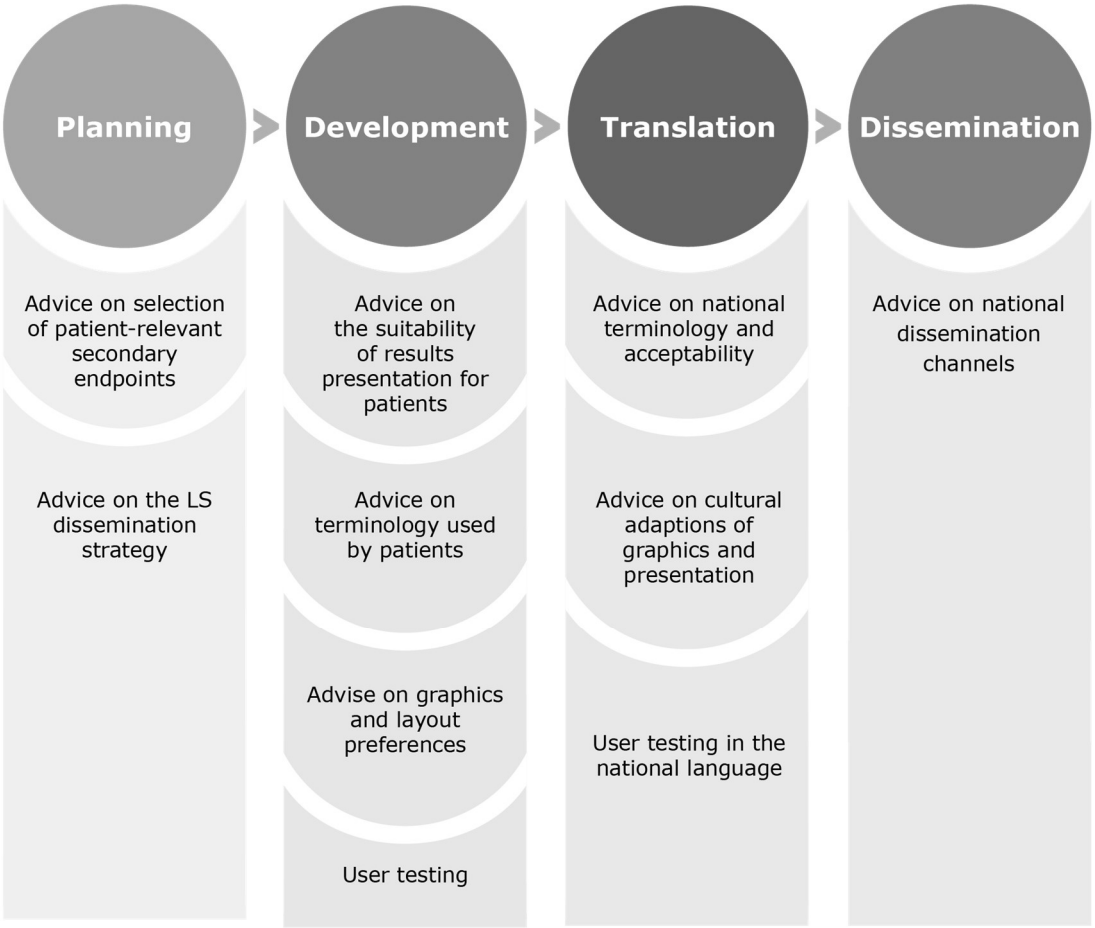
Table 2.1: Characteristics of Patients in Patient Engagement Activities

### 2.5.1 Timing and Type of Patient Involvement

The time frame is short between the end of the trial and the requested submission of the LS to the EU Portal. Seeking various input and joint opinion building takes time and resources. It is therefore particularly important to not only plan and prepare the development of the LS well in advance of the end of the trial but also to enable the patient advice, review, and user testing in due time. Early definition of the contributions desired, their timing and the level of disease and clinical trial methodology knowledge required can help reduce the time pressure and resource needs at the end of the trial. This is particularly relevant in clinical trials with fixed budgets where budget and resource deficits become most obvious towards the end of the trial.

Tasks that can be performed by patients with the respective level of expertise can be relevant in all four steps of the LS process, as illustrated in Figure **2.1** below.

Figure 2.1. Patient Involvement during LS steps




### 2.5.2 Planning

Patients' input can bring insights into a most suitable approach to the presentation of secondary endpoint results and respective selection of patient-relevant secondary endpoints. It may be useful to integrate the perspectives of both recently diagnosed persons, who may know little about the disease, and persons who have lived with the disease for a long time and experienced its different stages, treatments, and symptoms. It may also be interesting to obtain insights of people who indirectly live with the disease, such as informal caregivers or therapists interacting regularly with the patients. Patients, patient experts or patient organisations may in addition be able to contribute to the planning of a LS dissemination strategy beyond the CTIS route if the sponsor decides to do additional direct or indirect LS dissemination. Also, patient co-authorship of the LS is an option that is currently being explored.

### 2.5.3 Development

LS development can benefit from the patients' view on LS layout and results presentation taking into consideration the needs, interests, and potential physical and/or mental handicaps of the respective patient population. Review of the LS requires disease and a certain level of clinical research methodology experience. Patient experts, patient advocates and patient organisation representatives bring a solid knowledge about the patient community, their needs, and preferences. They may be able

to identify content and terminology which are potentially unclear, misleading, or which sound promotional. In addition, they may help develop alternative language recognised within the patient community. One or several patient representatives may perform the initial review of the LS.

Patient experts, advocates and patient organisation representatives represent a wide demographic mapping and may be well educated in clinical trial aspects without having the expertise to provide valuable feedback on the use and effectiveness of lay language. When performing review with patient experts, it is thus important not to preclude subsequent user testing of readability and understandability by patients who are not familiar with clinical trials or representatives of the public who do not have scientific insights.

It is recommended that patient- and public representatives who act as readability and understandability test persons do not have prior insights or knowledge of the clinical trial and that they represent various educational backgrounds, literature experience, age and gender, regardless of whether they are patients or represent the general public.

#### 2.5.4 Translation

When LS are translated into local languages, sponsors should consider user testing to confirm readability and understandability by native-language patients or representatives of the public. Consulting patients within the respective disease community in all relevant countries can offer valuable insight into any national terminology and cultural expressions that may not otherwise be identified during usability testing.

#### 2.5.5 Dissemination

Patient experts, patient advocates and patient organisation representatives can bring valuable input on local dissemination which may be subject to cultural practices, norms or different acceptability levels across different channels of communication. All dissemination methods may not be appropriate or effective in all countries or in all disease areas and age groups. Consulting patient representatives with local insights can help avoid ineffective and inappropriate dissemination efforts.

Additional considerations for planning patient involvement are discussed in Appendix 1, Section 7.1.4 - 7.1.7.

## 3. Development of the Lay Summary

This step focuses on the content of LS as defined in the EU CTR, Annex V, and as detailed in the Recommendations of the EU CT Expert Group on Clinical Trials for the implementation of EU CTR 536/2014[1,4].

### 3.1 General Principles

As the intended audience of the LS differs from that of the scientific Summary of the Results of the Clinical Trial, the amount of information in the LS should be reduced with focus on the elements relevant for trial participants and the public. Although not required by the EU CTR, a short abstract summarising the content of the LS is suggested by the EU Expert Group on Clinical Trials Recommendations[4].

In addition to the content that must be included according to the EU CTR, the GLSP encourages sponsors to thank trial participants for their contribution in the trial within the first paragraphs of the LS.

The LS should be dated (e.g., with the date of sponsor's approval), and it should be made clear that information disclosed in the LS is current at that time. It is strongly encouraged that this principle is adopted for all LS versions including any LS based on interim results and all translated versions into local languages.

### 3.2 Content as Laid Out by the EU Expert Group on Clinical Trials

The EU CTR Annex V lists the below 10 elements that must be included in the LS. The EU CT Expert Group on Clinical Trials provides examples of reader-friendly headings, covering the content of all 10 elements. Sponsors must cover all 10 elements but may combine them or change their order[4]. The headings below are identical to the headings in Annex V and the EU CT Expert Group offers advice on each element.

**Element 1: Clinical trial identification.**

The trial title (as given in the PIS/ICF), protocol number, the EudraCT number, and other identifiers. A simple lay title could be provided[9].

**Element 2: Name and contact details of the sponsor.**

Sponsors may need to establish procedures, specifying how to handle public contacts based on the information provided in the LS. National regulatory guidance and local law may need to be consulted regarding the provision of topics concerning medical information.

**Element 3: General information about the clinical trial.**

In addition to the information recommended by the EU CT Expert Group (including trial rationale, objectives, location, timing), an explanation of the trial design may be helpful.

This may include information on the type of randomisation, treatment arms, use of placebo, titration of medication, wash-out periods, and long-term follow up (where appropriate). Simple diagrams may be a helpful way to communicate trial design, particularly where multiple treatment groups/phases are concerned.

**Element 4: Population of subjects (trial participants).**

This should include main demographics and selection criteria. Care should be taken not to inadvertently identify specific individuals, particularly in trials involving rare diseases. Where there are differences in the numbers of randomised and treated trial participants, information should be presented clearly to avoid confusion. As far as possible, the numbers should align with the number of trial participants referred in the results section. Any differences should be explained in a simple way in the relevant section.

**Element 5: Investigational medicinal products used.**

The trial treatments should be named as in the protocol and trial registration. When describing investigational products and comparators, sponsors should not provide promotional information. Repetitive use of compound code names may impair readability. The route of administration should be stated together with the treatment regimen.

**Element 6: Description of adverse reactions and their frequency.**

Adverse reactions must be clearly defined and presented with their frequency. The EU CT Expert Group Recommendations specify that serious adverse reactions should be listed first, followed by other common adverse reactions listed by frequency given in numerical terms and percentages. It should be made clear that these are the results ofa single clinical trial. A detailed discussion of safety information in the LS is provided in Section **3.5** of the GLSP Handbook.

**Element 7: Overall results of the clinical trial.**

The LS must include the overall results of the trial. The sponsor must present the main objectives and overall results of the clinical trial[1]. According to the "Clinical Trials Regulation (EU) No 536/2014 DRAFT Questions & Answers" document, this means that the LS should reflect at a minimum the results ofthe primary endpoint(s) and potentially also patient-relevant secondary endpoints[10]. Since no broadly accepted definition for "patient-relevant" exists, sponsors may prefer to limit results presentation to the primary endpoint(s). However, if sponsors plan to select and include patient-relevant secondary endpoints, it is recommended that these endpoints are defined according to an established, documented framework for endpoint selection across all the sponsor's trials, ideally as early as trial finalisation but prior to availability of interim results, and no later than database look.

Secondary endpoints may lack statistical power and presenting such endpoints should therefore aim to avoid lay readers placing undue emphasis on these results[6].

Independent of the sponsor's choice on endpoint presentation a reference link to the complete list of outcomes in the scientific Summary of the Clinical Trial Results (Annex IV) in the EU Database should be included in the LS[4].

Additional safety data important to the overall results of the trial should complete the presentation of overall results.

**Element 8: Comments on the outcome of the clinical trial.**

This section should state whether the results are applicable to a specific population and should describe the most important limitations. Sponsors should reinforce that the LS reflects the outcome of one single trial and that other trials may show other resultsor other outcomes.

**Element 9: Indication if follow-up clinical trials are foreseen.**

Publicly available information about related trials should be provided and sponsors should ensure that the information disclosed is non-promotional. Reference literature should be chosen with caution, providing general sources of information only such as public databases or clinical trial registries. Sponsors may decide to combine the information given on this element with another element, e.g., "comments on outcome."

**Element 10: Indication where additional information could be found.**

This section may provide links to other websites deemed helpful (including industry-based websites and academic websites) or public trial registries. Sponsors need to make sure readers will not unintentionally be exposed to promotional content, or selective presentation of data, via such links.

### 3.3 Competencies to Enable Good Lay Summary Development

Developing LS requires insights and skills into writing for a general audience, and a fundamentally different approach to that of medical writing for regulatory purposes or a technical or scientific readership. A variety of competencies is needed for an optimal LS process. The term “competency” means possession of specific knowledge, skills and attitudes. Ideally, all know-how referenced in Table 3.1 should be available in the LS development team with the proficiency recommended there. However, depending on the setting and context, the different skills and the resulting roles may either be filled by individual specialists or by people with more general skill sets who are competent in performing the tasks required or willing to acquire the skills needed. Should a LS team realise that certain capabilities are underrepresented, it may be able to fill any such gaps from external resources. Where resource setting allows involving a LS development team, collaboration is key to successful LS writing. The finalisation of a LS needs discussion and alignment across many expert domains.

Table 3.1: Summary of Competencies Enabling Good Lay Summary Development

| Competency | Level |
|---|---|
| **Scientific knowledge** | |
| General knowledge of clinical trials and clinical research (phases, etc.) | **Intermediate** |
| Knowledge about the disease | **Intermediate** |
| Knowledge about the trial intervention (its clinical background and development) | **Intermediate** |
| Knowledge about clinical research methodology | **Intermediate** |
| Knowledge about reporting of safety data in clinical study reports (CSRs) and other sources | **Intermediate** |
| Knowledge about biomedical statistics | **Basic** |
| **Communication skills** | |
| Knowledge about the language LS is being written in | **Advanced** |
| Experience in writing for lay audiences | **Advanced** |
| Knowledge about how to avoid bias in communicating trial results | **Intermediate** |
| Writing and editing skills | **Advanced** |
| Knowledge of plain language/health literacy principles | **Advanced** |
| **Translation skills and ability to translate into lay language in the target language** | **Advanced** |
| **Knowledge of existing guidance for LS** | **Advanced** |
| **Ability to transfer statistical results into lay language** | **Intermediate** |
| **Quality control skills/knowledge** | **Basic** |
| **Visual design skills** | **Intermediate** |
| Good scientific graphic design principles | **Intermediate** |
| Accessibility principles (e.g. for people with visual impairments) | **Intermediate** |
| **Legal/compliance knowledge** | **Basic** |
| **Knowledge of the applicable regulations (e.g. EU CTR)** | **Advanced** |
| **Knowledge about validating the LS with users ("user testing")** | **Intermediate** |
| **Knowledge about patient involvement in advising on trial design and patient-facing material, including patient information documents and the LS** | **Advanced** |

### 3.3.1 Scientific Knowledge

To develop a LS, the writer or writing team needs to understand the purpose of the trial, its background, the population, and the medical intervention studied as well as the efficacy and safety results of the trial. In other words, s/he needs scientific knowledge, knowledge about clinical research in general and about the trial being summarised and/or knowledge about the disease. In addition, a good understanding of medical and clinical research terminology is important to prevent misinterpretation of

the scientific content. These skills also apply to some extent to translators who are responsible for translating the LS from one language into another language(s).

### 3.3.2 Familiarity with Source Documents

The CSR or full set of structured results describe the rationale, objective(s), and hypothesis and discuss the results and the conclusions of the trial. The PIS/ICF, which introduces the trial to potential trial participants in lay language may also be important references. Together, these documents serve as source documents for the scientific Summary of Clinical Trial results and the LS, and the writer or writing team therefore need to be able to interpret and use them.

Good LS communication practice requires that the data presented are consistent with the data in the source documents. Should the final version of the above-mentioned source documents not yet be available at the time the LS writing starts, an advanced draft CSR version may be used as a source. However, in such cases the content of the final LS should be checked against the final CSR or full set of structured results and consistency verified against the scientific Summary of Clinical Trial results.

### 3.3.3 Disease and Patient/Trial Participant Population

To present medical information in a lay-friendly manner, the writer or writing team should demonstrate a good understanding of the disease. Scientific knowledge will in addition facilitate the interpretation of the disease characteristics while critical scientific thinking is important for understanding the rationale for conducting the trial and how the trial answers the research questions.

A clinical trial protocol contains many inclusion and exclusion criteria, written in technical-scientific language. For the authoring of a LS, it is important to be able to interpret the selection criteria and their implications for the trial population. Knowledge about the background of the medical intervention, about basic pharmacology, and drug development is useful when having to render into lay language why the investigational medicinal product was tested alone, or in combination with another medication.

### 3.3.4 Clinical Research Methodology

Most clinical trials are performed to investigate the efficacy or the pharmacokinetic and/or pharmacodynamic properties and safety of the medicine. Different methods to increase objectivity of the investigation and to reduce potential bias of the involved stakeholders are applied, e.g., active comparator or placebo, randomisation, blinding, etc. These are difficult concepts that need to be explained to the LS readers in lay language as the basis for their understanding of the relevance of the results. The EU Expert Group on Clinical Trials Recommendations[4] provides helpful suggestions for phrasing of these concepts. The LS writer needs to have a good understanding of the significance of the methodological aspects and the relevance of potential deviations or changes during trial conduct to be able to adequately communicate the endpoint results.

### 3.3.5 Safety of the Intervention (Drug, Surgery, Other) under Investigation

As safety information is critical content in LS, writers need to have detailed insights into the terminology used to describe the side effects of medicines. In the source documents, clinical safety information is described in terms of adverse events (AEs), serious adverse events (SAEs), adverse reactions (ARs), serious adverse reactions (SARs), adverse events of special interest (AESI), and suspected unexpected serious adverse reactions (SUSARs). Mastering this terminology and the associated definitions is critical to communicate safety information appropriately and unambiguously.

Furthermore, familiarity with adverse event coding systems (such as the Medical Dictionary for Regulatory Activities (MedDRA) and Common Terminology Criteria for Adverse Event Reporting (CTCAE) is essential because adverse events are collected, coded and analysed using terminology from these systems. A good working knowledge of these is helpful for LS writers so that a consistent approach is used when transferring this information into lay language.

### 3.3.6 Statistical Knowledge

A sound knowledge of biostatistics is fundamental for LS content generation and presentation of statistical trial results should be treated with great caution. A LS author should appreciate and be able to explain that clinical trials are usually or often powered to demonstrate differences in the primary endpoint and are often not powered to show a difference in secondary endpoints. Results establishing a clear difference of active/placebo control may be easy to understand and translate into lay language. However, for trials where the interpretation of the statistical outcomes is complex, a good basic background in biostatistics will be necessary to appropriately explain the results without sacrificing scientific validity of the trial. Furthermore, most lay people have no understanding of statistical concepts and the writer therefore should decode them into lay language.

### 3.3.7 Communication & Language Skills

Since LS are designed for a general public audience, the language should be kept as simple as possible in order for the LS to be accessible to people with basic education and/or low health literacy skills. The LS writer should be able to render scientific content into simple everyday language which is based on a respectful tone of voice. Cultural sensitivities should not be underestimated but accommodated when pertinent, e.g., with regards to the use of certain medical terms.

For preparation of LS on results from multinational trials, translation and language skills are required to enable successful results communication to the lay audiences in all involved countries. Considerations on translation and language are further covered in Section **4**.

In case of LS intended for children, the cognitive development stages and the information-processing preferences of children in the different age groups shouldbe taken into account. Appendix 1, Table 7.4. provides information about child development, comprehension and learning strategies by age groups.

### 3.3.8 Skills for Quality Control (QC) and Accuracy Checks

Since the LS will be publicly disclosed, it is important that it is subject to an accuracy check before being released to the public. Quality Control (QC) of a LS entails checking of all numbers and all quantitative statements against the source documents. To ensure an objective unbiased QC process, the check should be performed by a professional who is not part of the immediate LS writing team, ideally a QC specialist. It is recommended to develop a checklist of all items that require QC review and to document any changes implemented.

### 3.3.9 Legal and Regulatory Knowledge

Writers of LS should possess sufficient regulatory knowledge to understand the purpose and context in which the LS is produced. This includes, above all, knowledge of the EU CTR. In addition, it is an advantage to be familiar with the EU Expert Group on Clinical Trials Recommendations[4].

There are additional relevant recommendations to consider: the TransCelerate Implementation Guide for Lay Summaries[6], the Recommendations for drafting Non-promotional Lay Summaries for Clinical Trial Results[17] and the MRCT Return of Aggregate Results Toolkit[18] as well as statements of patient advocacy groups such as the European Patient's Forum (EPF) and of pharmaceutical associations such as the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Pharmaceutical Research and Manufacturers of America (PhRMA).

### 3.3.10 Visual and Design Skills

Supporting the EU Expert Group on Clinical Trials recommendations, GLSP encourages the use of well-chosen and clearly designed visual aids to enhance understanding of scientific content. Graphics can be powerful communication assets as they can facilitate the accessibility and comprehension of the LS within the target audience. LS writing teams should be able to design easily understandable but accurate graphics. They should evaluate visual elements from a lay perspective and critically select graphical elements that aid unambiguous and non-promotional results communication. LS writers should have the competency to decide which content will benefit from visual presentation and where a combination of text and graphics is most helpful as well as its suitability for later translation to ensure technology compatibility and ease of translation of original design.

For LS of paediatric clinical trials, the writing team should have the ability to design illustrations, comics or infographics that can be easily understood by paediatric patients of different age groups. Table 7.6 in Appendix 1 provides further recommendations for paediatric lay-out and design.

### 3.3.11 Skills for Validation of Content

LS authors should be aware of the relevance of validation of LS content and therefore know how to enable consulting from patients experienced in clinical research methodology and ideally representing the LS target audience, but also from other involved stakeholders like healthcare providers. Knowledge about suitable user testing methodology for the LS and potential translations to determine readability and understandability by patients and members of the public at large is very relevant.

### 3.3.12 Attitudes and Collaboration Skills

Attitudes are also an element of competency for LS production. Writers, developers, reviewers, and other stakeholders directly involved in the LS process should be willing to work in a team setting, and display a collaborative, open-minded, and consultative mindset. They should be willing to listen to and act on feedback from stakeholders outside the scientific community including that from patient experts and representatives of the public. They should be committed to undertake training, including training on how to interact with the different stakeholders involved.

## 3.4 Writing and Presentation of the Lay Summary

One of the most demanding steps in the LS production process is authoring and presenting the LS in a way which meets the needs and literacy levels of the target audience. Efforts should be made to prepare LS which are understandable for the general public as of the age of 12 years. In contrast to scientific writing, which is designed for a narrow professional community, the LS should address the public at

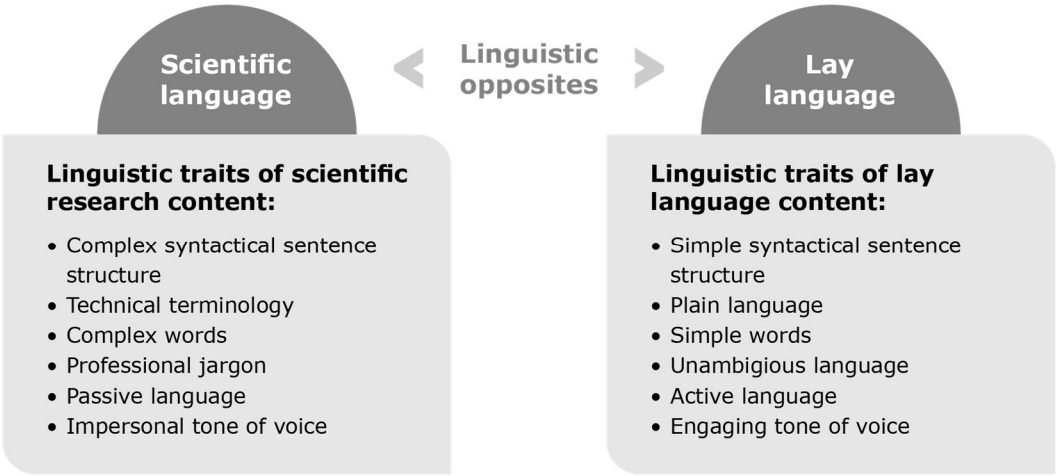
large and thus make the summary understandable, readable, and accessible for a heterogenous lay audience with no scientific knowledge.

Paediatric patient-focused LS may differ in terms of presentation and style (more illustrations or graphics) to assist children in understanding trial results.

LS addressing paediatric audiences are not established as a standard for presenting results of paediatric trials. Some sponsors have already developed paediatric LS but only few internal organisational practices appear to have evolved and there seems to be a lack of scientific research to support the development of LS aimed at children. The recommendations in GLSP therefore build on universal instructionson how to communicate with children based on existing guidelines about health, developed by UNICEF[19] and guidelines about children's reading skills from the Oxford Owl-website[20]. To address clinical trial specific topics, the GLSP offers additional advice and context with inspiration from IPPOSI/National Children's Research Centre[21] and Sant Joan de Déu Children's Hospital booklets[22] as well as existing recommendations for writing Assents for children.

As an offset for LS development, it is pertinent to recognise the difference in language conventions used within the scientific community and within lay audiences. Languages addressing these audiences are in fact opposites in all linguistic aspects, as illustrated in Figure **3.1**.

Figure 3.1: Linguistic Differences between Scientific and Lay Language




Clearly, the language employed within the scientific community is specialised and different in all linguistic aspects from plain language intended for a lay audience. Grammar and structure (morphology/syntax), terminology (nomenclature), style (jargon) as well as the generation of meaning (semantics) and the tone-of-voice used do contrast across the two types of communication. Being aware of these language differences will facilitate the creation and translation of LS which are understandable, culturally acceptable, and accessible to the target lay audience.

### 3.4.1 Health Literacy

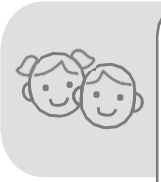
Health literacy is defined as "the capacity to make sound health decisions in the context of everyday life – at home, in the community, at the workplace, in the health-care system, in the marketplace, and in the political arena"[23]. Improving health literacy worldwide and increasing people's ability to understand and engage in their healthcare is an international priority[24]. In Europe it is estimated that one in five 16- to 65-year-olds have poor reading skills[25,26]**.** To address this, all people should be offered the same accessible information and services; everybody could benefit from clear health information.

The generally low level of health literacy combined with the need to convey the complicated messages related to clinical trial results is a challenge and requires different writing skills than for scientific or regulatory purposes. A fundamental principle when addressing a lay audience is using conversational, everyday language and avoid formal, medical jargon. In practice, this means to "write the way you talk." Most people do not read or write much and writing in conversational style can be a means of reaching out to them.

Table 3.2: Health Literacy Principles

| Health Literacy | |
|---|---|
| **Principles** | **Examples and Elaboration** |
| **Use simple everyday conversational language** | 'use' not 'utilise'<br>'long term' not 'chronic' |
| **Use short words, sentences and paragraphs** | To increase readability, it is recommended to use:<br>• words of 1–2 syllables<br>• sentences of 8–10 words<br>• paragraphs of 3–5 sentences |
| **Use active voice rather than passive voice** | Active voice is easier to understand with risk of misinterpretation - and can make sentences shorter.<br>"Researchers studied the effect of tamoxifen" not "The effect of tamoxifen was studied by researchers" |
| **Do not use technical or scientific language** | 'birth control', not 'contraception'<br>'high blood pressure' not 'hypertension' |
| **Present medical terms in brackets** | Present medical terms in brackets after the plain language version.<br>"Some people had side effects of feeling sick (nausea)" |
| **Use neutral non-promotional language** | See Section 3.4.6 for further guidance and examples. |
| **Do not use statistical terms** | Do not use terms like 'number needed to treat', 'odds ratio' and 'confidence interval'. |
| **Quantify words** | Quantify words like 'low', 'higher', 'faster', 'more', 'many'.<br>'Most were non-smokers (44) or former smokers (11)' |
| **Use words and terms consistently** | Do not alternate between interchangeable synonyms.<br>'study' versus 'trial' |
| **Be respectful in your language** | "People with cancer" rather than "cancer patients". |
| **Do not use Latin expressions** | 'such as' not 'e.g.'<br>'that means' not 'i.e.'<br>'in the laboratory' not 'in vitro' |

### 3.4.2 Paediatric Cognitive Development



Information about children's cognitive development is based on the Centers for Disease Control and Prevention (CDC)[27] and the National Academies Press (NAP)[28]. Both institutions advocate communication intended for children to be based on a broad understanding of children's levels of knowledge that also include cultural norms, values and children's age-specific perceptions of identity (being in the world). For information on child development, comprehension and learning by age, see Table 7.4 in Appendix 1. The table may help determine the level of complexity and focus for paediatric audiences when developing LS.

**Paediatric age groups**

Following IPPOSI and National Children's Research Center's booklets for children about clinical trials, three major age groups have been characterised in GLSP, whilst acknowledging that these groups are not rigid and that there is great variability within each age range. Also, the segmentation by age does not reflect a legal distinction between age groups:

**Age ≤8 years.** Storytelling and pictures constitute the most effective communication methods in this age range, although the oldest children in this segment begin to read and understand simple words. As this group has a limited attention span and understanding of numeracy, special attention should be given to LS content directed at the child and content directed at the parent.

**Age 9–11 years.** At this age, most children are capable of simple text reading and understanding of basic concepts. A combination of simple vocabulary, storytelling and pictures can aid comprehension at this cognitive development stage with attention to words commonly understood and relatable within this age group. At this stage, children are beginning to understand concepts, comparisons, theory, and process learning through personal experience.

**Age 12–17 years (adolescents).** In the 12 plus age range, children are generally capable of understanding more complex words, explanations, and concepts. At this stage children can distinguish between facts and fiction and they are able to process more complex information and comparisons than in the low age groups. Fact and figures can therefore be presented for this group without dependency on storytelling or imagery to get the message across.

### 3.4.3 Readability Formulae

The EU Expert Group on Clinical Trials Recommendations[4] encourages the use of readability formulae, although these tools have their limitations. Commonly known readability formulae apply an algorithm of the average number of words per sentence and syllables per word, without measuring context, difficulties of concept or the coherence of text. Hence, a short sentence with short words that make no sense at all will result in a good readability score because there is no direct correlation between an acceptable readability score and the actual readability of the content. Therefore, it is recommended

only to use readability formulae as a supplement to gauge the reading level and because current available tests are not developed in all official languages.

Commonly used readability formulae include the Flesch Reading Ease Readability Score[29] and the Flesch–Kincaid Readability Score[30]. With emerging technologies, more advanced readability formulae can also be obtained, e.g., by use of predictive analytics, and rules-based automated readability checks.

### 3.4.4 Length of Summaries

The EU Expert Group on Clinical Trials[4] recommends that the LS should be as short as possible, but also acknowledges that explaining technical information in simple language may require more words and result in a longer LS. Indeed, just translating medical terms into "simple" equivalents, without explanatory context, can be more misleading and confusing than technical language itself. The LS should be as brief as is consistent with an understandable and navigable document. A readable document can be achieved with a good layout and design for trials with intermediate complexity. More complex trials may require more description.

### 3.4.5 Health Numeracy

Health numeracy is the ability to understand, use and communicate quantitative health information, including the ability to understand information in text and non-text formats such as graphs. Some general numeracy principles are outlined in Table 3.3. Further details on how to apply principles of numeracy can be found in the MRCT Return of Aggregate Results Toolkit[18], and the HRA Information for participants[31].

Table 3.3: Health Numeracy Principles

| Numeracy | |
|---|---|
| **Principles** | **Examples and Elaboration** |
| **Use visuals for interpretation of numbers** | See Section 3.6.1 for examples |
| **Use whole numbers** | Round up to whole numbers if possible.<br>'5' instead of '4.87'<br>'1 in 1000' instead of '0.001' |
| **Keep denominators and units consistent** | "There is a 1 in 10 chance of nausea and a 2 in 10 chance of dizziness" instead of<br>"There is a 1 in 10 chance of nausea and a 1 in 5 chance of dizziness" |
| **Use percentages carefully** | Not everyone understands percentages - but percentages can be better understood than absolute numbers. To help with percentages, numbers can be visually presented e.g. in a pie chart (see also Section 3.6.1 on 'Graphics').<br>Frequencies can be expressed as 'natural frequencies' e.g. '1 out of 10' instead of '10%'. |
| **Use numerals rather than words for numbers** | '2' instead of 'two' |
| **Do not leave calculations to your reader** | Basic maths is beyond many people - so do the calculations for them e.g.<br>• Do not present a body weight loss in %, do the math or show examples.<br>• Use simple units: '1 year' not '52 weeks'; 'half a glass of water' not '120 mL water' |

### 3.4.6 Non-promotional Language

The content of the LS should be presented in factual and objective language and should not be designed as promotional or favourable. The EU Expert Group on Clinical Trials Recommendations[4],the MRCT Draft FDA Guidance on provision of Plain Language Summaries[7], the MRCT Aggregate Results Toolkit[18] and the TransCelerate Recommendations for Drafting Non-promotional Lay Summaries[17] give guidance and examples of neutral language. Table 3.4 lists recommendations that can be followed to reduce the risk that a LS could be perceived as being promotional.

Table 3.4: Recommendations for Non-Promotional Language

| Non-promotional Language | |
|---|---|
| **Dos** | **Don'ts** |
| **The overall tone should be factual and objective** | |
| ✔ Highlight both the positive and the negative.<br>✔ Present information accurately and in a non-misleading way. | ✗ Present no opinions that cannot be substantiated clearly from the results.<br>✗ Avoid making inferences or assessments: stick to fact.<br>✗ Do not criticise or oppose competitors. |
| **No commercial or marketing appearance** | |
| ✔ Use neutral colours and plain design.<br>✔ Ensure faithful reproduction and clear indication of source of quotations, graphs, diagrams, illustrations, etc.<br>✔ Name study products as in the ICF, protocol and on clinical trial disclosure sites (most often generic name[s]). | ✗ Do not use brand colours, glossy designs or sponsor logos<br>✗ Do not include approval status, as indication may vary between countries and may lead to a promotional concern.<br>✗ Do not use brand names, except where information can only be found knowing the brand name. |
| **Superlative and enthusiastic words should be avoided** | |
| ✔ Be careful using words like:<br>✔ 'safe', 'effective', 'better', 'best', 'strongest', 'highest' without quantification. | ✗ Do not use words which could lead to determination that the communication is promotional:<br>✗ 'the most', 'the best', 'extraordinary', 'unsurpassed'<br>✗ Avoid claims (e.g. 'the results proved') |
| **Be careful with high level statements** | |
| ✔ Specify the circumstances the statement is based on (e.g. "In this study, no safety issues were identified at the tested doses."). | ✗ Avoid generalising statements as<br>✗ "The study medicine is safe." |
| **Quantify statements** | |
| ✔ Present numbers, also for comparators:<br>✔ "# of # people (%) given X had low blood sugar". | ✗ Avoid unquantified statements such as:<br>✗ "Fewer people had too low blood sugar while on X". |
| **Reinforce that the outcome reflects only one single clinical study** | |
| ✔ Include relevant contrary evidence or limitations.<br>✔ Include a statement to emphasise that results presented are from one study:<br>✔ "The outcome of this study is from the results of this study only. Other studies may show something different."<br>✔ Reinforce that therapeutic changes should not be made based on results from a single study without consulting a healthcare professional. | ✗ Do not include results from other studies.<br>✗ Do not make comparison to other products than the ones included in the study. |
| **Ensure that additional information is readily available** | |
| ✔ Included statement with reference to where additional results from the study can be found (e.g. on external clinical trial disclosure sites): "Results from this study can be found on the listed websites."<br>✔ Consider including a statement on where to find results from other studies, if applicable. | |

### 3.5 Presentation of Safety Information

The EU CTR specifies that a “description of adverse reactions and their frequency” must be included in the LS.

The EU Expert Group on Clinical Trials Recommendations expand on this, acknowledging an intentional difference in the adverse reaction information presented in the LS compared with the adverse event information presented in the Summary of Clinical Trial Results. While recognising that it is not always possible to establish an exact causal relationship within a single clinical trial, the EU Expert Group on Clinical Trials Recommendations state that the sponsor should define adverse reactions as those adverse events for which the investigator has indicated at least a reasonable possibility of an established causal relationship between the event and the IMP based on an analysis of available evidence (EU CTR Annex III 2.1.3). The Recommendations suggest that a simple term such as “side effects” could be used to refer to adverse reactions. However, terms such as “side effects” and “adverse reactions” described in the product label may be confused with the adverse drug reactions (ADRs) described in a clinical trial, see Table 3.5. Whichever term is used, adverse reactions need to be clearly defined in the LS in words that are easily understandable to a non-scientific audience. Serious adverse reactions, defined as any untoward medical occurrence that at any dose requires inpatient hospitalisation or prolongation of an existing hospitalisation, results in persistent or significant disability or incapacity, results in a congenital anomaly or birth defect, is life-threatening or results in death (EU CTR Art. 2.2.33), also need to be explained in plain language.

A further difference between the LS and the scientific Summary of Clinical Trial Results is the sequence of information. The EU Expert Group on Clinical Trials Recommendations suggest that the serious adverse reactions be listed first in the LS, followed by the “other,” common adverse reactions listed by frequency. Clear separation of serious adverse reactions from the latter category is intended to avoid duplication of information within the LS.

The number of fatal adverse reactions and any adverse reactions that have led to early closure of the trial or withdrawal of participants should also be clearly stated per the EU Expert Group on Clinical Trials Recommendations. Depending on trial design, discontinuation of trial treatment does not always result in participant withdrawal from the trial. In these cases, the LS may provide information on adverse reactions resulting in discontinuation of trial treatment.

The advantage of describing only investigator-identified adverse reactions in the LS is that this may be more understandable, and the use of bulky tables covering many unrelated adverse events can be avoided.

The reader should not be expected to make analytical judgements based on the relative incidence of events versus a placebo group. Furthermore, the reader is not expected to make allowance for the underlying pathology in interpreting the information. These factors may be most significant for trial populations with advanced disease or involved in trials of long duration. Nonetheless, sponsors need to be aware of differences in information versus other publicly accessible sources, or versus informed

consent documentation provided to trial participants, and consider means of clarification. These clarifications could be applied as standard language for LS, for example within template text.

Regarding other safety information from the trial, the EU Expert Group Recommendations on Clinical Trials propose that clinical laboratory changes be included "only if they are useful/clinically relevant." Individual laboratory changes that have been reported as treatment-related adverse events are, by definition, adverse reactions, however, not in all cases clinically relevant[6].

In any case, clinical safety judgement should be applied also taking into account the trial results, and sponsors should aim to adopt a consistent approach across trials as far as possible.

Within the LS, the adverse reactions should be presented in a dedicated section. For those clinical trials for which the primary objective is a general description of safety and tolerability, this section may be interchangeable with the overall results section of the LS. For clinical trials for which the primary endpoint is based on the incidence of an adverse event irrespective of causality, this primary endpoint should be discussed separately within the overall results section, whereas adverse reactions should be presented in a separate, dedicated section. Examples of this might include a trial with a composite safety endpoint, or a trial comparing the rate of a specific adverse event between treatment groups.

In general, tables are likely to be a simple way of presenting adverse reactions, with graphs helpful in some cases. For trials with only a small number of adverse reactions, simple text may be more appropriate. Numerical information as well as percentages should be provided. Where specific adverse reactions coincide with endpoints, this should be noted. Medical dictionary preferred terms as defined in the Medical Dictionary for Regulatory Activities (MedDRA) will often need to be translated into terminology more understandable to a non-scientific reader. A plain language dictionary used for patient information documents may be a useful resource, where available.

The EU Expert Group on Clinical Trials Recommendations note that a reasonable and clearly communicated cut-off can be used when needed for common adverse reactions. However, the appropriate percentage cut-off is likely to vary according to the safety profile of the investigational product, the reporting interval, and the trial population. For each LS, the clinical and scientific experts involved in the trial's safety analysis should determine any percentage cut-off, to ensure meaningful representation of the data and should not be determined solely to shorten the LS.

Table 3.5: Cautions Related to Description of Adverse Reactions: Considerations for Development of Standard Lay Summary Template Language

| Caution | Considerations for developing a standard LS template |
|---|---|
| Potential confusion regarding "side effects" or "adverse reactions" described in the prescribing information/product label for approved products | • Sponsors may consider prefixing the term with "possible": "possible side effect" or "possible adverse reaction."<br>• Clear, plain language definition of what is meant by "adverse reaction" (or equivalent term used) for the purpose of the LS.<br>• Explanation that the LS only considers the results of this single trial. Researchers need to consider the results of many studies to understand if any medical problems may be related to an investigational treatment.<br>• Other wording to explain that the assignment of causality is not definite.<br>• Explanation that other studies may have different findings. |
| Potential confusion with respect to:<br>• Differences in numbers presented in other publicly available technical documents (although there will also be unavoidable differences in terminology due to translation into plain language)<br>• Information provided to trial participants in the informed consent document | • Explanation that the results may be presented differently elsewhere. |

Certain trial designs will have additional specific requirements. For example, clinical trials with solicited as well as unsolicited adverse event collection may require additional explanation. Writers should work with the clinical team to determine whether adverse events of special interest and those of particular clinical or patient relevance have to be described in the LS. For double-blind, placebo-controlled trials, it may be helpful to include a statement like: "The trial doctor did not know whether a participant was receiving the active treatment or placebo when judging whether an event was related to the treatment or not." In addition, for trials with both double-blind and open-label treatment periods, adverse reactions need to be discussed for the entire trial. However, sponsors need to determine the best approach: presenting adverse reactions for the different trial periods separately may be clearer than providing an additional explanation about the difference in reporting intervals. A sponsor choosing to deliver a LS after primary analysis would need to update the final LS with safety information collected up to the end of the trial.

### 3.6 Layout and Design of the Lay Summary

From a readability perspective, layout and design are as important as the wording in a LS by allowing people to use the document and navigate their way around it. The appearance and attractiveness of the document itself can make a difference to the reader. If the LS does not look easily accessible and relevant for the reader at a first glance, it may not be read at all.

The importance of design to readability is not addressed prominently by the EU CT Expert Group Recommendations[4]. A number of key points to consider related to layout and design are presented in Table **3.6**.

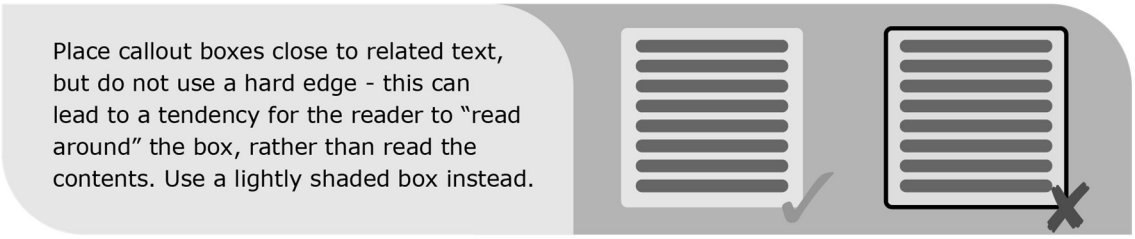


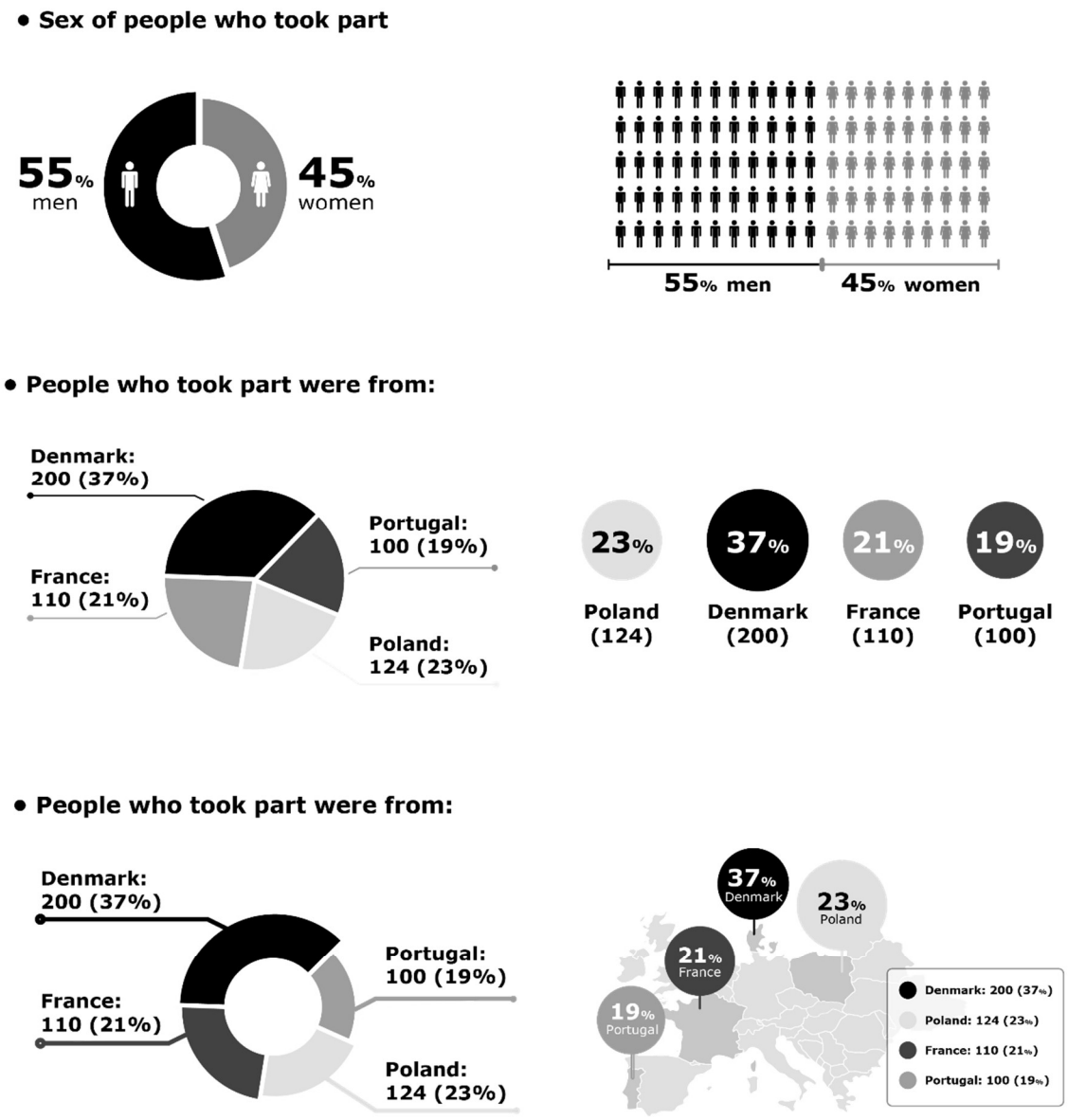
Table 3.6: Layout and Design

| Layout and Design | |
|---|---|
| **Points to Consider** | **Elaboration** |
| Use headings and descriptive subheadings | Use headings and subheadings to organise information. Descriptive subheadings make it easier to scan the text to find key points. |
| Use adequate white space | Densely packed text is tiring to the eyes, so allow space between lines, headings and paragraphs. Use white space to separate topics. When text is grouped together, it is assumed to belong together. |
| Use black text on white background | Sufficient contrast between the font colour and the background maximises legibility and accessibility. Most readable is black font on white background. |
| Limit use of unnecessary imagery, such as logos and icons | Logos may also be considered promotional. Icons should represent the content they accompany and should be used consistently. |
| Use visuals such as simple graphs | Visuals can be leveraged to aid written content. Visuals also may allow readers to extract information more quickly and easily. Make sure visuals are kept close to the text they correspond to (rather than the preceding or following text). |
| Use left justified text (also known as 'ragged right'). | Full justification with a straight line down both margins can lead to unusual spacing between words which some readers find difficult or distracting. |
| Do not use long lines of text | Use of columns produces shorter lines. Long lines are particularly difficult for less skilled readers. |
| Place column and page breaks carefully | If starting a new subsection or paragraph (bullet list), start on a new page or new column. Spanning both will disturb the reading flow. |
| Use of colour can make a document more attractive but do not over-use | Theme colours help to ensure the different elements (e.g. headings or call out boxes) align with each other and give a unified look. However, some colours pose difficulties for people with colour-blindness. |
| Use bold text to add emphasis, but do not use:<br>• underlining<br>• *italics*<br>• fancy fonts<br>• ALL CAPS | Emphasise information by bolding rather than put in CAPITALS, italics or fancy fonts, as these are more difficult to read. However, do not include too much bolding, or its impact will be reduced - only bold the most important items. |
| Use bullets formatting | Bullet formatting splits text into separate points and helps the reader to digest the message. |

### 3.6.1 Graphics

Well-chosen and clearly designed graphics or visuals can enhance comprehension of the text[4]. Graphics designed with the audience in mind can be powerful in supporting and facilitating the processing of numbers in the text. However, to avoid that too many graphics are presented, their selection needs to be considered carefully. In general, bar graphs are recommended for comparison across groups and pie charts for numerical proportions. Infographics or pictorial representation can also be useful. However, since even simple graphics can be misinterpreted and may be subject to cultural and age differences, it is essential to do user testing to ensure that the visuals are comprehensible and do not introduce ambiguity in the results communication. Figure 3.2 offers examples of how numbers can be presented graphically.

Figure 3.2: Examples of Graphics and Visuals



**General recommendations for using graphics include:**

- Make graphics simple and not overly complex; with one simple message per image. Do not display several relationships, or complex trial design diagrams and flowcharts.
- Use black and white print as a general rule. Colours may be used, however avoid brand colours which may be perceived as promotional. Some colours may be difficult for people with colour-blindness. If colour is used, remember that the LS may be printed in black and white – use of solid colour and hatching may also be helpful to distinguish sections.
- Use clear label captions and axes, along with meaningful scaling and labelling of axes. Do not exaggerate the positive or minimise negative results through the choice of axes.
- If space allows, place the caption inside each bar or pie slice - rather than using colour and a key. This means the reader has to do less work. Also, if possible, write the text describing the vertical axis horizontally – not vertically. This means the reader does not have to turn the LS on its side to read the graph. Labels inside graphical elements need to be able to be translated in the final country-specific LS. If using a translation vendor, ensure that the graphics are editable and not read-only, or that the source design-file is available.

### 3.6.2 Paediatric LS Presentation

It should be noted that storytelling and pictures can be effective communication methods across paediatric as well as adult audiences, as human beings have different cognitive learning preferences with some people being predominantly visual learners and others being auditory learners. Effective LS communication is about finding the balance between use of visuals, storytelling, and text to match the age group as well as the disease.

**Comprehension and understanding**

According to Oxford Owl, "comprehension" is the ability to read a text or a message and understand its meaning[32]. Comprehension builds on four underlying factors:

- **Background knowledge:** what the child already is familiar with and knows by experience or other sources of information.
- **Vocabulary:** the volume of words that the child knows (recognises) or reads, including the ability to decode new words by connecting them to known words.
- **Language structure:** the level of complexity that the child can process in sentences, including conjunctions and causations. For pictures/visuals the level and complexity of messages/information.
- **Inference:** the ability of the child to understand hidden messages; to read between the lines and to associate.

When processing information, the reader establishes a mental model – a picture in her/his head that creates meaning out of the content. The reader does not remember each and every word s(he) hears or reads but leverages the above four capabilities to extract meaning. The strategy for writing or creating a text, story, cartoon, or animation for children should therefore be to tap into their cognitive capabilities to ensure they understand the messaging. This may be achieved by designing the content based on an understanding of the four elements referenced above.

**Using narratives**

Empirical studies support a difference between typical science communication and narrative processing and suggest that narrative processing is generally more efficient. Narratives are often associated with increased recall, ease of comprehension, and shorter reading times[33].

Personification allows the reader a greater chance of identification and empathy compared with the full trial population, and it aligns better with the young child's way of perceiving and learning[34]. See also Table 7.4 in Appendix 1.

A narrative could exemplify multiple sides of the issue or variation of treatment/results through the eyes of a character who actively considers the options.

The accuracy of trial details may be compromised in order for the narrative to work as a whole. The narrative may also not be very detailed in presenting very accurate and precise descriptions of all inclusion criteria, settings, and time frames[35]. However, the time concerning cause-relations of the treatment/investigational product should be clearly described and not compromised.

**Ethical considerations**

When communicating trial results to children using narratives and/or cartoons, there are some ethical issues to acknowledge. Sponsors should carefully assess the benefits and risks of this approach.

- The avoidance of simplified messaging being inadvertently misleading is important with any LS but particularly when presenting LS in a child-friendly form. An example of this might be a cartoon implying that a study showed that a drug 'works' or is 'safe' in all circumstances. A solution in this case may be to make different characters or smaller groups represent the different results.
- By necessity, a LS aimed at a child will be a simpler version with less detail than one prepared for adults. This gap in information can be compensated by ensuring that all necessary detail is covered in the parent/carer's version of the LS.
- In the case of negative results in a trial for children with a terminal condition or a trial with high mortality, the sponsor should consider whether there should be a LS for children at all. If the decision is made to provide a LS for children, the sponsor should consider what information it could contain and how it could be disseminated.

For more detailed information on recommendations for paediatric LS layout and design, see Table 7.6 in Appendix 1.

### 3.6.3 Lay Summaries for People with Visual Impairment

For people with visual impairment, electronic copies of LS are the most accessible format. Common file formats such as PDF are most useful; however, it should be ensured that any security settings of the PDF file do not interfere with the screen reader's ability to convert the on-screen text to speech or Braille. As for sponsor websites, HTML or XML formats may be used and should be accessible for visually impaired readers as well. Effort should be made to ensure that information contained in the LS is accessible to people with visual impairment. This population includes both partially sighted readers, who will benefit from larger fonts and enhanced contrast, and users with very low to no vision, who access the web with screen readers. Indications for accessibility of internet sites are available, such as those provided in the guidelines produced by the Web Accessibility Initiative (WAI)[36] and should be followed when organising the LS content on web sites.

Charts or graphs can convey information effectively; however, they are not always legible with screen readers and they should be designed to also be accessible for people who are colour-blind. Therefore, a brief summary of the key messages of charts or graphs should be provided. A short caption describing any pictures present in the LS is desirable.

## 3.7 Review and User Testing of the Lay Summary

### 3.7.1 Review of the Lay Summary

Review is part of ensuring the overall quality of the LS. Review can include a medical review, legal review, lay language review, and/or translation review. As a minimum, reviewers of LS need to be aware

of the purpose of the document and the required content of LS. Reviewers also need to understand the key objective of a LS, which is to provide a summary of a single trial in a language accessible to people with low reading skills. Finally, reviewers should be instructed that LS must not be promotional and that biased language is to be avoided.

To ensure an efficient process and obtain the intended purpose of the LS review, the trial sponsor should instruct reviewers on the requirements and content of a LS. If there is a standard for LS in the institution, this should be communicated to the reviewers. Before being asked to conduct a review, reviewers should receive a training on the design of the LS, including the choice of visuals, graphs, and the use of white space. It is important that reviewers have clear instructions on the objective of their review. For example, a medical specialist is briefed to look at whether the description of the disease is adequate, a legal specialist may focus on aspects of compliance and on the non-promotional nature of the LS, and a language specialist will focus on the appropriate use of lay language. A patient reviewer may focus on the appropriateness of the language in the disease area. Thus, each reviewer should be briefed on his or her individual focus in the review of a LS. It is advisable to have LS reviewed by language specialists and by patient experts, patient advocates or patient organisation representatives.

**3.7.2 User testing of the Lay Summary**

- Later in the development of the LS, user testing by patients without experience in clinical research and/or public representatives is a helpful element of good LS practice. See Appendix 1, Table 7.3. Drafts for review can be distributed to multiple test individuals for written feedback. The quality of this type of review will depend on clear instructions on the input requested from testers, e.g., comments on content or literacy, numeracy, specific terminology, visuals, etc. In a written review, it is recommended to leave room for feedback which researchers may not have considered upfront. This will allow topics to surface which have not been evident to the sponsor but are important to patients and public readers.
- Valuable feedback can be obtained from an in-person review session, either a focus group discussion or a facilitated 'read-through' exercise. In a "read-through" session, the respondent is asked to provide insights into any perceptions, feelings or opinions triggered when reading the LS. In-person review sessions can be structured or unstructured depending on the input desired. A group of at least 6–10 people could be considered with a mix of patients with the disease (to test meaning and relevance) and people from the general public (for insights into general readability issues).
- The formal process of "user testing" identifies where there are potential issues in terms of readability and subsequently determines whether addressing those issues (using good practice in writing for lay people) leads to improvements[37]. It is a diagnostic and iterative process which is routinely used in readability assessment of medicine leaflets[38]. A key feature of this methodology is that respondents are initially asked to use the LS to find and answer questions and then enquired about their opinion on the actual use of the LS. Testing an example of a LS for each of the main types of medicines or types of trials the sponsor conducts may be helpful. An example of applying user testing to a LS was published in 2018[39].

## 4. Translation of the Lay Summary

Availability of a LS in patients' native language is an important element of fair access to information. Translating LS into the official languages of all countries in which the trial took place is considered good practice since a primary objective of the LS is to communicate results in clear and understandable local language. This section will focus on the translation of LS from one natural language to another natural language. Natural language refers to the language an individual or group of people use as a native tongue, and in the EU/EEA, a number of natural languages have been defined as official languages. A list of these languages per EU Member State can be accessed at the EMA website[40].

While the EU CTR does not request translations, the EU Expert Group on Clinical Trials Recommendations[4] suggest that as a minimum, the LS should be provided in the local language(s) of each of the countries where the trial took place, matching the languages employed in the PIS/ICF. Where resources allow, sponsors could consider preparing an English version if the trial did not include the Republic of Ireland or Malta to allow greater accessibility across the EU and globally.

### 4.1 Timing and Strategy of Language Translation(s)

The full LS development process – from authoring the LS to the final translated country-specific LS – should be approached as one integrated communication process. Furthermore, if the creation of the LS awaits the final CSR or full set of structured trial results, the authoring and translations of the LS may become time critical activities for meeting the regulatory deadlines. Sponsors may therefore choose to develop the LS in parallel with the source documents. In this case, it is advised to clarify upfront whether the language translation(s) can be performed in the above recommended single-step process based on the final master LS or whether a dual-step process with initial translation of a draft master LS followed by a final, adjusted translation is the only option.

While one version must be uploaded to the EU Portal within the legally required timeline, no time frame for additional translated LS is defined in the EU CTR. However, to ensure fair availability of information to all patients and the public, translated versions of the LS are recommended to be made available as soon as possible, ideally in parallel with the release of the version of the official language of the trial.

### 4.2 Planning and Preparation of Translations

It can be beneficial to commence the planning and preparation of language translations during the development of the PIS/ICF.

To control lay content throughout the trial (or even for all trials within a therapeutic area or a clinical development plan), it is ideal to set up a style guide for the writing and translation of the LS and to proactively develop a glossary of terms. This will facilitate reviews and minimise the occurrence of preferential changes, time consuming queries and content inconsistencies. Agreed terminology can help streamline the communication and specific phrases can be pre-defined in glossaries to ensure for example empowering language or an active tone of voice.

For regional or global trials, the sponsor may consider engaging with a language service provider that can manage the translation.

### 4.3 Translation Process

Language translation is a complex process which requires expertise, planning and control to help minimise poor, inaccurate outcomes. All country-specific language translations should be based on a master LS, and a successful final translation will thus rely on a high-quality master LS. Any ambiguous,

promotional or biased content in the master LS will carry over to the final translated LS. Given the importance of the source text during translations, it is highly recommended that the master LS be carefully reviewed, finalised, and approved before translations commence.

Three different resources can help obtain a sound translation:

- **Human expertise:** Translations should be performed by native or fluent translators and be checked by reviewers with the right expertise in clinical trial research and plain language communication.
- **Controlled workflows:** a well-defined process with built-in quality checks will help achieve a high translation quality.
- **Technology and automation tools:** Computer assisted translation and revision tools and translation memories can help ensure language accuracy, consistency and configure terminology to the trial at hand. Technology can be a powerful aid throughout the translation process and can run automated checks for linguistic and formatting issues.

Whilst the human expertise and well-defined processes are essential for a successful LS, technology and tools are no precondition if sponsor budgets are limited. Technology and tools can enhance the translation process and bring both consistency and efficiency and enable sponsors to develop language assets that can be re-used. This may be more relevant for sponsors with medium to large clinical pipelines.

#### 4.3.1 Translation Step-by-Step

Table 7.7 in Appendix 1 illustrates a step-by-step recommendation on how the language translation process can be set up. This process is widely recognised as a gold standard for patient-friendly communication in clinical trials. For resource limited organisations, the full process may not be an option and in this case, it should be considered which quality steps are reasonable to balance budget and quality in translation.

An ideal translation process involves forward translation and back translation by two different native speakers or translators fluent in the target, respectively source language and a subsequent review by a third person. However, the back-translation and review steps could be replaced by a partial or full linguistic review of the translated LS against the master LS. Whether a partial or full review of the translated LS is appropriate as an alternative to a back-translation depends on the complexity of the LS and the resources of the sponsor.

## 5. Dissemination of the Lay Summary

### 5.1 Dissemination through EU Database and Beyond

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In the interest of the broadest possible transparency about clinical trial results to the trial participants and the public, the EU CTR makes LS dissemination through the publicly accessible EU Database mandatory for sponsors[1].

Additional public dissemination of LS should be considered when the clinical trial also involved trial participants outside of the EU and/or when it is not ensured that EU trial participants have easy and

reliable access to the information in the EU Database. Although there is little to no control once the LS is in the public domain, it is important to ensure that its use and interpretation is consistent with its intended non-promotional purpose. Additional efforts may be made to facilitate and broaden the access to clinical trial results in lay language to maximise the impact of the new EU regulatory requirement.

### 5.2 Technical and Non-Technical Dissemination Methods

Dissemination of LS can be executed by using either technical or non-technical means. If LS are made electronically available on a public website, it is important to ensure document control to avoid any draft or obsolete LS being mistakenly disclosed.

**Examples of technical distribution methods:**

- Email
- Sponsor's investigator trial portal
- Investigator site/clinic's portal containing a patient portal
- Sponsor website
- Third-party website for trial participant LS registration and notification
- Patient organisation website
- Global open access portals providing support in various languages

**Examples of non-technical distribution methods:**

- Print/postal service
- Printed and handed to the trial participant
- Face-to-face meeting between the trial participant and the investigator

Some of the possible benefits and risks to each of the technical distribution methods are detailed in Appendix 1, Sections 7.1.13 and 7.1.14. These factors should be considered as sponsors select the most appropriate method. Multiple methods may work best.

### 5.3 Optional Dissemination Methods

Based on the overarching principles that the LS should ensure fair access to information for all study participants and the general public while being non-promotional in content and delivery, sponsors are encouraged to implement a LS dissemination policy. It should describe the principles, planning, strategies, and communication of the LS dissemination process for all trials. It should always be in-line with EU CTR and local laws, standards, or restrictions.

Should sponsors want to expand the availability of the LS beyond the EU Database, they should evaluate the risks and benefits of the various methods of LS dissemination and align their dissemination strategies with corporate or institutional priorities, budgets, and disclosure policies.

**Overall, there are two common dissemination methods employed to date:**

1. **indirect (unrestricted) dissemination** to trial participants and/or the public by providing the information on an open, publicly available website.
2. **direct (restricted) dissemination** to trial participants and investigators through a targeted, restricted delivery system.

**During the assessment of a suitable dissemination approach, sponsors should analyse the following best practices and adopt the most appropriate dissemination procedure:**

- Preparation for distribution of LS should be an element of trial planning, preparation, and closure; e.g., by mentioning the availability of a LS in the PIS/ICF.
- Potential dissemination of the LS outside the EU needs to occur in compliance with local restrictions and standards, especially in regions where guidelines are not in place.
- Patients may wish to share and discuss the LS with their treating physician or patient organisation and are free to share the LS they received or accessed in the EU Database.
- Investigational site agreements should set the expectation that the investigators will be available to address trial participants' questions after the LS and the scientific Summary of Clinical Trial Results are made available.

The benefits and risks described for the common methods of dissemination are not mutually exclusive. Sponsors should decide which solution works best, balancing regulatory and logistical concerns.

**5.3.1 Direct Dissemination**

One method of informing the trial participants about the results of the trial is either through printed material to be shared by the investigator personally, by postal service or by posting the results on the trial-specific electronic portal. Some sponsors that choose to enable this type of delivery method to trial participants do so:

- for a more personal approach, with direct investigator involvement, especially for vulnerable participant populations out of respect for and consideration of their illness.
- because trial participants selected printed hand-outs or postal service delivery as their preferred option.
- to engage the support of the investigator/trial participant relationship through direct communication with both. Trial participants can discuss results with the investigator, which may reduce the risk of misinterpretation (although this can also be achieved regardless of which dissemination method is selected by issuing separate communications to the investigator/trial participant).
- to leverage an existing communication channel such as a trial-specific portal through which trial details (i.e., trial material, trial progress, individual trial data) can be shared to benefit also in the final act of LS dissemination from the patient-centric IT infrastructure that has facilitated the clinical trial performance.

**Sponsors employing this approach should consider:**

- burden on investigator staff for printing and disseminating the LS by postal service.
- costs for maintaining a trial-specific portal or use of a third-party vendor.
- building in an option to view the LS to support the trial participant's autonomy.
- guidelines to investigators on how to respond to trial participant's queries about the results.
- supporting the logistics and investigator's administrative burden in low-tech distribution methods (i.e., printed material) months after the trial has ended and the trial has closed.
- likelihood of local, outside the EU, IEC/IRB request to review the LS since information is sent directly to trial participants as opposed to indirect dissemination.

**General considerations on achieving best possible result information**

The investigator-trial participant relationship should be held in the highest regard irrespective of the delivery strategy implemented and whether the investigator plays an active role in the dissemination of the LS. The sponsor might email the LS to the investigational site(s) with a request that the investigational site(s) distribute the LS to trial participants via a scheduled face-to-face meeting, email or postal service.

Non-technical distribution can be used as the back-up for technical distribution in cases where the trial participants request it, language is too technical or vulnerable populations require further assistance or support in reviewing the LS. The investigator may consider a face-to-face meeting to be more effective.

The benefit of the investigator directly disseminating the LS to trial participants is that the investigator can:

- facilitate the review and understanding of overall results especially if the trial was highly technical. The discussion or delivery can be done at the same time when individual results and/or treatment unblinding is revealed to the trial participant.
- organise face to face meetings to review results, which is an effective method for blind, illiterate or paediatric trial participants to increase comprehension.

There are, however, some logistical considerations in investigator dissemination directly to trial participants:

- It may be years between the first participant's last visit and the end of the study. The first participants enrolled will have to wait the longest for the LS and during that time the investigator may lose contact with these participants.
- The cost of efforts and delivery (i.e., cost for postage, supplies, effort by site personnel to coordinate delivery) may need to be negotiated in the site budget. There may be difficulties connecting with the investigator if a long time has passed after the trial was completed.

**Risk Mitigation Measures for Direct or Indirect Dissemination**

Many of the concerns can be mitigated by discussing dissemination plans with the site:

upfront at the investigator meeting and at study start,
- at the close-out meeting with sites,
- on follow-up call or correspondence to review the trial results and
- with correspondence upon LS circulation.

Experience shows that the following situations can occur:

- **Since LS are provided 6 or 12 months after the end of the trial it is likely that investigators and trial participants forget to check the availability of results. What can sponsors or third parties do to remind investigators/trial participants?**
    - If a password protected access portal is used, sponsors should develop, within the investigator trial portal, a password-recovery system and a confirmatory system when the investigational site downloads the LS (i.e., to implement IT solutions).
    - If LS are disseminated by the investigator, sponsors can leverage the end of trial time point when trial-related interactions with the investigator are occurring, e.g., when financial close

out information or formal closure of the site announcement are delivered, to remind the site of the planned availability of the LS and address any questions.

- **Sites are not typically open at LSLV + 12 months, investigators may no longer be available, or clinics are closed.**
  - Recommend planning distribution earlier (if possible) or limit to electronic dissemination to designated portal (i.e., upload LS to sponsor website or third-party website with open access) for those LSs.
- **The trial participant may forget the URL of the global domain used by the sponsor to disseminate LS which was provided at the last visit**.
  - The sponsor can provide the URL in printed information material or in a "Thank You Card or Letter" to be handed out at the participant's first patient visit, last treatment visit and/or last trial visit. This material can also include the information about LS availability after trial completion and include a location to retrieve it (investigational site, website, etc.).
- **The trial participant's email address may change, and the third party is not informed by the trial participant**.
  - In compliance with local privacy standards, the third party might ask the trial participant for a back-up email address or mobile phone number once the LS is available on the website.
- **The trial participant may not have email/internet access or may change his/her email address**.
  - When/if the participant agrees to email communication, the investigator site staff can ask the trial participant for a back-up email address/a relative's email address.
  - At the trial participant's last treatment visit (for mortality trials) and/or last visit, include an alternative way to retrieve the LS (e.g., "In case you do not have internet access, we suggest you ask your trial doctor to help you download the LS, go to a public internet site such as a library, ask a relative to help you").
- **Given the lapse of time between the participant's last visit and delivery of results, what can sponsors do to facilitate understanding of the clinical development process, purpose of the LS, and appropriate interpretation of results?**
  - Ensure investigator has a copy of the CSR synopsis to serve as learned intermediary.
  - Provide investigator with LS training at the investigator meeting and site close out.
  - Add a standard disclaimer in the LS, advising to not change any current treatment and to consult the treating physician or investigational site (if not closed) in case of need for explanation/questions.
  - Provide a statement in the LS directing trial participants to contact the investigator/site staff with questions and provide sponsor contact information.
- **What can sponsors do to increase access and communication on results to blind or illiterate trial participants?**
  - Suggest in the written material handed out at the participant's last treatment visit (for mortality trials) or last trial visit an alternative way to retrieve the LS (relative or the general practitioner, etc.).
  - Use of web-accessible tools for visually impaired (i.e., audio reader) or deaf-blind disabilities (i.e., refreshable braille display).
  - Post educational or informative video.

### 5.3.2 Indirect Dissemination

Sponsors may find it most convenient and effective to utilise web-based, indirect methods to disseminate the LS to the public at large beyond dissemination through the EU Database. However, in order to enable a non-promotional approach, sponsors should have a policy in place that ensures the dissemination of all their clinical trials' LS in line with their pre-specified policy options.

Indirect dissemination methods include (but are not limited to):

- uploading the LS to a sponsor's website dedicated to results disclosure and devoid of commercial information.
- uploading the LS to a third-party website with open access.

Some sponsors that choose to enable such type of delivery of the LS do so:

- to enable the LS to reach a wide audience, including trial participants, and to make it easily accessible globally.
- to make the website link to the LS easy to share.
- to avoid the investigator burden of producing printed materials and distributing the LS to the trial participants months after the trial has ended and staff have been allocated to other trials.
- to enable the sponsor to publish the LS in multiple languages and at reduced costs in comparison to printed materials to the investigational sites.

**Sponsors employing this method should consider:**

- the risk of misinterpreting the results in the LS since the LS will be a stand-alone one-way communication if not delivered by the site. To minimise this risk, the LS should explain its limitations and recommend that any questions be directed to an HCP or the trial participant's investigator.
- ways to support investigators who would need to provide paper copies to their participants locally.

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## 7. Appendices

**Appendix 1: Planning, Development, Translation and Dissemination of Lay Summaries**

### 7.1.1 Introduction

Appendix 1 offers additional recommendations from the Roadmap initiative stakeholders including current experiences of this group on lay summaries. More information on the Roadmap initiative is available at EFGCP[41] and EFPIA[42] websites.

### 7.1.2 Considerations on Secondary Endpoint Presentation

When deciding on the selection of secondary endpoints to be presented in the LS, sponsors could examine the list of endpoints defined in the protocol and consider the potential value to readers, considering factors such as:

- patient relevance (interest or value to patients),
- trial participant burden and risk (involvement of complex assessments, major time investment, invasive sampling),
- clinical relevance (representativeness of the main rationale of the trial, or identification as major or key in the protocol),
- statistical power considerations,
- complexity of concepts (feasibility of explanation in plain language),
- public availability of data elsewhere (e.g., EU Clinical Trials Register[8] or ClinicalTrials.gov[43]).

If sponsors choose to include secondary endpoint information in the LS, the following are important considerations:

- clear separation, in layout, description and emphasis, between the primary and the secondary endpoints.
- appropriate level of detail according to the statistical rigor with which the endpoint was analysed; consideration of whether the investigation was hypothesis testing or hypothesis generating:
    - e.g., quantitative presentation of data may be appropriate for discussion of a statistically powered comparison;
    - e.g., an aggregate approach with simple narrative statements may be suitable for complex descriptive data such as multiple pharmacokinetic parameters. Readers may be referred to other sources of more detailed information such as the technical summary, if applicable (per the EU CT Expert Group).
- including clear statements of limitations of the results (e.g., plain language explanation that some tests are not designed for comparison between groups, or that more participants would need to be studied to draw statistically valid conclusions).

### 7.1.3 Considerations on LS in Complex Clinical Trials

In planning the timing of delivery of individual LS within an overall complex design, sponsors need to consider the following:

- End of trial definitions in the protocol(s) (whether the end of a cohort or sub-protocol is defined as the end of that individual trial).

- Regulatory aspects (for example, whether sub-protocols are registered as individual trials with separate EudraCT numbers or as part of a single trial) and the timing of the regulatory requirement for LS delivery.
- The potential impact on data integrity of communicating results before the overall end of a complex trial (for example, the effect of knowledge of results from other cohorts on ongoing physician and participant perceptions)[13].
- The LS dissemination strategy presentation in the PIS/ICF if LS are planned before the complete end of the trial and upload of the LS on the final results to the EU Portal.
- Consistency with any publication/disclosure policy described in the trial protocol[16].

**7.1.4 Planning Patient Involvement**

The collaboration between industry or academic sponsors and patients or representatives of the public should be carefully arranged as part of the overall LS planning process. Finding a qualified partner and negotiating contractual conditions can be time consuming. Existing long-term relationships with acknowledged patient organisations or trained young patient groups can thus ease the involvement of patients into the LS process. It is recommended to work with the same group of patients for developing all patient facing materials for the same trial to ensure consistency.

It is important to plan the roles and expectations of patient or public representatives in each specific LS activity and to keep contributors motivated. The level of knowledge of the patient or public representative should be adequate to perform the task(s) requested in the LS process. In therapeutic studies, knowledge of the disease conditions and therapeutic options is a prerequisite; therefore, the involvement of representatives of the general public should be limited to user testing for LS readability.

Drawing up a patient involvement plan is strongly encouraged, and the plan should detail the assignments, time frame, location of task execution, expected R&D methodology, language, and IT skills. Furthermore, the process, criteria, and timelines of finding patient collaborators should be described, as well as the costs of recruiting and compensating patients and public representatives. The plan should also delineate the interaction management as well as the quality infrastructure for patient involvement in the LS process.

Patient experts conducting reviews of LS should as far as possible be independent of the clinical trial sponsor. The independence of the patient reviewer is fundamental for ensuring best practice in the relationship across investigators and sponsors for delivering an objective, unbiased patient input. Patient expert reviewers should not have been involved in developing the LS; nor should they have been participants in the specific clinical trial. However, prior participation in other trials may be a benefit to capturing valuable insights.

The written agreement between the patient(s) and the sponsor should include disclosure of interests.

**7.1.5 Inviting Patients as Contributors**

Sponsors are advised to appoint a single point of contact in the LS project team from the outset who is committed to support the invited representatives and act as a liaison for all interactions between the project team and the invited representatives regardless of the time commitment and other dimensions of their involvement.

An information sheet written in lay language should accompany the invitation to participants and describe:

- the project,
- the purpose of the patient contribution,
- the expected skills,
- time frame and
- the financial conditions of the collaboration.

Although not a legal requirement in all countries, it is recommended to lay out the scope of the collaboration, conditions, responsibilities, rights, and obligations in a legal agreement between the parties and to ensure the availability of all signatures before the engagement is initiated[44]. Intellectual property and publication rights might also be included, if appropriate. Widely accepted contract templates for such an advisor/consultant role with lay language explanations of the legal terms should be used[45].

**7.1.6 Compensation of Patients and Public Contributors**

- The contribution of patients provides tangible value and should therefore be compensated using established compensation rules. Available and broadly respected fair market value guidelines should form the basis for the compensation strategy. In addition, the financial ranges and conditions for compensation should be described in detail in the legal agreement.
- If the patient is requested to travel within the agreed frame of collaboration, the sponsor should organise the trip and cover justifiable travel and accommodation costs. The patient should not need to ask for more than minimal reimbursement amounts. This ensures that all patients are able to contribute to the LS development and dissemination process and it also reduces any bias against the ability to cope with economic burden.

**7.1.7 Follow up with Contributors**

It is highly recommended to follow up with people who contributed to the development, review and testing of the LS. Beside the option of a “Thank You Letter” it is also good practice to report back to contributors on how their input was implemented and the possible improvements their contributions made to the LS. Feedback may also include which impact patients’ input made to general considerations for researchers, writers or for the future process of developing LS.

### 7.1.8 Estimated Efforts for LS Production

Table 7.1: Table of Estimated Effort for Lay Summary Production According to Trial Complexity

| Complexity Parameters to Consider | Low complexity LS* | Medium complexity LS* | High complexity LS* |
|---|---|---|---|
| **Trial design** | Simple; either randomised, non-randomised or open-label, e.g. 1 or 2 treatment arms | More complex (e.g. cross-over), with standard or Bayesian statistics, multiple treatment regimens/arms | Complex, with multi-factorial design, or with multiple complex treatment regimens/arms |
| **Complexity of therapeutic background** | Low complexity | More complex concepts to explain trial rationale | Conceptually complex (e.g., schizophrenia) |
| **Number or nature of endpoints to be described**** | Small number of endpoints, straightforward to explain in plain language. | Multiple endpoints, or endpoints that are complicated to explain | Multiple complex endpoints |
| **Number of LS drafts produced** | 2 drafts, plus a final | 3 drafts, plus a final | 4 drafts, plus a final |
| **Estimated effort (hours)***** | 30–70 | 50–90 | 80-110 |

* Definitions of low, med, high complexity will vary depending on vendor, organisation and contractor.

**Estimates are for LS production only. Estimates do not include project management time (quality control, communication with reviewers, conducting reviews, translations and delivery). Resources are blended model, globally located.

*** Estimated hours may vary as a writer with less experience in writing lay language may take longer to write a shorter LS. The availability of a LS template could make a difference.

### 7.1.9 Examples of General Phrases

Table 7.2: General Phrases

| Term or concept and what the phrase may contain. | | Lay language examples<br>Please note that examples in this column are for inspiration |
|---|---|---|
| 1 | Lay summary | This summary gives the public information about a research study called a 'clinical trial'. It is also written for people who took part in the study.<br>This document is a summary of a research study, called a 'clinical trial'. It is written for a general audience and for people who took part in the study. |
| 2 | Clinical trial | The purpose of the clinical trial was to compare treatment A with standard treatment/medicine B<br>The purpose of the clinical trial was to look at how well the medicine works and how safe it is.<br>The purpose of the clinical trial was to find the dose that is most effective and with less side effects. |
| 3 | Phase 1 clinical trial | This was a phase 1 study where a small number of healthy people took the medicine.<br>This was a phase 1 study. In phase 1 a small number of healthy people take the medicine to see if it is safe. |
| 4 | Phase 2 clinical trial | This was a phase 2 study. A phase 2 study is the first time a small number of patients take the medicine. The purpose is to find out how well a medicine works in people with a condition/disease/symptoms.<br>Medicine 'A' was tested in a small number of patients with type 2 diabetes. Doctors compared it with existing treatment for diabetes. They wanted to know what impact it had on their blood sugar.<br>A small number of patients with type 2 diabetes took the medicine. Doctors compared Medicine 'A' with an existing treatment for diabetes to understand how it affects patients' blood sugar. |
| 5 | Phase 3 clinical trial | This was a phase 3 study. In a phase 3 study researchers look at how well a medicine/treatment works and how safe it is in a large group of people with <disease>.<br>A large number of patients with heart disease took the medicine 'A'. Researchers compared the medicine with another medicine 'B' that is normally used/commonly used to treat heart disease. |
| 6 | Phase 4 clinical trial | This was a phase 4 study. This was carried out after the new drug was approved for use and a large number of patients took part. It looked at how well the treatment worked in the long-term and if there were side effects that researchers did not know about.<br>This was a phase 4 study. A phase 4 study is carried out after the drug was approved for use and a large number of patients take part. Researchers looked at how safe the medicine is in the long-term. |
| 7 | Only 1 single study – do not make treatment decisions based on only 1 study. | This summary only shows the results from this one study. Other studies may find different results. Do not use this summary to make decisions about or changes to your medicines without discussing it with your doctor. |

| | | |
|---|---|---|
| 8 | Randomisation | People in the study were split into x groups by chance (randomly). The researchers did this to make the groups as similar as possible. People in group 1 were given Medicine A and people in group 2 were given Medicine B. Medicine A is the new treatment that researchers study. Medicine B is the common treatment for this condition. By comparing Medicine A with Medicine B, researchers can tell if Medicine A works and/or is safe to use. |
| 9 | Arm of the study | This study had three groups or 'arms'. The first group took Medicine A. The second group took Medicine B. The third group took Medicine C (normal/common treatment for this condition/disease.) |
| 10 | Multi-arm | This is a multi-arm study. In this study, each of the four (3, 5, 6) different groups of patients received a different treatment. |
| 11 | Multi-stage | In this study, researchers found that Treatment A did not work as well as Treatment B. Because of this people in this group stopped taking Treatment A earlier than planned. And a new Treatment C was added to the study at this point. |
| 12 | Approved vs non-approved product (investigational product) | Treatment A is already approved for use by authorities. Doctors can prescribe the Medicine A to treat <disease/ condition>.<br>Treatment A is not yet approved by authorities to treat <disease/condition>.<br>Treatment A is already approved by authorities to treat <disease/condition X>. Researchers now wants to see how well it works to treat <disease/condition Y>. |
| 13 | Placebo | The new Medicine A was compared with a placebo. A placebo does not contain any medicine but looked like Medicine A. Comparison with placebo helped the researchers to understand how well Medicine A works and how safe it is. |
| 14 | Purpose of blinding | The study was a 'double-blind' study. This means that the doctor and the people in the study did not know who was getting which medicine. The researchers did this to make sure the results were not bias.<br>This study is called a 'single-blind' study. This means the study doctor did know which patients took the new treatment (Medicine A) and which took the comparison treatment (Medicine B). However, the patients did not know which medicine they took. The researchers did this to make sure the results were not bias. |
| 15 | Open-label treatment | Patients were either taking Medicine A or Medicine B. In all cases both the patients and the doctor knew which medicine they were taking |
| 16 | Differences in the numbers of randomised and treated participants. | In this study, xx men and women agreed to take part. Of these, only yy people took the medicine. |
| 17 | Statistical power – explaining the lack of power | The number of people who took part in the study was not large enough to show a real difference in outcomes between the groups. The differences could have happened by chance. |

| | | |
|---|---|---|
| 18 | Adverse reaction | Like all treatments, these medicines can cause side effects - although not everybody gets them. Adverse reactions are unwanted events that the study doctor/we thinks are related to the treatment in this study/trial. The table shows the number of patients who had adverse reactions. More adverse reactions were seen with the study treatment / medicine A/B.<br><br>The table shows the most common adverse reactions that people in the study reported. We have only shown those adverse reactions that were reported by more than 1 in 5 people.<br><br>We have only shown those adverse reactions which happened in more than 1 in 5 people in the study. |
| 19 | Serious adverse reactions (SAR) | A small number of people in this study had a serious adverse reaction. Two people had an abnormal heartbeat after taking drug A and both were sent to hospital. The study doctor considered both reactions to be related to the study medicine. |
| 20 | Adverse reaction of special interest | The researchers were particularly interested to know if any of the people had suicidal thoughts after taking Medicine A. Because of the seriousness of this adverse reaction, people in the trial were asked to report this if it happened to them. |
| 21 | Endpoints | The focus of/endpoint in this clinical trial of cancer treatments was 'Overall survival'. The study defines Overall survival as the number of people alive five years after treatment.<br><br>The endpoint in this clinical trial of cancer treatments was 'survival'. In this study we said that survival meant the number of people still alive five years after treatment. |
| 22 | 2nd endpoints | This trial also collected info about heart attack and stroke.<br><br>The secondary endpoints in this trial were the number of people who had heart attack and stroke. The study was not designed to determine if there was a difference between the groups.<br><br>Researchers were looking for additional effects on heart attack of the study medicine. We cannot be sure that there is a difference in the number of people having a heart attack or stroke between the group who took Medicine A and the group who took Medicine B. It may have happened by chance. |

| | | |
|---|---|---|
| 23 | Patient reported outcomes and HrQoL | The study also collected information on outcomes directly from patients. These outcomes were:<br>• pain, breathing, fatigue (symptoms)<br>• how well patients were able to walk/move (physical functioning)<br>• mood, coping (psychological state)<br>• ability to go to school, work, take part in community (social functioning)<br>• quality of their daily lives with the treatment<br><br>As well as the primary endpoint measuring blood glucose, the study also had a secondary endpoint. This was based on a 'patient reported outcome' which collected information about symptoms and side effects patients had - as well as the impact of the treatment on their daily lives.<br><br>Doctors measured the Quality of life of the people in the study with a questionnaire, called EQ-5D. |
| 24 | Absolute risks | The study was of 10,000 women who took oestrogen plus progestin for one year. The study found that there will be 8 more cases of breast cancer in hormone users compared with if they had not taken the medicine. So, the risk to the individual woman is low. |
| 25 | Other useful phrases | This study is just one of many studies. The studies are done to find out how best to use <generic drug or device name> to treat people with <disease/condition>.<br><br>In this study, researchers found/studied <describe the study outcome and how it will help patients and researchers>.<br><br>Findings from this study will be used: <select the most applicable from below or add text as appropriate for study><br>• in other studies to learn how <generic drug or device name> may help people.<br>• in other studies to compare <generic drug or device name> with other treatments/medicine/medical tools for <disease/condition>.<br>• to combine <generic drug or device name> with other treatments in people with <disease/condition>.<br>• to seek approval for using <generic drug or device name> to treat people with <disease/condition>.<br>• to further study the safety/efficacy of <generic drug name>.<br>• to further improve the most effective use of <generic drug name>. |

### 7.1.10 User Testing

Table 7.3: User Testing Steps

| Key steps in user testing | |
|---|---|
| 1. | Identify the key points in the summary – as a guide, this may be 12–15 points. |
| 2. | Test the information with potential readers of the summary - with a range of reading abilities and ages. |
| 3. | Develop a questionnaire which will:<br>• test findings and understandings of each point.<br>• elicit participants' general views on the LS. |
| 4. | Pilot the questionnaire on 2–3 users. |
| 5. | Administer the questionnaire individually to a cohort of 10 users. |
| 6. | Analyse the quantitative and qualitative data to identify the strengths and weaknesses of the LS. |
| 7. | Revise those parts of the LS where there have been shown to be problems, using good practice in information writing and design. |
| 8. | Test again on a new cohort of 10 users. |

### 7.1.11 Paediatric Trials

Table 7.4: Child Development, Comprehension and Learning by Age Group

| | Age ≤ 8 years | Age 9-11 years | Age 12-17 years |
|---|---|---|---|
| **Comprehension** | **5-6 years:**<br>Make connections based on what is said and done in a story. Able to link to their own experiences.<br>Use pictures to decode meaning and decode short words.<br>Limited attention span.<br>Begin to comprehend time.<br>**7-8 years:**<br>Understand books they can read themselves and those they listen to.<br>Create meaning from several details in a text or story.<br>Understand simple cause-effect concepts. | Use interesting words and phrases. Use evidence from text when discussing. Use glossaries to check meaning of words.<br>Able to identify details that support main messages.<br>Learn to justify inferences with evidence.<br>Develop understanding of concepts.<br>Able to make simple comparisons.<br>Begin to understand mutual dependence, and that people have different experiences and views. | Able to apply known concepts to new theoretical understanding.<br>Have a clear understanding of distinction between facts and fiction and the way they are presented.<br>Able to handle complex information and make comparisons.<br>Able to comprehend complexity/coherence/ inference in what they experience, read and are being told.<br>Have strong (own) sense of right and wrong, good and bad. |
| **Learning strategies** | Learn through storytelling and find it easier to engage with topics and issues they can make personal or emotional connections to (egocentric perspective). | Learn through personal experience and basic theoretical thinking, especially if interlinked.<br>Learn by mirroring other children of the same age.<br>Belonging to a group is becoming important. | Highly influenced by peer groups.<br>Focus on themselves and belonging to a group. Family support seems not important.<br>May want to challenge rules and recommendations. |

continued...

| | Age ≤ 8 years | Age 9-11 years | Age 12-17 years |
|---|---|---|---|
| **Scientific understanding** | Objects are made of specific materials.<br>There are different kinds of materials.<br>Objects have certain properties: weight, length, area, and volume. Properties can be described, compared and measured. (Observable properties: colours, hardness, flexibility, fluidity, solid forms).<br>Measurements are more reliable than common-sense impressions.<br>Measurement involves comparison.<br>Ideas can be evaluated through observation and measurement.<br>Instruments, such as microscopes, can extend our ability to observe and measure. | Solids, liquids, and air are forms of matter and share general properties.<br>There can be invisible pieces of matter (too small to see).<br>Combining two or more materials can produce a product with properties<br>different from those of the initial materials.<br>Measurements can be more or less precise.<br>Sources of measurement error can be examined and quantified.<br>Hypotheses and data are distinct. Ideas get strong arguments when they are supported by a pattern of data rather than simply one observation. | All matter is made of a limited number of different kinds of atoms, which are commonly bonded together in molecules and networks.<br>The properties of materials are determined by the nature, arrangement, and motion of the molecules that they are made of.<br>In chemical changes new substances are formed as atoms are rearranged into new molecules. The atoms themselves remain intact.<br>In physical changes, molecules change arrangement and/or motion but remain intact, so the chemical substanceremains the same. |
| **Numbers and maths** | **5-6 years:**<br>Able to count to 100.<br>Understand ½ and ¼ of a part or of a group.<br>**7-8 years:**<br>Understand and work with numbers up to 1000.<br>Understand simple fractions: 2/5 = 4/10. | **9-10 years:**<br>Learn basic percentages.<br>Understand and work with negative numbers.<br>Round numbers to nearest 10, 100 and 1000.<br>Understand and work with decimals. Round decimals to nearest whole number. | Work with ratio, proportion and percentages.<br>Round to nearest 10.000.000.<br>Understand basic ratio, scale factors, and equations.<br>Understand unequal sharing and grouping.<br>Work with infographics: pie-charts, 2D-diagrams: column, line and bar-charts. |
| **Grammar** | **5-6 years:**<br>Read one syllable words.<br>Use (read) capital letters and punctuation.<br>Use (read) common exception words.<br>**7-8 years:**<br>Read one-or two-syllable words that they can **decode** already but with a prefix or **suffix** added on.<br>Use (read) simple sentences made of main clauses. | Understand verbs to describe relationships of time and cause.<br>Understand expanded noun phrases to convey complicated information concisely.<br>Understand relative clauses: who, which, where, when, whose, that or with an implied relative pronoun.<br>Understand commas to clarify meaning or avoid ambiguity.<br>Understand the use of a column or bullet points to introduce a list. | Principles on writing for this age group follow recommendations for adults. Please see table 3.2. Health Literacy Principles (currently p.39) |

Table 7.5: Recommendations for Paediatric Lay Summary Content

| | Age ≤ 8 years | Age 9-11 years | Age 12-15 years |
|---|---|---|---|
| **Background knowledge** | Write at relevant level of knowledge about/experience with disease and intervention – this will vary according to the trial and the patient group. | | |
| **Perspective** | Write from the child's point of view. Focus on what the child did during trial participation and less on doctor, staff or lab-procedures. | Write from a group perspective including a limited number of people and how their different contributions helped researchers create new knowledge. | Write at population level. |
| **Representa-tiveness** | Use a limited number of people or characters:<br>Child, or boy and girl Doctor or nurse<br>Parent(s)<br>Make sure to reflect diversity of race, gender, ethnicity, class, disability and age. | Describe main characters and their connection to a larger group of maybe 10 or 20 children.<br>Make sure to reflect diversity of race, gender, ethnicity, class, disability and age. | May be easier to follow the study-flow and procedures when writing about specific characters.<br>Present variations at population level. |
| **Storyboard** | **Start:** Introduce characters. Present disease characteristics, relevant symptoms and how this affects the child. Frame the child as a unique contributor to research.<br>**Middle:** Describe trial-related actions, procedures and the child's experiences incl. side effects.<br>**End:** What the child learned, achieved, succeeded in – and what researchers learned. Acknowledge the child's contributions as part of the 'research-team'. | | |
| **Story** | Use familiar words to explain what happened / was done.<br>Reflect the child's point of view.<br>Describe:<br>• who were involved<br>• tool<br>• procedure<br>• purpose<br>Focus on what the child did during procedure/trial. Less on doctor's actions or scientific explanations.<br>Avoid time shifts, and changes in point of view. Choose content or stories with straightforward and time-reflecting descriptions that are easy to follow. | Reflect child's independence from parents in a narrative if applicable to the trial.<br>More children can be included in the narrative/story to show what different participants did or if they experienced different effects. | |

| | | | |
|---|---|---|---|
| **Treatment** | Describe how the treatment works/is expected to work in the body.<br>Describe the effect on the disease/symptom and how the child reacted – if any changes. | | |
| **Adherence** | Describe/show what the participant took/had, how often and for how long.<br>Example: "The child took two pills each morning for 28 days". | | |
| **Side effects** | Describe/show how the side effect made the child feel and how often. Include causation.<br>When presenting side effects always have an adult as part of the description/picture to make child-readers feel safe. | Describe how the side effect made the child feel and how often. Include causation.<br>E.g.: "The pill made the boy feel dizzy for 2-3 minutes", rather than "Dizziness occurred". | |
| **Numbers and scaling** | Use small denominators that are closer to "plausible" group sizes in human society (x/20).<br>Show percentages as infographics. | | |
| **Equality between participants** | Make sure that all participants are described as "heroes and "important contributors". Include children who took part in a control group, placebo group, group with negative results etc. | | |

Table 7.6: Recommendations for Paediatric Lay Summary Layout and Design

| | Age ≤ 8 years | Age 9-11 years |
|---|---|---|
| **Text, cartoon and animation** | The use of pictures, cartoons and storytelling is recommended.<br>Use text only to describe roles and names of characters and to support main messages in pictures and figures. | Simple text can be provided. |
| **Words / vocabulary** | Simple words, one-two syllable words are preferred.Common English exception words for age 6 and 7 – please see links. (helpful links are provided in the reference list) | Use words that they already understand with simple suffix (endings) E.g.: "cats", "'sleeping", and "quicker".<br>Common English spelling, words of ages 9 and 11 – please see links. (helpful links are provided in the reference list) |
| **Numbers, proportions and risk** | Use characters to show numbers and limit the size of numbers. | Use small denominators that are closer to "plausible" group sizes in human society (x in 5, 10, 50 or 100 people). |
| **Length of words, sentences, lines and paragraphs.** | Simple and short words can be used to present people or support messages of pictures.<br>E.g.: BOY, GIRL, MUM, DAD, DOCTOR, NURSE.<br>Names of characters: ANN, BEN. | Create sentences with 8-10 words.<br>Create paragraphs of 3-5 sentences.<br>Do not use subordinate clauses. |
| **Colours** | Use solid colours and limit the number of different colours | |
| **Paper, if printed** | Thick paper is best to avoid the other side from showing through.<br>Matt paper is better than glossy. | |

### 7.1.12 Step by Step Translation Process

Table 7.7: Step-by-Step Translation Process

| Step | Process |
|---|---|
| **1.Planning** | Before language translation is initiated, the source file (master LS) should be analysed in order to identify potential areas of ambiguity, regulatory compliance or risk areas of promotional or biased language. The analysis will enable decisions to be made regarding any specific instructions, checklists, glossaries, reviews or tools needed during the translation process for a specific trial. Translation planning should also cover any implications of interim reporting on the translation process. Finally, any specific file format requirements or translations to support visual/graphic elements should be considered. |
| **2.Forward translation** | Forward translation is the process of translating a source text (in this case the master LS) into a target language or languages (the country-specific LS in local language). Forward translation is performed by a qualified translator who is a native speaker or is fluent in the target language and has experience in the medical field/with clinical trials. |
| **3.Back translation (optional)** | This step is a strong quality control step which is recommended in communication of complicated, sensitive or patient-directed content. Back translation is the translation of a target text (the results of the forward translation) into the original source language (same language as the master LS). Back translations serve to control the quality of the forward translations, and, in some cases, they also serve a regulatory purpose. The back translator will not have access to the master LS but only the forward-translated file, which ensures an unbiased quality control check. This process will reveal any discrepancies or language "drifts" resulting from the translation process. A back translator is independent of the forward translator and is typically a native speaker or is fluent in the source language. |
| **4.Comparative review (optional)** | A third resource will perform a comparative review in which the back translated LS will be compared with the master LS to detect and investigate any discrepancies between the source LS and the translation. The forward translation may be revised during the review process to resolve any issues and arrive at the best possible "faithful" translation. Comparative reviewers have access to the master LS and the back translated summaries and are typically native speakers of the original source language. |
| **5.Final Quality Assurance inspection** | A final thorough quality inspection is recommended if DTP (Desktop publishing) or other production quality steps have been included as part of the final file production. |
| **6.Delivery and certification** | The final output is the translated LS along with any translation certificates, in cases in which the sponsor wishes to engage a language service provider and obtain translation certification. |
| Note that step 3. Back translation and step 4. Comparative review can be replaced by a linguistic review in case of resource or other restraints. | |

### 7.1.13 Technical Distribution Method

Table 7.8: Technical Distribution Methods: Benefits and Risks

| Distribution method | Benefits | Risks |
|---|---|---|
| **Direct methods** | | |
| **Email** from the investigator to the trial participant. | More rapid distribution than awaiting a scheduled face-to-face meeting with the investigational site.<br>Some LS research indicates that trial participants prefer email notification.<br>Blind or illiterate trial participants may have the application to convert text to voice. | The trial participant may not have email/internet access or may change his/her email address.<br>Receiving the LS without explanation or the possibility for immediate clarification on questions/potential misconceptions from the investigator.<br>Investigational site budgets may increase. |
| LS posted to the **sponsor's investigator trial portal**. The investigational site is requested to distribute the LS via a face-to-face meeting and/or email/ postal service. | The LS alleviates potential investigator concern on how to simplify technical results for review with the trial participants.<br>Facilitates the investigator's discussion with trial participants about the overall results, individual results and the medicine that the trial participant received.<br>Efficient distribution method if the sponsor has a trial investigator portal established.<br>Confirmation that the investigational site accessed the LS on the portal. | The sponsor has no trial investigator portal.<br>The investigational site may forget their sponsor's trial portal password.<br>There is no guarantee that the investigational site(s) will retrieve the LS from the trial portal.<br>There is no guarantee that the investigational site will distribute the LS to the trial participants via a face-to-face meeting and/or email/postal service.<br>The sponsor trial investigator portal may have technical issues.<br>Investigational site budgets may increase. |
| LS posted to the **institution's individual patient portal** which only the trial participant can access with direct login credentials. | Efficient distribution to trial participants through the investigator's institutional patient portal.<br>Trial participant has access to all personal medical records, tests and the LS from the trial.<br>The trial participant receives an email notification when new information is posted to their own portal. | The trial participant may not have internet access.<br>The trial participant may not access to the institution's portal for the LS.<br>The investigator's institutional portal has technical issues.<br>There is a risk of misinterpretation of the LS by the trial participant receiving the LS without explanation from the trial investigator.<br>Blind/illiterate trial participants may not be able to access the portal autonomously |

| | | |
|---|---|---|
| Sponsor uses **social media** (Facebook, Twitter, LinkedIn, etc.) to announce location of the LS. | Distribution method reaches a wide audience.<br><br>May facilitate participation interest in future research. | May require sponsor legal review of this distribution method.<br><br>Not all trial participants use social media.<br><br>The LS is written to trial participants. May need to change the text.<br><br>There is a risk of misinterpretation of the LS by the trial participant/public without explanation from a trial investigator or clinical professional.<br><br>The sponsor may need to expand call centre funding to address calls to understand the results.<br><br>Blind/illiterate trial participants may not be able to access the portal autonomously. |
| **Indirect methods** | | |
| LS posted on a **sponsor's public website**. | The trial participants and the public at large have access to the LS.<br><br>The trial participants receive a card at their PLV notifying them of the sponsor's public website and the future posting of the LS.<br><br>Cost effective if the sponsor public website exists.<br><br>Metrics are easily obtained.<br><br>A link to sponsor's public website is provided on ClinicalTrials.gov or other public registries or on the investigator's institutional/clinic patient portal.<br><br>IEC/IRB review is not required. | The investigational site does not notify the trial participant at their individual PLV explaining where and when the LS will be available.<br><br>There is a risk of exposure to promotional material on the website which the reader will encounter on the way to accessing the LS.<br><br>The sponsor website is not available in local languages.<br><br>The trial participant may forget the URL which was provided at their individual LPLV.<br><br>The trial participant does not have access to the internet.<br><br>Blind/illiterate trial participants may not be able to access the portal autonomously.<br><br>There is a risk of misinterpretation of the LS by the trial participant without an opportunity for an explanation from the trial investigator. |

| | | |
|---|---|---|
| LS is posted by the sponsor on a **third-party public website**. | The trial participants receive a card from the investigational site at their LPLV notifying them of the third-party public website.<br><br>Option of the trial participant to self-register for an email notification when the LS is posted on the third-party managed public website.<br><br>Option of the third-party website to contain an "opt in or opt out" by the trial participant before viewing the LS<br><br>Metrics are easily obtained.<br><br>A link to the third-party public website is provided on ClinicalTrials.gov or other public registries or on the investigator's institutional/clinic patient portal. | This distribution method requires additional sponsor funding for the third-party website and for each LS to be posted publicly.<br><br>The investigational site does not notify the trial participant at their PLV explaining where and when the LS will be available.<br><br>The third-party website is not available in local languages.<br><br>The trial participant may forget the URL, which was provided at their PLV.<br><br>The trial participant does not have access to the internet.<br><br>The trial participant's email address may change, and the third party is not informed by the trial participant.<br><br>Blind/illiterate trial participants may not be able to access the portal autonomously.<br><br>There is a risk of misinterpretation of the LS by the trial participant without an opportunity for an elaboration from the trial investigator. |
| Step 1: Sponsor emails the link of the LS public location to specific patient organisations at global, regional and/or local levels.<br><br>Step 2: The patient organisations use their channels (**email, social media**) to distribute the LS link. | Efficient use of an existing Sponsor Patient Advocacy network.<br><br>Distribution method reaches public sector with or interested in the disease.<br><br>May facilitate participation interest in future research. | The sponsor has no contact with Patient Advocacy networks.<br><br>Incomplete notification of global, regional, local patient organisations.<br><br>The patient organisation shuts down (no website).<br><br>The patient organisation publishes the LS rather than providing the link to a sponsor or third-party public website.<br><br>There is a risk the LS viewer thinks the patient organisations could address any questions about the LS.<br><br>Blind/illiterate trial participants may not be able to access the portal autonomously.<br><br>The patient organisation may ask for sponsor funding, increasing development costs. |

### 7.1.14 Non-technical Distribution Method

Table 7.9: Non-Technical Distribution Methods: Benefits and Risks

| Distribution method | Benefits | Risks |
|---|---|---|
| **Direct methods** | | |
| A **face-to-face** meeting is scheduled and conducted by the investigational site(s) with the trial participant. | Alleviates potential investigator concern on how to simplify technical results for review with trial participants.<br>Facilitates the investigator discussion with the trial participant about the overall results, individual results and the medicine which the trial participant received.<br>Trial participants can ask questions/ obtain dialogue. | There is no guarantee that the investigational site(s) will conduct a face-to-face review of the LS with the trial participant.<br>The trial participant may opt out of a face-to-face meeting with the investigator.<br>The investigational site budgets may increase. |
| **Indirect methods** | | |
| Mailed via **postal service** from the investigational site to the trial participant. | More rapid distribution than awaiting a scheduled face-to-face meeting with the investigational site.<br>Some LS research indicates that trial participants prefer postal notification. | Investigational site does not mail the LS to the trial participants.<br>Trial participants may move and not leaving a forwarding postal address.<br>Risk of misinterpretation of the LS by the trial participant receiving the LS via postal service without explanation from the trial investigator.<br>Blind/illiterate trial participants may not be able to access the portal autonomously.<br>Investigational site budgets will increase. |

**Appendix 2: List of Glossaries**

Most glossaries provide definitions of various terms rather than accurate translations into lay words.

**Drug Discovery Glossary**
University of Oxford
**http://russell.chem.ox.ac.uk/resources/Drug_Discovery_Glossaryv2.PDF**

**Drugs@FDA Glossary of Terms**
**https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms**

**EunetHTA Glossary**
The aim of the Glossary of Health Technology Assessment (HTA) Adaptation Terms is to identify and highlight key words and concepts that are easily misunderstood between countries. It provides a series of descriptions for such terms and contains examples of where the usage of these terms may differ between countries.
This glossary is intended to be a resource for identifying issues related to different uses and meaning of various HTA terms with a view to aiding the adaptation of HTA reports between settings.

**https://www.eunethta.eu/glossary-of-hta-adaptation-terms/**

**European Union Clinical Trial Register**
The explanations are provided for the benefit of public users of the system and to enhance general understanding of terms used. They are not intended as the regulatory definitions and should not be used or substituted for the regulatory definitions and guidelines.
**https://www.clinicaltrialsregister.eu/doc/EU_Clinical_Trials_Register_Glossary.pdf**

**European Medicines Agency (EMA) Glossary**
This glossary gives definitions for the main regulatory terms used on this website and in EMA documents.
**https://www.ema.europa.eu/en/about-us/about-website/glossary**

**European Patients' Academy on Therapeutic Innovation (EUPATI) Toolbox Glossary**
The search machine Toolbox Glossary contains lay person terms and information on medicines research and development for patients and the general public. The Toolbox Glossary is available in Danish, Dutch, English, French, German, Italian, Japanese, Polish, Portuguese, Romanian, Russian, Spanish and Swedish.

**https://learning.eupati.eu/mod/glossary/view.php?id=109**

**FDA Drug Development Tool (DDT) Glossary**
**https://www.fda.gov/drugs/drug-development-tool-qualification-programs/ddt-glossary**

**FDA Glossary of Terms on Clinical Trials for Patients Engagement Advisory Committee**
**https://www.fda.gov/media/108378/download**

**FDA Patient-Focused Drug Development Glossary**
This glossary defines terms that will be used in the series of methodological Patient-Focused Drug Development (PFDD) Food and Drug Administration (FDA) guidance documents that are required by the 21st Century Cures Act, and part of commitments made by FDA under the 6th authorisation of the Prescription Drug User Fee Act (PDUFA VI). The goal of this glossary is to provide standardised nomenclature and terminologies related to patient-focused medical product development. As the science of patient input matures, or in response to comments received on the FDA's guidance, this

glossary may be updated.
**https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary**

**Glossary of Evaluation Terms for Informed Treatment (GET-IT) Glossary**
The GET-IT glossary provides plain language explanations of terms that people might need to understand if they wish to assess claims about treatments. The glossary is specifically intended to be useful to people without a research background, particularly those wanting to make an informed choice about a treatment, communicating research evidence to the general public or teaching others about how to assess claims made about treatments.
**http://getitglossary.org/**

**Glossary of Drug Safety Terms**
Some terms used in drug safety can vary in how they are interpreted and used. This glossary largely reflects relevant International Council for Harmonisation (ICH) (www.ich.org) and/or European regulatory agency definitions. Sometimes more than one interpretation has been added.
**https://globalpharmacovigilance.tghn.org/resources/glossary/**

**Glossary of Terms used in Drug Development/Access**
**https://voisinconsulting.com/glossary**

**Glossary of Terms and Symbols Used in Pharmacology – Boston University**
**http://www.bumc.bu.edu/busm-pm/academics/resources/glossary/**

**Just Plain Clear Glossary**
United Health Group
**https://www.justplainclear.com/en**

**Lay Glossary of Medical Terms**
Stanford University Research Compliance Office
**https://researchcompliance.stanford.edu/panels/hs/forms/definitions**

**Medical Terms in Lay Language - University of Iowa**
Portal glossary for alternative lay language for medical terms in consent forms.
**https://hso.research.uiowa.edu/medical-terms-lay-language**

**Multi-regional Clinical Trials Center (MRCT) - Health Literacy in Clinical Research**
The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard
Portal for health literacy in clinical research throughout the trial life cycle including glossary.
**https://mrctcenter.org/health-literacy/tools/overview/glossary/**

**National Cancer Institute - Dictionary of Cancer Terms**
Portal with interactive search glossary for 8,465 English terms related to cancer and medicine
**https://www.cancer.gov/publications/dictionaries/cancer-terms/search?q=heman&redirect=true**

**National Comprehensive Cancer Network (NCCN) Informed Consent Language (ICL) Database**
Portal with interactive search glossary that contains more than 2,300 standardised lay language descriptions of risks and events associated with clinical research
**https://www.nccn.org/clinical_trials/informed_consent.aspx**

**National Center for Biotechnology Information (NCBI) - BEST (Biomarkers, Endpoints, and other Tools) Resource**
**https://www.ncbi.nlm.nih.gov/books/NBK338448/**

**National Institute for Health Research (NIHR) Involve - Jargon Buster**
Portal with interactive search glossary. The glossary contains definitions of terms commonly used in public involvement in health research.
**https://www.invo.org.uk/resource-centre/jargon-buster/**

**Pharma-IQ Glossary**
A glossary of keywords, acronyms and general terminology used in day-to-day professional work, compiled by Pharma IQ
**https://www.pharma-iq.com/glossary**

**Plain Language Medical Dictionary - University of Michigan Taubman Health Sciences Library**
Portal with interactive search glossary for medical terms in plain language, contains 1,100 terms in English.
**https://www.lib.umich.edu/plain-language-dictionary**

**R&D Chemicals Glossary**
This is a glossary of terms and abbreviations used in the drug discovery industry.
**https://www.rdchemicals.com/glossary.html**

**World Health Organization (WHO) Glossary**
**https://extranet.who.int/pqweb/content/glossary**

**Appendix 3: Other Guidance References**

**General Guidance on Lay Summaries**

**European Patient Forum (EPF) Position: Clinical Trial Results – Communication of the Lay Summary**
March 2015
**https://www.eu-patient.eu/globalassets/policy/clinicaltrials/epf-lay-summary-position-final_external.pdf**

**Multi-Regional Clinical Trials (MRCT) Draft Food and Drug Administration (FDA) Guidance on Provision of Plain Language Summaries**
The MRCT Center, in collaboration with TransCelerate Biopharma, Inc. submitted to FDA for consideration a draft guidance document on provision of plain language summaries for trial participants. The document was endorsed by 36 signatories, including patient advocacy groups and professional associations. **https://mrctcenter.org/wp-content/uploads/2017/06/2017-06-13-MRCT-Draft-FDA-Guidance-Return-of-Aggregate-Results.pdf**

**Multi-Regional Clinical Trials (MRCT) - Return of Aggregate Results**
Launched in 2013, the MRCT Center and its collaborators developed resources to lower barriers for returning results, created a number of useful tools and published a guidance for the clinical trial community. The practical guidance document and toolkit were developed for use by all clinical trial sponsors, including academia, industry, non-profit and government organisations**.** As of December 2017, version 3.1 is available
**https://mrctcenter.org/blog/projects/return-of-results-to-participants/)**

**Reflection Paper – EFPIA Guiding Principles on Layperson Summary**
**https://www.efpia.eu/media/25661/reflection-paper-efpia-guiding-principles-on-layperson-summary.pdf**

**Summaries of Clinical Trial Results for Laypersons.**
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. Version 2, 5 February 2018.**https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf**

**TransCelerate Biopharma Inc. Layperson Summaries of Clinical Trials: An Implementation Guide**
This guide provides general principles helping sponsors prepare and distribute layperson summaries to the general public and trial participants to implement the obligations of the European Union Clinical Trial Regulation (EU CTR) No 536/2014.
**http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/02/Implementation-Recommendations_20Jan17_Final.docx**

**TransCelerate Recommendations for Drafting Non-Promotional Lay Summaries of Clinical Trial Results**
A guide intended to provide general principles to help sponsors prepare LS in a manner that reduces the risk that the summaries could be perceived as promotional, which would raise regulatory concerns
**http://www.transceleratebiopharmainc.com/wp-content/uploads/2015/04/TransCelerate-Non-Promotional-Language-Guidelines-v10-1.pdf**

**Guidance on Patient Involvement**

**EUPATI Guidance for Patient Involvement in Industry-led Medicines R&D**
The guidance article is for all stakeholders aiming to interact with patients on medicines research and development (R&D). The EUPATI guidance documents aim to support the integration of patient involvement across the entire process of medicines research and development. This relates to activities pre-approval and post marketing, involving individuals and groups of patients.
**https://www.frontiersin.org/articles/10.3389/fmed.2018.00270/full**

**Good Participatory Practice (GPP) Guidelines**
AVAC and UNAIDS
The guidelines provide trial funders, sponsors and implementers systematic guidance on how to effectively engage with all stakeholders in the design and conduct of biomedical human immunodeficiency virus (HIV) prevention trials, including development, planning, implementation, and conclusion of a trial, including dissemination of trial results. The guidelines are available in multiple languages, Arabic, Chinese, English, French, Khmer, Portuguese, Russian, Spanish, Thai and Vietnamese.
**https://www.avac.org/good-participatory-practice**

**INVOLVE Briefing Notes for Researchers, NHS**
National Institute for Health Research - Involve
The briefing notes explain the different ways that patients and members of the public are involved in research. They will help to plan, resource and support patient and public involvement in research.
**https://www.invo.org.uk/wp-content/uploads/2014/11/9938_INVOLVE_Briefing_Notes_WEB.pdf**

**Meaningful Engagement of People with Dementia - A Resource Guide**
The Resource Guide provides tools, resources and strategies to assist organisations in promoting meaningful engagement with people who have dementia. The guide contains principles for collaboration, practical strategies and resources that enhance the process of engagement. Also, assessment tools are included for the organisation to assess how well they are engaging with people who have dementia.
**https://alzheimer.ca/sites/default/files/files/national/meaningful-engagement/meaningful_engagement_e.pdf**

**PFMD Patient Engagement Quality Guidance**
This is a practical guide to **planning, developing and assessing the quality of patient engagement** activities and projects throughout the development and lifecycle of medicines. The guidance is for patient engagement that takes place at any point along the research and development continuum and can be applied to health and social research.
**https://patientfocusedmedicine.org/the-patient-engagement-quality-guidance/**

**Guidance on Writing for Specific Groups/Populations**

**Writing Dementia-friendly Information**
The document provides tips for writing easy to read and understand information to people with dementia. Language, style, length and format can all have a big impact on making a document understandable. However, people with dementia find written information difficult to read and understand.

**https://www.dementiavoices.org.uk/wp-content/uploads/2013/11/DEEP-Guide-Writing-dementia-friendly-information.pdf**

**Guidance on Readability Formulae**

**The Fry Readability Formula**
Edward Fry, A Readability Formula That Saves Time, Journal of Reading, Vol. 11, No. 7 (Apr., 1968), pp. 513-516, 575-578
**https://www.jstor.org/stable/40013635?seq=1**

**The Flesch–Kincaid Readability Score.**
**https://www.webfx.com/tools/read-able/flesch-kincaid.html**

**Guidance on User Testing**

**Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use**
Revision 1, 12 January 2009 by the European Commission
**https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf**

**Tips for Organisations Wanting to Consult People with Dementia about Written Documents**
The Dementia Engagement and Empowerment Project (DEEP) guides aim to support the involvement of people with dementia. Some are aimed at DEEP groups, others at organisations wanting to work well with people with dementia. They have all been co-produced with people with dementia.
**https://www.dementiavoices.org.uk/wp-content/uploads/2013/11/DEEP-Guide-Consulting-about-written-documents.pdf**

**List of References for Patients on Medicines R&D**

**Testing Treatments Interactive (TTi)**
An interactive website about how we tell whether one treatment is better than another; in other words, about what constitutes a “fair test” of the effects of treatments. The English National Institute of Health Research is funding the development of TTi. The e-book, testing Treatments, included shows how everyone can play a part in promoting better research for better healthcare.
**http://www.testingtreatments.org/**