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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>ADR</td>
<td>Adverse Drug Reaction</td>
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<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>AESI</td>
<td>Adverse Event of Special Interest</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>COA</td>
<td>Clinical Outcome Assessment</td>
</tr>
<tr>
<td>CSR</td>
<td>Clinical Study Report</td>
</tr>
<tr>
<td>CTCAE</td>
<td>Common Terminology Criteria for Adverse Event Reporting</td>
</tr>
<tr>
<td>CTIS</td>
<td>Clinical Trials Information System</td>
</tr>
<tr>
<td>CTR</td>
<td>Clinical Trial Regulation</td>
</tr>
<tr>
<td>DDT</td>
<td>Drug Development Tool</td>
</tr>
<tr>
<td>DEEP</td>
<td>Dementia Engagement and Empowerment Project</td>
</tr>
<tr>
<td>EEA</td>
<td>European Economic Area</td>
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<tr>
<td>EFGCP</td>
<td>European Forum for Good Clinical Practice</td>
</tr>
<tr>
<td>EFPIA</td>
<td>European Federation of Pharmaceutical Industries and Associations</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
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<tr>
<td>EPF</td>
<td>European Patient Forum</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>EUPATI</td>
<td>European Patients’ Academy on Therapeutic Innovation</td>
</tr>
<tr>
<td>eYPAGnet</td>
<td>European Young Person’s Advisory Group Network</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>GET-IT</td>
<td>Glossary of Evaluation Terms for Informed Treatment</td>
</tr>
<tr>
<td>GPP</td>
<td>Good Participatory Practice</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HTA</td>
<td>Health Technology Assessment</td>
</tr>
<tr>
<td>IALS</td>
<td>The International Adult Literacy Survey</td>
</tr>
<tr>
<td>IBD</td>
<td>Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>ICF</td>
<td>Informed Consent Form</td>
</tr>
<tr>
<td>ICH</td>
<td>International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use</td>
</tr>
<tr>
<td>ICL</td>
<td>Informed Consent Language</td>
</tr>
<tr>
<td>IPPOSI</td>
<td>Irish Platform for Patient Organisations, Science and Industry</td>
</tr>
<tr>
<td>IRB/IEC</td>
<td>Institutional Review Board/Independent Ethics Committee</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
</tr>
<tr>
<td>ISPOR</td>
<td>The Professional Society for Health Economics and Outcomes Research</td>
</tr>
<tr>
<td>LS</td>
<td>Lay Summary</td>
</tr>
<tr>
<td>LPLV</td>
<td>Last Participant/Patient Last Visit</td>
</tr>
<tr>
<td>MDR</td>
<td>Medical Device Regulation EU 2017/745</td>
</tr>
<tr>
<td>MedDRA</td>
<td>Medical Dictionary for Regulatory Activities</td>
</tr>
<tr>
<td>MRCT</td>
<td>Multi-Regional Clinical Trials</td>
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<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>NAP</td>
<td>National Academies Press</td>
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<tr>
<td>NCBI</td>
<td>National Center for Biotechnology Information</td>
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<tr>
<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
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<tr>
<td>NIHR</td>
<td>National Institute for Health Research</td>
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<tr>
<td>PDUFA</td>
<td>Prescription Drug User Fee Act</td>
</tr>
<tr>
<td>PFDD</td>
<td>Patient-Focused Drug Development</td>
</tr>
<tr>
<td>PFMD</td>
<td>Patient-Focused Medicines Development</td>
</tr>
<tr>
<td>PhRMA</td>
<td>Pharmaceutical Research and Manufacturers of America</td>
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<tr>
<td>PIS</td>
<td>Patient Information Sheet</td>
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<tr>
<td>QA</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>QC</td>
<td>Quality Control</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research and Development</td>
</tr>
<tr>
<td>RA</td>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
</tr>
<tr>
<td>SAR</td>
<td>Serious Adverse Reaction</td>
</tr>
<tr>
<td>SME</td>
<td>Small and Medium-sized Enterprise</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
</tr>
<tr>
<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
</tr>
<tr>
<td>TTi</td>
<td>Testing Treatments interactive</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
<tr>
<td>WAI</td>
<td>Web Accessibility Initiative</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
1. INTRODUCTION

This “Good Lay Summary Practice” (hereinafter referred to as the “GLSP”) provides recommendations for the patient-centric preparation and dissemination of summaries of results from clinical trials in lay language as required by the EU Clinical Trial Regulation 536/2014 and by global transparency commitments of pharmaceutical and academic sponsors.

Regulation (EU) No 536/2014 of the European Parliament and of the Council, (hereinafter referred to as the “EU CTR”), was issued on 16 April 2014. Article 37 of the EU CTR requires trial sponsors to submit a summary that is understandable to laypersons (hereinafter referred to as a “lay summary” or “LS”) for each clinical trial with pharmaceuticals. The content required in such lay summary is listed in Annex V of the EU CTR and will accompany a technical results summary, the content of which is laid out in Annex IV.

At the time of publication of this GLSP, the date of application of the EU CTR has not yet occurred.

1.1 Background

Transparency and the right of citizens to access clinical study and toxicology reports submitted to the European Medicines Agency (EMA) is a guiding principle which was endorsed in January 2020 by the European Court of Justice. In addition, consistently and reliably presenting the results of all clinical trials in easily understandable language to the public and in particular to patients, has been recognised by global stakeholders involved in Patient Engagement.

Lay summaries can serve multiple beneficial purposes including to ensure transparency, knowledge- and trust building in clinical research in the public domain and to benefit current and future clinical trial participants. However, the practice of patient involvement in the lay summary process and with the purpose of supporting sponsors’ efforts to better meet patients’ needs has not yet been consistently established. By the same token, the sharing of multi-stakeholder developed best practices, such as those presented in this GLSP, are expected to facilitate patient engagement as well as the development and dissemination of LS which are understandable to laypersons (as intended in Article 37 of the EU CTR).

Discussions across industry and academia have revealed that there is not yet enough awareness among researchers, sponsors, patients/trial participants and healthcare professionals about the EU CTR requirements for LS. The core management group of the “Roadmap Initiative to Good Lay Summary Practice,” led by the European Forum for Good Clinical Practice (EFGCP) and the European Federation of Pharmaceutical Industries and Associations (EFPIA), was thus established to work with representatives from various stakeholder groups to find a systematic, realistic and tangible approach to implement LS by the date of application of the EU CTR.

Purpose & Scope of the Good Lay Summary Practice

Per EU CTR, lay summaries are required for interventional clinical trials with medicinal products in adult and paediatric populations conducted in the EU/EEA, and per EU Paediatric Regulation 1901/2006, Recital 31 for trials included in a paediatric investigation plan (including trials executed outside the EU/EEA). The EU CTR does not call for LS on non-interventional or medical device trials. However, the recommendations provided in the GLSP can be useful in the preparation of lay summaries for such trials, albeit considering that some EU CTR-defined elements may not apply, including 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."

The GLSP expands on the existing recommendations of the “Expert Group on clinical trials for the implementation of EU Clinical Trial Regulation 536/2014” (hereinafter referred to as the “EU Expert Group”)\(^5\). It offers advice and practical considerations to trial sponsors for the planning, development, translation and dissemination of the LS (For the full text of the EU Expert Group Recommendations, refer to Appendix 2).

As for the scope and intentions of the GLSP, the following should be observed:

- Patient involvement is generally recommended in the preparation and dissemination of a LS to ensure its suitability, relevance and successful communication to the intended lay audience.
- Although the GLSP is founded on the EU CTR, it may also provide useful recommendations for lay summaries of trials in regions outside the EU/EEA territory.
- LS recommendations in this document apply to aggregate clinical trial results only; therefore, return of patient-level data to individual trial participants is out of scope.
- The need for specific skills and strategies for LS on paediatric trials is recognised and addressed in this document, although highlighting the limited experience available so far.
- 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.
- Where researchers or sponsors choose to voluntarily disseminate LS beyond EU/EEA, the scope will be at the discretion of the sponsor. However, some of the guiding principles described in the GLSP will still be relevant.

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

The target audience for the GLSP constitutes professionals who have been assigned the responsibility to develop and upload lay summaries to the Clinical Trials Information System (hereinafter referred to as the “CTIS”), as well as professionals who wish to provide LS outside of the mandatory EU CTR requirements. Developing summaries in plain language 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 (See also Section 3.3).

**Target Audience for the Lay Summary**

The target audience for the lay summary is "laypersons," which is the term referenced in the EU CTR, Article 37. The EU Expert Group also indicates that a primary audience for the LS is expected to be the general public\(^8\). It is a common conception that the actual audience of lay
summaries concentrates on people affected by disease, living with a condition or otherwise with an interest in the research results.

**Target audiences may therefore primarily include:**

- Participants/people who took part in the clinical trial.
- People from patient organisations who communicate with patients within specific disease areas.
- Individual patients who receive or seek treatment.
- Caregivers, including family members or other close relatives.
- Investors, funders or Payers/HTA professionals.

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".

**Terminology and Language**

Different terms are used for lay summaries 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 used throughout this document. Other terms used elsewhere include, but are not limited to, "Plain Language Summary", “Trial Results Summary” and “Simple Language Summaries”.

The GLSP includes a combination of legal obligations enforced by the EU CTR and recommendations based on experience across the stakeholders involved in the Roadmap Initiative. As a general principle, the use of the word “should” in this document refers to optional recommendations (anchored in ethical obligations and best practices), whereas use of the word “must” refers to legal requirements, as laid out in the EU CTR. In addition, recommendations are kept in general terms in acknowledgement of the diversity of the existing operating models and practices of different sponsors.

Unless otherwise stated, the order in which information is presented does not indicate or prescribe a linear process or suggest any correct order of priority. Company or research institutional standard operating procedures (SOPs) and other considerations may require activities to be performed in another sequence.

The content of the GLSP may evolve as lay summaries become more widely adopted. This includes practices and experience from developers and target audiences along with advancements in technological infrastructures. Also, any new regulatory requirements may demand updates to the GLSP.

**1.2 How to Use This Document**

The LS process can be organised into four overall phases including a Planning phase, a Development phase, a Translation phase and a Dissemination phase. While a phased approach is neither part of the EU Expert Group Recommendations, nor a regulatory requirement, a
stepwise approach will help sponsors secure proactive planning as well as a controlled execution and quality of the LS.

The phases and core activities suggested per each phase are depicted in the flowchart below and each phase is further defined in terms of input and output. It is recommended that the trial sponsor determines which output or deliverables may be desired before a next phase is initiated. For example, sponsors are encouraged to ensure that any LS templates are final and approved before the LS Development phase commences, and that the master LS in source language is reviewed, approved and "locked" before translations are initiated.

For easy navigation, this document is organized into the four phases mentioned above with Chapter 2 covering the Planning phase, Chapter 3 the Development phase, Chapter 4 the Translation phase and Chapter 5 the Dissemination phase.

The APPENDICES offer supplemental information with reference to chapters, sections or phases throughout the document. Appendix 1 is a list of members of the Roadmap Initiative that contributed to this Good Lay Summary Practice. Appendix 2 is a full copy of the EU Expert Group guidance document, and Appendix 3 contains additional useful information related to each phase. Finally, a list of glossaries is included in Appendix 4 as well as a number of additional guidance references in Appendix 5. For convenience, hyperlinks are included where feasible to enable cross-chapter or cross-section navigation.
1.3 Conclusions

This GLSP has been developed to accommodate legal requirements under the EU CTR while offering practical advice on the development and dissemination of high-quality results summaries designed for the lay audiences defined in this chapter. The document is organized into four phases to facilitate navigation not only during the LS process but also in the GLSP itself. The recommendations offered in this document are written by professionals to professionals who are responsible for lay summaries. As such, the language applied throughout the document is not itself reflective of the language recommended for successful results communication to a lay audience.

The following four chapters will cover the Planning, Development, Translation and Dissemination phases of LS projects.
2 PHASE 1: PLANNING OF THE LAY SUMMARY

Planning of the lay summary should commence during protocol development. Some aspects, such as cost implications and matters related to trial design, are pertinent prior to trial start whereas others may be considered closer to the time of LS production. Careful and proactive planning are strongly encouraged to ensure timely delivery of a high-quality and compliant LS. This chapter discusses various facets, such as timing, templates, costs, effort, communication and trial design, which should be taken into account during the Planning phase.

2.1 Timing of the Lay Summary

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 plain language terminology. If the documents are prepared by different writing teams, collaboration between these teams will be imperative.

According to Article 37, EU CTR (for clinical trials in adults only), the LS must be submitted no later than 12 months from the end of the clinical trial, defined as the last patient last visit (LPLV), or at a later point in time, as specified in the protocol. This requirement applies in all EU Member States concerned irrespective of the trial outcome and is consistent with the timing of the integrated Clinical Study Report (CSR) submission. For trials which include paediatric participants (participants less than 18 years old), the submission is due no later than six months from the end of the clinical trial. (Paediatric LS are addressed in Section 3.7 and in Appendix 3 Paediatric Trials. A LS should be available at the same time as the CSR and must be published in parallel with the technical summary.

Article 37, EU CTR, allows exceptions to be granted to the above regulatory timelines provided that the sponsor can present valid scientific reasons, and that such reasons are detailed in the protocol\(^5\). The LS must be based on the results presented in the CSR, and hence compliance is dependent on timely delivery of the information provided in the CSR and in the technical summary.

In addition, in order to protect commercially confidential information, a deferral may be accepted for up to 30 months after the end of the clinical trial in cases of non-therapeutic pharmaceutical development trials (Phase 0 or Phase 1)\(^6\).

Due to the regulatory constraints enforced by EU CTR, the timely delivery of clinical trial results calls for careful planning. The dissemination of lay summaries should be coordinated with the publication plans for the clinical trial in general but also with the regulatory requirements for posting results on databases such as EU Clinical Trials Register, CTIS (upon implementation of the EU CTR), ClinicalTrials.gov or similar. For multinational and multicentre trials, LS dissemination should be coordinated across trial sites, if distribution is planned via investigational sites, and in the interest of sharing identical information across all sites.

Finally, proactive planning of translations is imperative for successful results communication in local language. These aspects are discussed in Sections 4.2 and 4.3.

2.2 Lay Summary Production Overview

LS development approaches may differ according to the type of sponsor (commercial or academic) and may be adapted depending on available resources and the volume of clinical trials undertaken.
Use of a LS template (e.g., in line with the EU Expert Group’s Recommendation) is likely to aid efficient and consistent preparation of lay summaries. It may be helpful to pre-populate the template with general information on the trial, and hence create an outline ‘shell’ document, in advance of database release and trial results availability. Once final trial data are available, complete LS drafts 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 CSR. Trial team members, including the physician and scientific/statistical experts, can confirm that the LS represents the results accurately. Depending on organisational setup, sponsors may consider other reviewers to be involved, e.g. from legal or regulatory affairs. Also, patient(s) should be involved in the review process to ensure readability, as presented in Section 2.5. Quality control on the final LS should be carried out by independent reviewer(s) 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.

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 lay summary. Having finalised and “locked” the LS content in source language, the document can then be translated and disseminated as described in Chapters 4 and 5, respectively.

### 2.3 Cost Implications

For academic researchers, planning of the process and resources required for production and dissemination of a lay summary should begin with budgeting at the time when a research proposal for a clinical trial is submitted to a funding source. Cost implications are particularly important for academic, charity and Small Medium-sized Enterprise (SME) sponsors of clinical trials, who may not have existing in-house resources or the expertise to produce LS.

The major costs will account for staff with the proper communication skills and availability to invest the necessary working hours for the production of LS – mainly the preparation, writing and review of the LS. In addition, costs include translations of LS into local languages. Sponsors who decide to provide LS beyond mandatory EU requirements will need to plan for additional translation costs and/or dissemination costs.

Depending on the scale of the trial (number of participants, number of sites), and the geographic location of the LS responsible sponsor, the efforts and costs of disseminating a LS vary considerably and may be difficult to estimate at the time of funding application.

Additionally, remuneration for the functions involved in LS generation, including patient advisors and reviewers, may be considerable and should be taken into account in the Planning phase. If appropriate, representative patient involvement in relation to the development of the LS may require additional funding. (For additional information, see also Appendix 3 Compensation of Patients and Public Contributors).

It should be observed that funding bodies do not currently foresee budget allocation for LS preparation. Moreover, most funding bodies require eligible costs to have been incurred during the funding period. As previously mentioned, the LS is due six months or 12 months after LPLV, with a deferral period of up to 30 months for some trials. Therefore, if the LS is produced years after the initial 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 agency in advance.
2.4 Advance Stakeholder Communication

Investigators

Investigators should be made aware of their roles pertaining to the LS as early as possible. Introductory communications should explain the purpose of the lay summary and how trial participants will access the LS. The introduction should also indicate whether and how investigators expect to become involved in the dissemination of LS and where they can find further information. In case investigators are actively involved in the dissemination, it should be considered to include such responsibilities in the investigator agreement due to the time lapse between LPLV and trial results.

Ethics Committees

According to Recital 39 of the CTR, a summary of the results of the trial and a summary that is understandable to a lay person must be submitted to the single portal within the specified timelines and will thus be available to all involved ethics committees. LS are thus an element of a sponsor’s reporting obligations. In the EU regulatory framework under Directive 2001/20/EC², LS are not foreseen and are thus not an element of ethics committees’ review obligations. However, preparation of LS is becoming professional practice in pharmaceutical companies to increase transparency on research results to trial participants and the public.

In cases in which sponsors choose to disseminate LS beyond the EU/EEA territories or in certain cases deliver LS during trial conduct, it should be noted that different IRBs/IECs may have varying requirements. Compliance with local restrictions and standards in such cases is the responsibility of the sponsor. (For more information on interim reporting and LS dissemination during trial conduct, see Section 2.7)

A “Thank You Letter” to be sent to trial participants after the end of their participation in a running trial may be subject to ethical review in some countries, especially if it contains information on procedures after the end of the trial, such as availability of a LS and/or follow-up treatment options. Such “Thank You Letter” might require ethical review and favourable opinion in line with requirements for all other information provided to study participants in a running trial.

Trial Participants

At a minimum, for trials applicable under the EU CTR, the trial participant should be informed that LS will be made available in the CTIS and, to the extent possible, when the LS will be available through other distribution channels. To preserve their autonomy, permission from the trial participant or recipient may be needed before receiving the information³. However, generally there is now a greater appreciation that trial participants expect summary findings to be shared with them upon completion of the trial.

It is good practice to proactively inform trial participants in the ICF¹⁹ how and when they can access the trial results. In a short trial, it may suffice to make trial participants aware of the forthcoming LS via information contained in the PIS. However with a longer trial, it may be necessary to contact the trial participants before the end of the overall trial, e.g. at the individual patient’s last visit via direct communication such as a “Thank you Letter” (See Section 5.2).

2.5 Patient Involvement

Involving patients can be instrumental for achieving the objectives of lay summaries, and the expertise of patients should be regarded as valuable in ensuring the suitability of the LS for
patients, trial participants and the public at large. Patients add a different perspective on the
effects of a drug and can therefore bridge any gaps between what clinical researchers assume
matters to patients and what in reality matters to patients who live with the disease. Depending
on the patient input desired, one or several patients should be involved in the process of LS
planning, development, translation and dissemination.

The EU Expert Group encourages sponsors to “consider involving patients, patient
representatives in the development and/or review of the summary to assess comprehension and
the value of the information provided” (See Appendix 2 EU Expert Group Recommendations).

In order to clarify terminology applied for potential patient interaction presented in the GLSP, the
following distinctions are made, as defined by EUPATI:

Table 2.1: Types of Patients in Patient Engagement Activities

<table>
<thead>
<tr>
<th>Individual patients</th>
<th>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&amp;D) or regulatory processes, but their main role is to contribute with their subjective disease and treatment experience.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carers</td>
<td>Carers include persons supporting individual patients, such as family members, paid- or volunteer helpers.</td>
</tr>
<tr>
<td>Patient advocates</td>
<td>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.</td>
</tr>
<tr>
<td>Patient organisation representatives</td>
<td>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.</td>
</tr>
<tr>
<td>Patient experts</td>
<td>Patient experts, in addition to disease-specific expertise, have the technical knowledge in R&amp;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&amp;D.</td>
</tr>
</tbody>
</table>

It is important to bear in mind that involving individual patients in LS discussions does not ensure patient representativeness. Yet, patients contribute by providing perspectives that may be different than those of researchers and healthcare providers, and patients may also be able to identify important considerations, issues or terminology used in the patient community.

Timing and Type of Patient Involvement

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

Input may include:

- Consultation regarding the planning, identification and prioritisation of patient-relevant outcomes and endpoints. Can be performed or contributed to by patient experts.
Co-authoring or consultation regarding terminology used by patients, format and presentation of the LS. Can be performed by patient experts, patient advocates or patient organisation representatives.

Review results of the CSR. Can be performed by patients, patient advocates, or patient organisation representatives. User testing for readability can potentially also be assigned to representatives of the public.

Consultation regarding translations and dissemination of LS. Can be performed by patient experts or patient organisation representatives.

**Figure 2.1: Patient Involvement during LS Phases**

**Planning Phase**

Patients’ input can bring value if their insights are proactively included into the planning and design stages of a clinical trial when endpoints, assessments, trial duration, etc. are determined. 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. Patient experts can help determine which trial information is meaningful for patients, e.g. when it comes to the inclusion of endpoints or indicators for quality of life. Patient involvement initiated during trial design to inform content decision for trial design, PIS and ICF may also be useful for preparation of the LS.

Patients may in addition be able to contribute to LS content planning, particularly for sponsors considering inclusion of secondary endpoint information (See Section 2.7).

Development Phase

Review of the LS requires disease experience. Patient experts 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 unacceptable, and help develop alternative language recognised within the patient community. One or several patient experts may provide the initial review of the lay summary.

Patient expert reviewers should be able to understand the principles of good science writing and should be trained in the LS review criteria as described in Section 3.6. Their review should be true to the data and in line with the CSR or the technical summary. They may also observe the non-promotional content or presentation of the LS.

Patient experts represent a wide demographic mapping and may be well educated 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 different educational backgrounds, literature experience, age and gender, regardless of whether they are patients or represent the general public.

Translation Phase

When lay summaries 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.

Dissemination Phase

Patients can bring valuable input on local dissemination which may be subject to cultural/sub-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. Consulting patients with local insights can help avoid ineffective and inappropriate dissemination efforts.

Additional considerations for planning patient involvement are discussed in Appendix 3 Planning Patient Involvement.

2.6 Country-specific Planning

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.

### 2.7 Decisions on Trial Specific Endpoints and Complexity

The EU CTR requires the LS to include the overall results of the trial. 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. While the presentation of results from the primary endpoint is obvious to include in the LS, there is discussion about presentation of results from secondary endpoints that are particularly relevant for patients. However, inclusion of select secondary endpoints entails that the sponsor has to make a selection that could be biased.

Standardised planning for elements common to all LS is an efficient approach. Nevertheless, there will be trial-specific considerations, related to both content and timing of delivery, that need to be factored into LS planning. It is important that sponsors address these in advance and use a consistent, non-promotional approach across trials. The sections below discuss trial-specific planning.

#### Endpoint Inclusion

Making content-related decisions before trial results are available (i.e. before database lock) may help reduce bias in endpoint selection for the LS. Limiting the presentation of results to the primary endpoint of the trial is the recommended approach in order to keep the LS short and focused on the outcome of the key research question in that trial. Sponsors who decide to summarise secondary endpoints will need to define a clear policy for planning non-promotional, prospective selection of patient-relevant information to be consistent across trials.

#### Secondary Endpoint Inclusion

Secondary endpoints may be of interest to the general public, particularly to participants or patients represented in the trial population. Sometimes secondary endpoints could be more relatable to patients/trial participants than the primary endpoints. For some studies, secondary endpoints may be confirmatory for efficacy claims for product indications. Additionally, certain secondary endpoints involve invasive or time-consuming procedures for trial participants who will want to know the results. This may often be the case for patient-reported outcomes. Draft question and answer documents from the European Commission also refer to inclusion, at a minimum, of patient-relevant secondary as well as primary endpoints. Since patient relevance is subjective, and not all endpoints can be presented in detail in the LS, secondary endpoint inclusion inevitably involves a selective process. As discussed below, approaches to reducing bias in selection should be considered.

It is also important to recognise that there are risks and challenges associated with summarising secondary endpoints. For some trials, the sheer number of potentially patient-relevant endpoints may seem to be incompatible with a concise, readable LS. Often, secondary endpoints lack statistical power, which could be misleading to non-scientists and result in readers placing undue emphasis on certain results. If sponsors choose to include secondary endpoint information, there should be clear separation, in layout and in emphasis, between the primary and the secondary endpoints. It also needs to be explained in plain language that some tests are not designed for
comparison between groups, or that more participants would need to be studied to draw statistically valid conclusions.

Perhaps the most significant challenge is the absence of regulatory guidance and the fact that selectively presenting secondary endpoint information could put sponsors at risk of being perceived as intentionally promoting or “cherry-picking”. Consequently, an influence of results on selective incorporation of secondary endpoints should be avoided. If sponsors opt to include secondary endpoints, it is recommended that these endpoints should be defined before results are available and that this exercise should be built into the LS Planning Phase. The aim would be to ensure consistent inclusion principles across a sponsor’s trials. This would require an established, documented framework for endpoint selection, to be implemented as early as trial protocol finalisation or submission, and no later than database lock. At this stage, sponsors could examine the list of endpoints defined in the protocol and consider the potential value to the general public, considering factors such as:

- patient relevance (e.g. patient-reported outcome measures and quality of life measures)
- trial participant burden (involvement of complex assessments or major time investment)
- secondary endpoints that were identified as major or “key” in the protocol
- clinical relevance (representativeness of the main rationale of the trial)
- statistical power considerations
- complexity of concepts (feasibility of explanation in plain language)
- public availability of data elsewhere (e.g. technical summaries on the EU Clinical Trials Register [clinicaltrialsregister.eu] or ClinicalTrials.gov [https://www.clinicaltrials.gov/]).

At a minimum, the clinical and statistical experts involved in protocol development should participate in this process. Pilot exercises to test the prospective endpoint selection strategy could be valuable. Sponsors may also consider consultation with patients regarding the most patient-relevant endpoints and the value of information to be provided. It may be useful to outline the prospectively defined secondary endpoint information in a LS outline “shell document” prepared in advance of results availability. It should be ensured that the results to be discussed will be reflected by logical and consistent information in other sections describing the trial objectives and what happened during the trial.

Having considered endpoints to discuss, the scope of presentation also requires careful deliberation. Again, factors such as conceptual complexity and statistical power need to be weighed. In some cases, it may be appropriate to combine multiple secondary endpoints into a single qualitative description. For example, an aggregate approach with simple narrative statements may be suitable for complex descriptive data such as multiple pharmacokinetic parameters. In developing a presentation strategy, sponsors would need to consider the level of detail compatible with different phases of product development, as well as statistical power. High-level narrative statements may be optimal for an early pharmacodynamic trial, explaining the broad value of the information instead of describing the results. In contrast, quantitative presentation of data may be needed for discussion of a statistically powered comparison within a late-stage pivotal trial. In all cases, the reader should be referred to other sources of more detailed information such as the technical summary, if applicable (per the EU Expert Group).

To sum up, sponsors may choose to summarise only the information specifically required by the EU CTR, namely, the primary endpoint and important safety data. Any sponsor deciding to summarise secondary endpoint results will need to define a clear policy for non-promotional, prospective definition of patient-relevant information. It may be advisable to test such an approach in pilot exercises.
Interim Results

Generally, it should not be considered to routinely develop LS for interim analyses but to aim for a single master LS after protocol-defined trial completion. Any decision to share interim trial data should not be based on results, since selective early disclosure of favourable results could be perceived as being promotional or compromise the validity of the final results. As with other trial-specific planning activities, a consistent, predetermined strategy is advisable.

There are circumstances in which earlier delivery of interim information to the general public might be considered, e.g. for a trial with a long-term, open-label extension within the same protocol. Furthermore, for trials with survival follow up continuing for several years after both primary analysis and publication, delivery of a LS after main analysis may be of greatest value to trial participants. Any summary of results provided before the end of the trial (as defined in the trial protocol) would effectively be delivering interim results. Consequently, such interim LS would need to be updated with final results after trial completion. In contrast, extension studies that start after the defined end of trial and are described by independent protocols would be expected to have separate LS.

The EU Expert Group acknowledges that some trials have an extended follow-up period during which it may be appropriate to upload some interim findings. Furthermore, the “Multi-Regional Clinical Trials (MRCT) Draft FDA Guidance on Provision of Plain Language Summaries” states that, for some studies, sponsors may be interested in communicating results after the primary endpoint has been obtained but while the trial remains open for completion of secondary endpoints. Sponsors should consider whether provision of a LS in an ongoing trial may introduce bias on the side of study participants or investigators and thus compromise the integrity of the research data in the rest of the trial. Accordingly, LS should be postponed until trial completion if communication of interim results could compromise trial integrity. Independent evaluation of these scientific considerations by the trial steering committee in advance of trial conduct could be useful in judging the appropriate timing of LS dissemination. Other factors in this judgement would include alignment with results disclosure elsewhere, e.g., via technical summaries or publications. The relative risk of misinterpretation of interim results disclosed in simplified, plain language compared with technical results disclosure should be appraised.

In addition, careful consideration should be given to the potential impact of interim results on trial participants, in particular for vulnerable trial populations. The likely survival status of the trial population and possibilities for delivery of the LS to family members, or any individuals designated by participants, also need to be considered.

Complex Trials

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. 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 complex trial, which may have a master protocol and multiple sub-protocols, or as separate linked trials. A complex trial with several arms sharing common control arms must be submitted as one trial. In this case, publication of sub-protocol results will be delayed until after the overall clinical trial is completed. As such, complex trials, including basket, umbrella and platform designs, present challenges for data transparency planning. From a trial participant’s or patient’s perspective, timely availability of information on sub-protocol results is needed.
The EU Expert Group recognizes that some arms in multi-arm trials may close and publish results long before the overall trial closes. They suggest that in these circumstances, the sponsor may decide to develop multiple LS for the same trial. Accordingly, for a complex design comprising several separate parts, preparation of multiple individual LS is likely to be the clearest approach.

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

- 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)\(^2\).
- Implications for data transparency, and value to participants, of waiting until the overall end of the trial for delivery of LS.
- 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.
- 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).
- LS for sub-protocols defined as part of a single trial may need to be reviewed by IRBs/IECs if delivered before the overall end of the trial.
- Consistency with any publication/disclosure policy described in the trial protocol\(^11\).

In summary, clarity on the end of trial definition(s) applicable to individual parts of a complex trial is of utmost importance. This, and the planned dissemination strategy should be considered during development of the trial design. For adaptive trials with substantial amendments, changes to the end of trial definitions will need to be tracked carefully during the trial. Since the use of complex trials is still limited, shared sponsor learning is likely to be fundamental to developing best practices.

### 2.8 Conclusions

Planning of the LS should commence during protocol development as diligent planning will help ensure a high-quality and compliant lay summary. Critical decisions regarding publication of results and any interim results should be taken prior to LS Development phase to avoid introducing unintended bias into the results communication. Also, due to the strict regulatory timelines for results disclosure and CTIS submission, sponsors should plan translations, review and testing to avoid any unforeseen delays in the availability of the LS. For content and timing decisions, sponsors should consider applying predetermined LS planning strategies to ensure consistent approaches across trials.

Depending on the geographic footprint and complexity of the trial, the Planning phase may call for several iterations in the trial team to ensure that the LS project is properly scoped for a successful development, translation and dissemination of the LS.
3 PHASE 2: DEVELOPMENT OF THE LAY SUMMARY

Phase 2 focuses on the content of LS as defined in the EU CTR, Annex V and as detailed in the Recommendations of the Expert Group on clinical trials for the implementation of EU CTR 536/2014\textsuperscript{1}. The chapter includes recommendations on resources, competences and important considerations for the authoring, design and testing of lay summaries which can be understood by the target audience and adhere to principles of health literacy, numeracy as well as non-promotional results communication.

3.1 General Principles

As the intended audience of the LS differs from that of the technical summary, some information should be presented differently, and the technical summary will contain more information than the LS. Although not required by the EU CTR, a short abstract summarising the content of the LS is suggested by the EU Expert Group.

In addition to the content laid down by the EU CTR, the GLSP encourages sponsors to thank trial participants for their contribution within the first paragraphs of the LS. While not a legal requirement, this acknowledges the efforts of trial participants who voluntarily undertook the inconvenience and risks associated with the trial without any guarantee of direct, individual benefit.

LS should be dated (e.g. with the date of sponsor’s approval), and it should be 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 language.

3.2 Content Laid Out by the EU CTR

The EU CTR Annex V lists 10 elements that must be included in the LS. The EU Expert Group provides examples of reader-friendly headings, covering the content of all 10 elements (See Appendix 2 EU Expert Group Recommendations). Sponsors must cover all 10 elements listed below but may combine them or change their order. The headings below are identical to the headings in Annex V and offer advice on each element.

Element 1: Clinical trial identification. The trial title, protocol number, the EudraCT number, the phase of the trial and other identifiers (e.g. Investigational New Drug number, China drug trials, Japanese register, NCT number). A simple lay title should be provided.

Element 2: Name and contact details of the sponsor. Local regulations (e.g. data protection law) may apply. Sponsors may need to establish procedures, specifying how to handle public contacts based on the information provided in 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 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, inclusion of placebo, titration of medication, wash-out phases and long-term follow up. 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 key demographics and entry 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 simply in the relevant section.

**Element 5: Investigational medicinal product 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
should be clearly defined, and 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 Appendix 3
Adverse Reactions and Safety Information.

**Element 7: Results of the clinical trial.** The EU Expert Group states that the LS should
include the primary endpoint(s) and additional safety data important to the overall results of the
trial. They recommend that sponsors reference the complete list of outcomes based on all
endpoints available in the technical results summary including patient-relevant secondary
endpoints. On the other hand, draft Question and Answer documents from the European
Commission refer to inclusion at a minimum of patient-relevant secondary as well as primary
endpoints. As such, there is no EU regulatory requirement to detail secondary endpoint data in
the LS. Sponsors may thus choose to summarise only the information specifically required by
the EU CTR. Additional considerations are discussed in Section 2.7 on Secondary Endpoint
Inclusion.

**Element 8: Comments on outcome of the clinical trial.** This section should state if 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 something different.

**Element 9: Indication if follow-up clinical trials are foreseen.** Public domain 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 of where additional information could be found.** This section
may provide links to other websites deemed helpful (including industry-based websites as well as
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 these
links.

### 3.3 Competencies to Enable Good Lay Summary Development

This section summarises the competencies needed for an optimal LS process. The term
“competency” means possession of sufficient knowledge, skills and attitude. Ideally, all know-how
referenced should be available in sufficient depth in the team working on LS. 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 realize that certain capabilities are underrepresented, it may be able to fill any such gaps from external resources.

The compilation of required knowledge detailed below was developed to optimally support a mature LS process in a larger institution. The list may help teams that are newly tasked with the development of LS to identify and develop the resources that might not be fully available at the outset. Based on a collaborative attitude, appropriate solutions can be developed in the absence of a large supporting organisational background. The skills and knowledge recommended are listed in Table 3.1 and some considerations are offered below to facilitate resource allocation to the LS team.
Table 3.1: Summary of Competencies Enabling Good Lay Summary Development

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

**Source Documents**

The clinical trial protocol and the CSR describe the rationale, objective(s), and hypothesis and discuss the results of the trial. The PIS and the ICF, which introduce the trial to potential participants in plain language, may also be important references. Together, these documents serve as source documents for the LS, and the writer or writing team therefore need to be able to interpret and use them.

**Disease and Patient/Trial Participant Population**

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

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 plain language why the investigational product was tested alone, or in combination with another medication.

**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, pdf files should not be password protected. 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) 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. Therefore, a brief summarising description of the key messages of charts or graphs should be provided. A very short caption describing any pictures present in the LS would also be desirable.
Safety of the Intervention (Drug, Surgery, Other) under Investigation

As safety information is critical content in lay summaries, writers need to have detailed insights into the terminology used to describe the side effects of drugs. In the source documents such as the CSR, clinical safety information is described in terms of adverse events (AEs); serious adverse events (SAEs); adverse drug reactions (ADRs); serious adverse reactions (SARs); adverse event 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 the Medical Dictionary for Regulatory Activities (MedDRA) is essential because adverse events are collected, coded and analysed using MedDRA terminology. A LS writer needs a good working knowledge of the MedDRA system to be able to transfer this information into lay language. For particular disease areas such as oncology, proficiency within additional adverse event recording systems are important such as Common Terminology Criteria for Adverse Event Reporting (CTCAE).

Statistical Knowledge

A sound knowledge of statistics is fundamental for LS content generation and presentation of statistical trial results should be treated with great caution. A LS author should appreciate that clinical trials are statistically 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 from a control/placebo may be easy to understand and translate into plain language. However, for trials where the interpretation of the statistical outcomes is complex, a basic background in statistics will be necessary to appropriately explain the results without sacrificing scientific validity of the trial. Furthermore, most lay people have little or no statistical capabilities, and the writer therefore must decode the statistical terminology into plain language which is void of statistical jargon.

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 lay summary 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 sensitive and 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 or in disease areas that may be subject to sentiment. These aspects are considered in more detail in Sections 3.4 and 4.1.

Good LS communication practice requires that the data presented are consistent with the data in the source documents, i.e. the CSR. In addition to relevant scientific knowledge, authors as well as translators of LS should know how to transform complex information into plain, neutral and local language without losing important nuances or introducing bias or promotional incentives. Authoring and editing skills, and knowledge of lay language writing are specific skills important for LS production.

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 Chapter 4.
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, e.g. the CSR. 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.

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 and the recommendations of the EU Expert Group. It is in addition an advantage to be familiar with existing guidance on results communication, e.g. the TransCelerate Implementation guide for lay summaries, the MRCT Return of Results Guidance Document, and statements of patient advocacy groups such as the European Patient Forum (EPF) and of pharmaceutical associations such as European Federation of Pharmaceutical Industries and Associations (EFPIA) and Pharmaceutical Research and Manufacturers of America (PHRMA).

Visual and Design Skills

In line with the EU Expert Group recommendations, well-chosen and clearly designed visual aids can help enhance understanding of scientific content and for the same reason, their use is strongly encouraged in this GLSP. 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 have the ability 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 or writing teams should have the competence to decide which content will benefit from visual presentation and where a combination of text and graphics is most helpful (See also Section 3.5).

Skills for Validation of Content

The process of developing a lay summary should include feedback from non-scientists to ensure that the information presented is relevant and appropriate and that the document is understandable outside of the scientific community. Validation of LS content is best achieved by consulting members of the public and/or patients, e.g. through an advisory group. To ensure actionable input for user validation, patients and members of the public involved should be representative of the target audience of the LS. User testing is one method by which to test and validate LS content, e.g. to determine readability and understandability by members of the public at large. Involving patients or members of the public may not be feasible for all LS, e.g. under resource constraints in SMEs or academic trials, but may be particularly helpful for the development of LS templates. Section 2.5 and Appendix 3 Planning Patient Involvement discuss patient involvement in more detail.

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 lay persons. They should be committed to undertake training, including training on how to interact with patients and members of the public.

### 3.4 Writing and Presentation of the Lay Summary

One of the most demanding steps in the LS production process is authoring and presenting lay summaries 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 must address the public at large which is inherently more heterogeneous and demanding from a communication effectiveness perspective. Any successful communication starts with insights into the target audience and the primary objective of LS should thus be to make the summary understandable, readable, and accessible for a diverse lay audience with no scientific knowledge. As pointed out in Section 1.1, the LS audience potentially spans a diverse group including trial participants, people from patient organisations, patients and carers who directly or indirectly live with the illness and may or may not be affected by this research and its results.

This section offers guidance on how to generate understandable LS content for the general public as well as recommendations on good layout and design. This adds to the EU Expert Group Recommendations; See Appendix 2 EU Expert Group Recommendations. The section also covers aspects of user testing with lay people which is equally important for readability and understandability.

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. Language 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**

![Linguistic Differences between Scientific and Lay Language](image)

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.

**Health Literacy and Numeracy**

Health literacy is low worldwide. Increasing people’s ability to understand and engage in their healthcare is an international priority\[^13\]. In Europe it is estimated that one in five 16- to 65-year-olds have poor reading skills.\[^14\] To address this, all people should be offered the same accessible information and services - everybody could benefit from clear health information.

> “Health literacy is 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.”


The general low level of health literacy combined with the need to convey the complicated messages related to clinical trial results is a challenge. Writers working within clinical development are often schooled in a writing style suited for regulatory purposes but writing for people without a healthcare background requires a different sort of writing. However, following established good practice principles described here, along with user testing with lay people, provides a good start.

A fundamental principle when addressing a lay audience is using conversational language. 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

<table>
<thead>
<tr>
<th>Principles</th>
<th>Examples and Elaboration</th>
</tr>
</thead>
</table>
| **Use simple everyday conversational language**      | ‘use’ not ‘utilise’  
‘long term’ not ‘chronic’                                                                                                                            |
| **Use short words, sentences and paragraphs**        | To increase readability, it is recommended to use:  
• words of 1–2 syllables  
• sentences of 8–10 words  
• paragraphs of 3–5 sentences                                                                                                               |
| **Use active voice rather than passive voice**       | Active voice is easier to understand, reduces the risk of misinterpretation - and can make sentences shorter.  
“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’  
‘high blood pressure’ not ‘hypertension’                                                                                                           |
| **Present medical terms in brackets**                | Present medical terms in brackets after the plain language version.  
“Some people had side effects of feeling sick (nausea)”                                                                                         |
| **Use neutral non-promotional language**             | See Section 3.4 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’.  
‘Most were non-smokers (44) or former smokers (11)’                                                                                               |
| **Use words and terms consistently**                 | Do not alternate between interchangeable synonyms.  
‘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.’  
‘that means’ not ‘i.e.’  
‘in the laboratory’ not ‘in vitro’                                                                                                              |
Readability Formulae

The EU Expert Group 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 since currently available tests are not developed in all official languages.

Commonly used readability formulae include the Fry readability formula\textsuperscript{16} as well as the Flesch Reading Ease text score and the Flesch–Kincaid readability test. With emerging technologies, more advanced readability formulae can also be obtained by use of predictive analytics, rules-based automated readability checks and so-called Lexical Profiling tools.

Length of Summaries

The EU Expert Group\textsuperscript{5} recommends that 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 of four to six pages can be achieved with a good layout and design for trials with intermediate complexity. More complex trials may require more description.

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 guidance on returning results to participants\textsuperscript{17}, and the HRA Information for participants\textsuperscript{18}. 

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Table 3.3: Health Numeracy Principles

<table>
<thead>
<tr>
<th>Numeracy</th>
<th>Examples and Elaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principles</strong></td>
<td></td>
</tr>
<tr>
<td>Use visuals for interpretation of numbers</td>
<td>See Section 3.5 for examples</td>
</tr>
<tr>
<td>Use whole numbers</td>
<td>Round up to whole numbers if possible.</td>
</tr>
<tr>
<td></td>
<td>‘5’ instead of ‘4.87’</td>
</tr>
<tr>
<td></td>
<td>‘1 in 1000’ instead of ‘0.001’</td>
</tr>
<tr>
<td>Keep denominators and units consistent</td>
<td>“There is a 1 in 10 chance of nausea and a 2 in 10 chance of dizziness”</td>
</tr>
<tr>
<td></td>
<td>“There is a 1 in 10 chance of nausea and a 1 in 5 chance of dizziness”</td>
</tr>
<tr>
<td>Use percentages carefully</td>
<td>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 3.5 on ‘Graphics’). Frequencies can be expressed as ‘natural frequencies’ e.g. ‘1 out of 10’ instead of ‘10%’.</td>
</tr>
<tr>
<td>Use numerals rather than words for numbers</td>
<td>‘2’ instead of ‘two’</td>
</tr>
<tr>
<td>Do not leave calculations to your reader</td>
<td>Basic maths is beyond many people - so do the calculations for them e.g.</td>
</tr>
<tr>
<td></td>
<td>• Do not present a body weight loss in %, do the math or show examples.</td>
</tr>
<tr>
<td></td>
<td>• Use simple units: ‘1 year’ not ‘52 weeks’; ‘half a glass of water’ not ‘120 mL water’</td>
</tr>
</tbody>
</table>

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. Both the EU Expert Group and the MRCT Draft FDA Guidance LS give examples of neutral language, as well as the MRCT Center toolkit. In addition, TransCelerate has provided guidance on drafting non-promotional LS. 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

<table>
<thead>
<tr>
<th>Non-promotional Language</th>
<th>Dos</th>
<th>Don’ts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The overall tone should be factual and objective</strong></td>
<td>✓ Highlight both the positive and the negative.</td>
<td>✓ Present no opinions that cannot be substantiated clearly from the results.</td>
</tr>
<tr>
<td></td>
<td>✓ Present information accurately and none misleading.</td>
<td>✓ Avoid making inferences or assessments: stick to fact.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Do not criticise or oppose competitors.</td>
</tr>
<tr>
<td><strong>No commercial or marketing appearance</strong></td>
<td>✓ Use neutral colours and plain design.</td>
<td>✓ Do not use brand colours, glossy designs or sponsor logos.</td>
</tr>
<tr>
<td></td>
<td>✓ Ensure faithful reproduction and clear indication of source of quotations, graphs, diagrams, illustrations, etc.</td>
<td>✓ Do not include approval status, as indication may vary between countries and may lead to a promotional concern.</td>
</tr>
<tr>
<td></td>
<td>✓ Name study products as in the ICF, protocol and on clinical trial disclosure sites (most often generic name[s]).</td>
<td>✓ Do not use brand names, except where information can only be found knowing the brand name.</td>
</tr>
<tr>
<td><strong>Superlative and enthusiastic words should be avoided</strong></td>
<td>✓ Be careful using words like:</td>
<td>✓ Do not use words which could lead to determination that the communication is promotional:</td>
</tr>
<tr>
<td></td>
<td>without quantification.</td>
<td>✓ Avoid claims (e.g., ‘the results proved’)</td>
</tr>
<tr>
<td><strong>Be careful with high level statements</strong></td>
<td>✓ Specify the circumstances the statement is based on (e.g. “In this study, no safety issues were identified at the tested doses.”).</td>
<td>✓ Avoid generalising statements as “The study medicine is safe.”</td>
</tr>
<tr>
<td><strong>Quantify statements</strong></td>
<td>✓ Present numbers, also for comparators:</td>
<td>✓ Avoid unquantified statements such as: “Fewer people had too low blood sugar while on X”.</td>
</tr>
<tr>
<td></td>
<td>✓ “… of … people (%) given X had low blood sugar.”</td>
<td></td>
</tr>
<tr>
<td><strong>Reinforce that the outcome reflects only one single clinical study</strong></td>
<td>✓ Include relevant contrary evidence or limitations.</td>
<td>✓ Do not include results from other studies.</td>
</tr>
<tr>
<td></td>
<td>✓ Include a statement to emphasise that results presented are from one study:</td>
<td>✓ Do not make comparison to other products than the ones included in the study.</td>
</tr>
<tr>
<td></td>
<td>✓ “The outcome of this study is from the results of this study only. Other studies may show something different.”</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Reinforce that therapeutic changes should not be made based on results from a single study without consulting a healthcare professional.</td>
<td></td>
</tr>
<tr>
<td><strong>Ensure that additional information is readily available</strong></td>
<td>✓ 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.”</td>
<td>✓ Consider including a statement on where to find results from other studies, if applicable.</td>
</tr>
</tbody>
</table>

3.5 **Layout and Design of the Lay Summary**

From a readability perspective, layout and design are as important as the wording in a lay summary. 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. Layout and design are equally important in allowing people to use the document and navigate their way around it.
The importance of design to readability is not addressed prominently by the EU Expert Group. A number of key points to consider related to layout and design are presented in Table 3.5. A central principle is to chunk the content. This can be achieved through extensive and appropriate use of headings and subheadings in a clear hierarchy. Also, information can be broken down into a series of short paragraphs.

Place callout boxes close to related text, but do not use a hard edge - this can lead to a tendency for the reader to "read around" the box, rather than read the contents. Use a lightly shaded box instead.
### Table 3.5: Layout and Design

<table>
<thead>
<tr>
<th>Points to Consider</th>
<th>Elaboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use headlines and descriptive subheadings</td>
<td>Use headings and subheadings to organise information. Descriptive subheadings make it easier to scan the text to find key points.</td>
</tr>
<tr>
<td>Use adequate white space</td>
<td>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.</td>
</tr>
<tr>
<td>Use black text on white background</td>
<td>Sufficient contrast between the font colour and the background maximises legibility and accessibility. Most readable is black font on white background.</td>
</tr>
<tr>
<td>Limit use of unnecessary imagery, such as logos and icons</td>
<td>Logos may also be considered promotional. Icons should represent the content they accompany and should be used consistently.</td>
</tr>
<tr>
<td>Use visuals such as simple graphs</td>
<td>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).</td>
</tr>
<tr>
<td>Use left justified text (also known as ‘ragged right’)</td>
<td>Full justification with a straight line down both margins can lead to unusual spacing between words which some readers find difficult or distracting.</td>
</tr>
<tr>
<td>Do not use long lines of text</td>
<td>Use of columns produces shorter lines. Long lines are particularly difficult for less skilled readers.</td>
</tr>
<tr>
<td>Place column and page breaks carefully</td>
<td>If starting a new subsection or paragraph (bullet list), start on a new page or new column. Spanning both will disturb the reading flow.</td>
</tr>
<tr>
<td>Use of colour can make a document more attractive but do not over-use</td>
<td>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.</td>
</tr>
<tr>
<td>Use bold text to add emphasis, but do not use: • underlining • <em>italics</em> • fancy fonts • ALL CAPS</td>
<td>Emphasise information by bolding rather than put in CAPITALS, <em>italics</em> 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.</td>
</tr>
<tr>
<td>Use bullets formatting</td>
<td>Bullet formatting splits text into separate points and helps the reader to digest the message.</td>
</tr>
</tbody>
</table>

### Graphics

Well-chosen and clearly designed graphics or visuals can enhance comprehension of the text. Graphics designed with the audience in mind can be powerful in supporting and facilitating the
Good Lay Summary Practice

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. However, since even simple graphics can be misinterpreted and may be subject to cultural differences, it is essential to do user testing to ensure that the visuals are comprehensible and do not introduce ambiguity in the results communication (See Section 3.5). Figure 3.2 offers examples of how numbers can be presented graphically.

Figure 3.2: Examples of Graphics and Visuals

- Sex of people who took part

- People who took part were from:

- People who took part were from:
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 Review and User Testing of the Lay Summary

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 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 expert 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, patients or public representatives.

User testing of the Lay Summary

- Later in the development of the LS, patients and people from the public can contribute as reviewers or test persons (See also Section 2.5, and Appendix 3 User Testing. 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 reviewers, 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 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 should be included with a mix of patients with 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 documents have potential issues in terms of readability and subsequently determines whether addressing those problems (using good practice in writing for lay people) leads to improvements. It is a diagnostic and iterative process which is routinely used in readability assessment of medicine leaflets. A key feature of this methodology is that the respondent is initially asked to use the LS to find and answer questions and then enquired about their opinion on the actual use of the document. 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 layperson summary was described in a paper in 2018.

### 3.7 Writing Paediatric Lay Summaries

This section provides recommendations specific to lay summaries targeting children and for communicating with children across different age groups. If not specifically addressed in this section, the general recommendations in previous sections for LS apply to summaries for children as well.

It is anticipated that the CTIS will accept LS to be uploaded in a pdf file format, although the sponsor will need to check the requirements once the CTIS is launched. 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. The recommendations below are focused mainly on written content and cartoons to convey storytelling that would be compliant under the EU CTR, but sponsors are free to develop videos and animations in their LS for separate dissemination.

**Current status and sources of inspiration**

The EU Expert Group Recommendation states that a well written LS would normally be accessible by young people from the age of 12 years upwards. 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, particularly where they have already developed an Assent for the paediatric patient’s information about trial participation. Paediatric patients focused LS may differ in terms of presentation and style (more illustrations or graphics) to assist children in understanding trial results, over and above what is required by the EU CTR.

Lay summaries 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 lay summaries aimed at children. The recommendations in this section therefore build on universal instructions on how to communicate with children based on existing guidelines about health, developed by UNICEF, and guidelines about children’s reading skills from the Oxford Owl-website. To address clinical trial specific topics, the GLSP offers additional advice and context with inspiration from IPPOSI/National Children’s’ Research...
Information about children’s cognitive development is based on the Centers for Disease Control and Prevention (CDC) and the National Academies Press (NAP). Both institutions strongly 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 3.5 in Appendix 3 Paediatric Trials. The table may help determine the level of complexity and focus for paediatric audiences when developing lay summaries.

**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 the 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.

**The age groups are:**

**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 12–15 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.

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. 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. 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. See also Table 3.6 in Appendix 3 Paediatric Trials.

A narrative could exemplify multiple sides of an issue or the 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. 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 lay summary 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 and discuss with the IEC/IRB 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 lay-out and design, see Table 3.7 in Appendix 3 Paediatric Trials.
3.8 Conclusions

Developing LS is a multidisciplinary effort requiring a combination of clinical research, communication, and language competencies. In order for LS to be successful, the development process should focus on the respective population’s needs, build on principles of health literacy and numeracy and leverage visual communication to facilitate the reader experience. This chapter has offered recommendations for the authoring, review and testing of LS that can facilitate the production of lay summaries which are understandable, non-promotional, attractive and user-friendly for the target audience, while preserving the scientific integrity of the clinical trial results. The right mix of resources, review and user testing will always depend on the sponsor infrastructure, funding, the scope and complexity of the trial as well as the disease.
4 PHASE 3: TRANSLATION OF THE LAY SUMMARY

This chapter will focus on language aspects and the translation of LS from one natural language to another natural language.

To meet the EU CTR requirements, at a minimum, translations must cover the languages of each EU Member State in which the trial took place which will be equivalent to the languages of the PIS/ICF. Translating LS into the languages of all countries in which the trial took place (also outside EU/EEA) should be considered the best practice solution from a patient-centric view since a primary objective of the LS is to offer results communication in clear and understandable local language.

Sponsors should consider preparing an English version of the LS, also if the trial did not include a country where English is an official language, to enable broader accessibility and the upload of an English version to CTIS. Many sponsors already author the master LS in English in line with other essential clinical trial documents.

Since the GLSP is made available before the launch of the CTIS, sponsors must check which language versions are required for upload to the relevant database to ensure regulatory compliance.

A list of official languages per country in EU can be accessed at the EMA website.

4.1 Lay Summaries as an End-to-End Translation Process

The LS development process is depicted in Figure 4.1 as a three-step language process in which the scientific results are initially translated from scientific language into a master LS, and then subsequently translated into natural languages. Each step represents a linguistic “translation,” where the quality of the output of each step relies on the quality of the prior rendition. Focusing on both the LS development starting from the CSR and LS creation to the subsequent language translation as one end-to-end process can therefore help ensure consistency in the communication of results and avoid “drifting” language or “skewed” results disclosure. Also, focus should continuously be kept on the target audience and health literacy not only during the authoring of the master LS but also during the translation into local language. Focus on the target audience will help avoid the misinterpretation of results once they have gone through all text renditions.
**Figure 4.1: End-to-End Translation Process**

Translation Process from Lay (Source) Language to Local (Target) Language

All country-specific language translations should be based on the same master LS, and a successful final translation output 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 since the primary purpose of a professional translation is to reflect its source document. Given the importance of the source text in natural language translations, it is highly recommended that the master LS be carefully reviewed, approved and “locked” before any language translations commence. Any in-country or affiliate reviews of the master LS should be complete, and ambiguities addressed, to help ensure that the master LS will not be a source of potential misunderstandings during the rendition into local language. Besides the risk of miscommunication, any revision of the master LS after having initiated local language translations may bring inconsistencies between the different language versions.

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

Since language is the primary vehicle for the successful communication of results, along with visual and formatting elements, it is recommended to plan and control language proactively including potential external translation resources, even if translations may not seem compelling during the LS Planning Phase. Language translations are often mistakenly seen as a last-minute undertaking and are therefore not well planned. 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, the authoring and translations of the LS may become time critical activities for meeting the regulatory deadlines enforced in the EU CTR. Some sponsors may therefore choose to develop the LS in parallel with the CSR. 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.

### 4.3 Planning and Preparation of Translations

It can be beneficial to commence the planning and preparation of language translations during the development of the ICF since the style and language of both the master LS and translations into local languages should be consistent with the PIS/ICF. If interim results are expected to be
Good Lay Summary Practice

disclosed before the end of the trial, it will also be necessary to plan any additional translations and make sure that the terminology is consistent across the interim and final LS.

To control lay content throughout the trial (or even for all trials within a therapeutic area or a clinical development plan), it is advised to set up a style guide for the writing and translation teams and proactively develop a glossary of terms. This will facilitate reviews and minimise the occurrence of preferential changes, time consuming queries and content inconsistencies. Controlled terminology or phrases can help streamline the communication and specific phrases can be pre-defined in glossaries to ensure empowering language or an active tone of voice. If the sponsor engages a language service partner, such terminology can be managed via use of translation memory tools, and language assets can be established for results communication across more trials. Benefits from such technologies requires preparation and that controlled terminology is defined up front.

4.4 Translation Process

Translation Process

Three different resources can help obtain a sound translation:

- **Human expertise:** a thorough vetting process ensures the right multidisciplinary skills required for language translations including the selection of native or fluent translators and reviewers with the right expertise to manage the nuances of clinical trial research and plain language communication (See also Section 3.3).

- **Controlled workflows:** a well-controlled end-to-end process with clear workflows and built-in quality checks steps will help drive translation quality, content consistency, document management and de-risk translations on the critical path toward dissemination of results.

- **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. The benefits of translation tools are that they can be customised if the sponsor wishes to control certain terms to ensure they are consistently translated in the local language LS. Even terms that may be prone to bias or specific to a disease indication can be added to such automated assets. Quality assurance (QA) tools have no language limitations and work on bilingual files, which enables the sponsor to implement automated checks in all relevant languages. Another advantage is that tools can help reduce the burden on in-country reviewers since they can help avoid past mistakes, preferential changes and redundant reviews.

Whilst the human expertise and controlled workflows 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.

**Translation Step-by-Step**

Table 3.8 in Appendix 3 Step by Step Translation Process illustrates a step-by-step recommendation on how the language translation process can be set up. This process is widely recognised as a standard for essential clinical and patient-sensitive communication in clinical trials. There is no regulatory-defined process for LS translations, but ISO 17100 sets requirements for the process, resources and other aspects necessary for the delivery of quality translation services, and the ISPOR recommended standards for translations of Clinical
Outcome Assessments (COA) may also be helpful, although these standards include linguistic validation, which is a specific step to ensure that measurement properties are comparable between an original COA instrument and the corresponding translations.

The recommended process involves forward translation and back translation by two different native speakers or translators fluent in the target, respectively source language and a comparative review of the master LS and the back translated LS by a third person. The back-translation and comparative review steps can 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 and comparative review depends on the risk of the translation, the complexity of the LS, and the resources of the sponsor.

4.5 Conclusions

Translations should be approached as an integrated part of the LS project. Sufficient upfront planning and scoping should be invested already during the Planning phase to enable an efficient, compliant and timely translation of LS. Control of the LS master, the translation process and language assets such as glossaries and terminology can make the difference between a successful and a failed results communication in local language which is the end product of the entire LS production. Technology and linguistic skills should be leveraged with the right balance depending on the trial at hand and sponsors’ own internal procedures. Even with limited resources or budget, proactive language management will facilitate the quality, timeliness, and accuracy of LS to the final target audience.
5 PHASE 4: DISSEMINATION OF THE LAY SUMMARY

5.1 Mandatory CTIS Dissemination and Beyond

The dissemination of results has been discussed and outlined in existing implementation guidance documents. Sponsors have been proactively sharing lay summaries with trial participants and the public and have developed best practices around several methods of dissemination. The following section describes the dissemination of LS as practiced by industry, patient advocates, and academia.

Based on the overarching principle that the LS should be non-promotional not only in content but also in delivery, sponsors are strongly encouraged to consider how and when the finalised LS will be shared with trial participants and the general public. In addition to LS submission to the publicly accessible CTIS as requested by the EU CTR, the GLSP recommends distribution of LS beyond the CTIS in the EU and generally for trials also conducted outside the EU, by using other distribution channels.

Global delivery of LS is voluntary but requires identification of non-promotional distribution channels in compliance with any local restrictions/standards. It is advisable for researchers to choose publicly accessible distribution channels for the broadest possible dissemination to the public and patients including those who serve in a patient supportive role (i.e., patient organisations, healthcare professionals).

Generally, trial participants should be asked if they are interested in receiving the results.

5.2 Optional Dissemination Methods

Should a sponsor decide to expand the availability of the LS beyond the CTIS, they will be doing so voluntarily and should evaluate the risks and benefits of the various methods of lay summary disseminating. This section evaluates different dissemination channels with the purpose of helping sponsors identify suitable dissemination strategies which align 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:

- Delivery of the LS needs to occur in compliance with local restrictions and standards, especially in regions where guidelines are not in place.

- Preparation for distribution of LS should be an element of trial planning, preparation, and closure: e.g. by mentioning the availability and dissemination of LS in the protocol, PIS/ICF, investigator site selection visit, investigator meeting, and site initiation visit. For participants leaving the trial, a “Thank you” letter could be prepared as a means to inform the participant.
about the indirect and direct availability of a LS after the end of the trial if the participant wishes
to receive this. For the site close out visit information on the envisaged dissemination timeline
and process including the investigator’s role in dissemination of the LS to trial participants
should be prepared.

- Global, public dissemination of LS may fall outside the safe harbour of scientific exchange
and could be deemed promotional (i.e., pre-approval or off-label promotion). There is little to
no control, once in the public domain, that its use or interpretation will be consistent with its
intended non-promotional purpose.

- Patients may wish to share and discuss the LS with their treating physician or patient
organisation and are free to accordingly share the LS they received. However, direct LS
dissemination by the sponsor to healthcare professionals (HCP) outside the clinical trial
setting would fall under the special relationship between sponsors and HCP which is governed
by specific policy and regulations to conduct business in an ethical manner. EFPIA describes
it as a “well-regulated relationship” in which scientific and medical knowledge is exchanged to
improve patient outcomes. Since the LS is not a document intended for scientific exchange,
it would not be advisable for sponsors to directly share it with HCP or other stakeholders
outside the clinical setting without first seeking legal and regulatory advice.

- Investigational site agreements should set the expectation that the investigators will be
available to address participants’ questions after the LS and the CSR synopsis 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.

**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.

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

The benefits of this method include:

- This method of electronic dissemination enables the LS to reach a wide audience, including
  trial participants, and makes it easily accessible globally.
- The website link to the LS is easily shared and may facilitate participation in future research.
- LS of a completed trial available on a public website does not require IEC/IRB review (For
  more information on IEC/IRB review, see Section 2.4).
- Indirect dissemination will reduce 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.
- The sponsor can publish the LS in multiple languages and at reduced costs by providing
  electronic versus printed materials to the investigational sites.

Sponsors employing this method should consider:

- 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.

- The LS should also contain a globally accessible number or email address for the sponsor’s customer care call centre (or equivalent) to which inquiries can be addressed.
- Good Documentation Practice should be ensured for electronic LS including version control for all LS files and updates shared on CTIS or disclosed in the public sphere.

**Direct Dissemination**

An alternative method of disseminating the LS is directly to trial participants either through an electronic portal, or via printed material to be shared by postal service or by the investigator. Some sponsors that choose to deliver the LS directly 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
- to reach trial participants who do not have internet access or where printed hand-outs or postal service delivery is the trial participant’s 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 by which trial details (i.e. trial material, trial progress, individual trial data) can be shared to enhance the participants’ overall clinical experience
- because electronic access to the LS is optional, supporting the trial participant’s autonomy to either access a sponsor’s public website or self-registering to a third-party website to receive an email notification when the LS is made public.

**Sponsors employing this approach should consider:**

- choosing an electronic patient portal can reduce the burden on investigators of disseminating LS to trial participants themselves, whereas printing and disseminating the LS by postal service would increase the investigator burden on staff who have to handle the dissemination 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 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
- higher likelihood of local IEC/IRB request to review the LS since information is sent directly to trial participants as opposed to indirect dissemination.

Both direct and indirect methods of dissemination 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.
**Table 5.1: Examples of Technical and Non-Technical Distribution Methods**

<table>
<thead>
<tr>
<th>Technical</th>
<th>Non-Technical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Email</td>
<td>• Print/postal service</td>
</tr>
<tr>
<td>• Sponsor’s investigator trial portal</td>
<td>• Printed and handed to the trial participant</td>
</tr>
<tr>
<td>• Investigational site/clinic contains a patient portal</td>
<td>• Face-to-face meeting between the trial participant and investigator</td>
</tr>
<tr>
<td>• Sponsor website</td>
<td></td>
</tr>
<tr>
<td>• Third-party website for trial participant LS registration and notification</td>
<td></td>
</tr>
<tr>
<td>• Patient organisation website</td>
<td></td>
</tr>
<tr>
<td>• Social media</td>
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</table>

Some of the possible benefits and risks to each of the technical distribution methods are detailed in Appendix 3 under Sections Technical Distribution Methods and Non-technical Distribution Methods. These factors should be considered as sponsors select the most appropriate method. Multiple methods may work best.

The investigator-trial participant relationship should be held in the highest regard irrespective of the delivery strategy implemented and if 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.

Direct or indirect non-technical distribution can be used as the back-up for technical distribution in cases when 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
- face to face meetings to review results are an effective method for blind or illiterate trial participants to increase comprehension.

There are, however, some logistical considerations in investigator dissemination directly to trial 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 difficulty connecting with the investigator. For example, the investigational site may not open the email from the sponsor
- The site’s email address has changed
- The site has closed, or the investigator is no longer employed at that site.
5.3 Risk Mitigation Measures

- Since LS are provided six to 12 months after the end of the trial (or longer for Phase 1 studies), it is likely that investigators and participants may forget to check their results, passwords, etc. What can sponsors do to remind investigators/participants?
  - 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 the CSR synopsis, unblinding data, financial close out information are delivered to remind the site of the LS and address any questions.

- The trial participant may forget the URL which was provided at their last visit.
  The sponsor can provide the URL in writing in a “Thank You Letter” or printed information material to be handed out at the participant’s last trial visit. This material can also include the information about LS availability after trial completion and include a location at which 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.
  The third party might ask the trial participant for a back-up email address or mobile phone number to text once the LS is available on the website.

- 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.
  - Sponsors can monitor these activities, but it will increase the burden and costs as site closure and staff reassignment may occur prior to completion of the LS.
  - Once the LS is delivered to the site, follow up 1–2 weeks later to confirm they received the documents and if they shared them with the trial participants, and address any questions or concerns they may have.

- The investigational site does not explain to the trial participants at their last visit where and when the LS will be available.
  - Outline the investigator’s obligations in the Investigator Agreement.
  - Third-party notification to the trial participant about the availability of the LS through mobile phone text after self-registration.

- The trial participant may not have email/internet access or may change their email address.
  - At the time of email address communication: the trial participant can be asked by the investigational site staff for a back-up email address/a relative’s email address.
  - At the trial participant’s 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, etc.”)

- Writing LS in simple language for a non-technical audience has a risk of misinterpretation, again, given the length of time between the participant’s last visit and delivery of results. What can sponsors do to increase understanding of the clinical development process, purpose of the LS, reinforcing results?
o Ensure investigator has a copy of the CSR synopsis to serve as learned intermediary.

- Provide investigator LS training at the investigator meeting and site close out.

- Insert a disclaimer at the beginning of 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 of explanation/questions.

- Provide a statement in the LS directing participants to contact the investigator/site staff with questions. Provide sponsor customer care phone numbers from EU/United States (US) registry.

- **What can sponsors do to increase access and communication results to blind or illiterate trial participants?**

  - Suggest in the written material handed out at the participant’s last 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

### 5.4 Conclusions

This chapter has evaluated various methods of dissemination available for trial sponsors who wish to go beyond the mandatory EU CTR requirement of uploading the LS to the CTIS. LS can be indirectly disseminated through unrestricted or open channels, such as publicly available websites, or via more restricted pathways targeted at trial participants or investigators. In addition, LS can be channelled through technical or non-technical distribution methods or a combination of both. Irrespective of the strategy implemented, sponsors should weigh the benefits against the risks of the various dissemination methods and consider any partnering necessary 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.
6 LIST OF REFERENCES


12. Web Accessibility Initiative (WAI). http://www.w3.org/WAI


34. WECAN. Reference agreements. https://wecanadvocate.eu/rapp/
7. APPENDICES
## Appendix 1: List of Members of the Roadmap Initiative for Good Lay Summary Practice

<table>
<thead>
<tr>
<th>Organization</th>
<th>Contact Information</th>
</tr>
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<tbody>
<tr>
<td>Abbott Established Pharma Division</td>
<td>Abbvie</td>
</tr>
<tr>
<td>ABPI – The Association of the British Pharmaceutical Industry</td>
<td>AEDEM COCEMFE - Confederación Española de Personas con Discapacidad Física y Orgánica</td>
</tr>
<tr>
<td>AGAH - Association for Applied Human Pharmacology</td>
<td>AJH Associates</td>
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<tr>
<td>Akeso Biomedical</td>
<td>Aparito</td>
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<td>AstraZeneca</td>
<td>Benzi Foundation</td>
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<tr>
<td>BMS – Bristol-Myers Squibb</td>
<td>Boehringer Ingelheim Pharma</td>
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<tr>
<td>Boog Study Center</td>
<td>CEIC – National Ethics Committee for Clinical Research, Portugal</td>
</tr>
<tr>
<td>Chiesi Farmaceutici</td>
<td>CISCRP - Center for Information and Study on Clinical Research Participation</td>
</tr>
<tr>
<td>DORP – Dutch Oncology Research Platform</td>
<td>EATG – European Aids Treatment Group</td>
</tr>
<tr>
<td>ECRIN – European Clinical Research Infrastructure Network</td>
<td>EFA – European Federation of Allergy and Airways Diseases Patients’ Organisations</td>
</tr>
<tr>
<td>EFGCP – European Forum for Good Clinical Practice</td>
<td>EFNA – European Federation of Neurological Associations</td>
</tr>
<tr>
<td>EFPIA – European Forum for Pharmaceutical Industry and Associations</td>
<td>EORTC- European Organisation for Research and Treatment of Cancer</td>
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<tr>
<td>EPF – European Patients Forum</td>
<td>ETOP/IBCSG – International Breast Cancer Study Group</td>
</tr>
<tr>
<td>France Parkinson</td>
<td>EUPATI – European Patients Academy on Therapeutic Innovation</td>
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<td>EUFEMED – European Federation for Exploratory Medicines Development</td>
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<td>Ligue contre le Cancer</td>
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<td>Lionbridge Technologies</td>
<td>Masaryk University, Faculty of Medicine</td>
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<td>Medizinische Hochschule Hannover</td>
<td>Merck KGaA</td>
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<tr>
<td>MSD - Merck Sharp &amp; Dohme Corporation</td>
<td>Multiple Sclerosis Patient Organisation</td>
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<td>Novo Nordisk</td>
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<td>Pfizer</td>
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<td>Primary Sclerosing Cholangitis</td>
<td>Sanofi</td>
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<tr>
<td>Servier</td>
<td>Teddy Network – European Network of Excellence for Paediatric Clinical Research</td>
</tr>
<tr>
<td>The Association of Cancer Patients in Finland</td>
<td>Trinity College Dublin</td>
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<td>UCB - UCB Biopharma SRL</td>
<td>UNICANCER</td>
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<td>University Hospital of Parma</td>
<td>University of Leeds/Luto Research</td>
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Appendix 2: EU Expert Group Recommendations


<table>
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<tr>
<th>Document history</th>
<th>Version 2</th>
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<tbody>
<tr>
<td>Date of discussion of the revised version by the expert group on Clinical Trials</td>
<td>5 February 2018</td>
</tr>
<tr>
<td>Date of publication</td>
<td>22 February 2018</td>
</tr>
<tr>
<td>Date of entry into force</td>
<td>On application of the Clinical Trials Regulation (EU) No 356/2014</td>
</tr>
<tr>
<td>Supersedes</td>
<td>Version 1 of 26 January 2017</td>
</tr>
<tr>
<td>Changes compared to superseded version 1.0</td>
<td>Update to Annex 1 Section 7 regarding secondary endpoints.</td>
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</table>
Good Lay Summary Practice

1. Introduction

The EU Clinical Trials Regulation 536/2014 (Article 37) (EU CT Regulation) requires sponsors to provide summary results of clinical trials in a format understandable to laypersons. These layperson summaries will be made available in a new EU database once it becomes available and is approved according to the timelines set forth in the Regulation. Prior to this Regulation and the creation of a new EU database, the EudraCT Results data model, launched in July 2014, had been used for posting of scientific results written in technical language under the Commission Guidelines 2012/C 302/03, which was not easily accessible or understandable to the layperson.

Annex V of the EU CT Regulation sets out ten elements that must be addressed in the lay summaries. This document includes guidance and templates to help authors writing these lay summaries. Consistency in the way trial results are presented will help improve familiarity and comprehension by the general public, participants, patients, and others.

2. Scope

This document provides sponsors and investigators with guidelines and templates for the production of summaries of clinical trial results for laypersons. These guidelines will only apply to lay summaries included in the EU database. The lay summary section of the EU database will be publicly available. The general public are expected to be the primary audience for the lay summaries. The lay summaries may also be accessed by others, such as research participants, healthcare professionals, and academics. Given this wide audience, the summaries will need to take into account the average literacy level of the general population, provide simple explanations, and apply other measures to support health literacy.

3. Responsibility of sponsor

It is the responsibility of the trial sponsor to ensure that the lay summary is developed and submitted to the EU database within the timelines required by applicable regulation.

4. General Principles

- Develop the summary for a general public audience and do not assume any prior knowledge of the trial, of medical terminology or clinical research in general.
- Develop the layout and content for each section in terms of style, language, and literacy level, to meet the needs of the general public.
- Keep the document as short as possible, avoid simply copying text from the technical summary. Explaining technical terms in a simple language may increase the number of words and translation to some languages will result in longer documents than others. All content must be carefully considered for inclusion since additional content worded in plain language may add considerable length which in and of itself may decrease comprehension. Focus on unambiguous, factual information.
- Ensure that no promotional content is included (See neutral language guidance in Annex 2).
- Follow health literacy and numeracy principles (see section 5 ‘Health Literacy Principles and Writing Style’ and section 7 ‘Numeracy’).
- Consider involving patients, patient representatives, advocates or members of the public in the development and/or review of the summary to assess comprehension and the value of the information provided. This won’t be feasible for some studies, but where it is a

1 “Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.”
http://health.gov/communication/literacy/quickguide/factsbasic.htm
possibility, it may enhance the final version. Medical writers with particular experience of writing in plain language for the public who are also able to incorporate health literacy and numeracy principles may be helpful in developing summaries for the lay person.

5. Health Literacy Principles and Writing Style

Communications written for the public should use simple everyday language to ensure ease of reading and understanding.

- Text should be suitable for people with a low to average level of literacy. Across Europe, the average proficiency level is 2-3. A proficiency level of 2 is defined as being able to identify words and numbers in a context and being able to respond with simple information, such as being able to fill in a form. A proficiency level of 3 is defined as being able to identify, understand, synthesize and respond to information, be able to match given information that corresponds to a question. This level corresponds roughly with high (secondary) school completion levels.

- Avoid long and complex sentences that include many clauses as these are difficult to understand.

- Use simple vocabulary familiar to non-medical people:
  - Avoid jargon, technical, medical or scientific language (for example, use “high blood pressure” rather than “hypertension”)
  - Remove unnecessary or complex words (for example, “use” rather than “utilise”)
  - Be consistent in the use of terms/words throughout the document, and define them
  - Ensure that the underlying concepts are clear and easy to understand. Where necessary, explain the underlying concept
  - Avoid ambiguous words and phrases (for example, “felt badly”)

- Use active, rather than passive, voice:
  - Active voice: “Researchers studied the effect of tamoxifen on breast cancer”.
  - Passive voice: “The effect of tamoxifen on breast cancer was studied by researchers”.

- Use the following elements to help improve comprehension:
  - Headlines and descriptive subheadings to organise information
  - Presentation of the “big picture” before the detail (inverted pyramid writing style)
  - Bullet points instead of paragraphs
  - Numeracy principles to describe data and statistics (see section 7 below)
  - Adequate “white space”. For example, separate topics by one or two lines
  - 12-point font should be used (where needed, readers may enlarge print when viewing electronically or print pdf in larger font)
  - The most readable colour combination is black text on a white background. Please avoid using white text on a coloured background as this can be harder to read. Keep in mind how documents will look when online or printed.
  - Links to additional information, and resources for online summaries and background information. Such links need to be minimal since hyperlinks can become out of date over time.

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2 Based on research across Europe, text for the lay summary should be aimed at a literacy proficiency level of 2-3. The International Adult Literacy Survey (IALS) identifies five levels of proficiency ranging from level 1 (lowest level of proficiency in literacy, that is basic identification of words and numbers) to level 5 (highest level of proficiency in literacy, that is able to understand and verify the sufficiency of the information, synthesize, interpret, analyse and discuss the information. At level 5, the individual demonstrates sophisticated skills in handling information).
Good Lay Summary Practice

- Limited use of unnecessary imagery that does not enhance understanding (icons, logos, etc.)
- Avoidance of text in ALL CAPS and underlining
- Use visuals (for example, simple graphs) to convey messages where helpful. Avoid overwhelming the reader with too much information.

Where possible, avoid using acronyms, abstract, medical/technical, or multisyllabic words (such as, “unanticipated”, “hematopoietic”). If such words are to be used (for example, where commonly used medical terms will also aid in finding other medically relevant information and referencing other documents), add clear language to define the word followed by the term in parenthesis. For example, cancer that has spread to another part of the body (metastases). Also, where medical terminology refers to defined stages of a condition, it may be helpful to express the stages as mild (stage 1), moderate (stage II), severe (stage III) and very severe (stage IV) as appropriate.

Finally, it is helpful to use language in a way that is respectful and empowering for patients. For example, words such as “demented” in dementia research should be avoided. Similarly, avoid using the words “sufferers” or “victims” that have negative connotations. A preferable term is “people living with …” or “people affected by …”.

Sponsors should note that there is no limit placed on the size of the lay summary document that will be uploaded as a pdf document. However, it should be as succinct as possible while relaying the required information in a form that is readily understandable. Whilst brevity is preferable, explaining technical terms and complex concepts in a simple language will often use more words than a technical term.

6. Readability and use of plain language

Sentences should be kept short and succinct. The summary should remain factual and objective, avoiding any promotional language (See neutral language guidance in Annex 2) or promotional perception through formatting or tone.

Sponsors are encouraged to use a language-specific reading test to assess the literacy level of each lay summary produced. Sponsors should understand, however, that even though lay summary text may indicate an optimal reading level, the summary may not be clear or readily understandable. Many simple sentences together may explain little or nothing despite the fact that each sentence is simple, straightforward and grammatically correct. Nonetheless, these readability tests may be useful tools in striving to make often complex information understandable. While approaches were initially only developed for the English language, tools are now available in other languages (See Annex 3 for further information). These tools use a variety of metrics to provide a corresponding grade level (for example, average numbers of words per sentence and syllables per word).

A well written lay summary would normally be accessible by young people from the age of 12 years upwards. Sponsors of paediatric studies may consider developing a child-focused version of the lay summary, particularly where they have already developed child-focused Patient Information Sheets. Paediatric focused lay summaries may differ in terms of presentation and style (more illustrations or graphics) to assist children in understanding trial results, over and above what is required under the EU CT Regulation. Enabling increased understanding of results

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3 See ‘Recommendations for Drafting Non-Promotional Lay Summaries of Clinical Trial Results’
Good Lay Summary Practice

by the general public will also help parents and caregivers explain results to others, including children who have participated in a trial.

Where feasible, sponsors should consider testing the readability of the summary with a small number of people who represent the target population. Depending on the nature of the trial, this could be patients with a particular disease or members of the public. Their feedback and suggestions could be helpful in developing a summary that lay people will understand.

7. Numeracy

Trial results summaries are likely to include a variety of numerical data that should be easily understandable by the target audience. Some key principles to consider when using numbers in a lay summary are:

- Present absolute numbers but also consider conveying numerical information in other ways such as a percentage, rather than relative risks, odds ratios etc.
- Use whole numbers rather than decimals to the extent this is possible without increasing confusion. The lay summary should be cross referenced with the scientific summary.

Further detail on how to apply principles of numeracy can be found in Appendix 4 of the MRCT Return of Results Guidance Document, Version 2.1, July 13 2016 – Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard.

8. Visuals

Well-chosen and clearly designed visual aids can help enhance understanding of text and their use is encouraged. Summaries of clinical trial results that combine clear infographics with explanatory text can be a good way of presenting information. Basic principles to follow include:

- Where used, visuals should present a simple message and be clearly labelled with captions; consider how a visual aid helps to reduce the need for lengthy text. Visuals should always be accompanied by a simple textual explanation and placed near the text that they illustrate.
- Avoid using overly complex images, such as graphs showing several relationships, since they can be easily misinterpreted.
- Graphs using potentially misleading axes labels should be avoided. Consider the scales you are using in any graph and whether the axes need to start at zero to avoid confusion. Ensure that all your graphical images are clearly labelled.
- Creative solutions to ensure understanding could include cartoons and illustrations.
- Finally, although colour adds interest, any visuals or graphics should still be clear if printed in black and white.

For examples of clearly laid out visuals which aid understanding see the Understanding Immuno-oncology for kidney cancer website which uses infographics to display clinical trial results.

9. Language

As a minimum, the summary is expected to be provided in the local language of each of the EU countries where the trial took place. The specific local languages selected should match the languages employed in the Patient Information Sheet for that trial in each country (pdf versions of translated lay summaries will need to be uploaded separately). Where resources allow, sponsors should consider including an English version if the trial did not include the Republic of Ireland or Malta, as the use of a common language will allow greater accessibility across the EU and globally, however this is not mandatory.
Where translation is required for multi-country trials, care should be taken to ensure that the original meaning and non-promotional nature of the summary are maintained. Translated summaries should also take into account the cultural validity of the medical or technical terminology used.

10. Communication of return of results to participants

The summary for lay persons in the EU database should not be regarded as the only way of communicating with trial participants. Although not required by regulation, sponsors may provide trial results to investigators or third parties to feedback to patients who have taken part in their trials, along with an acknowledgement of their contribution and an expression of appreciation, rather than solely directing them to the lay summaries on the EU portal.
References for the EU Expert Group Recommendation

Health literacy:


Center for Information and Study on Clinical Research Participation (CISCRP) (www.ciscrp.org)


http://www.hsph.harvard.edu/healthliteracy/resources/teaching-patientswith-low-literacy-skills/

Health Literacy Missouri Best Practices for Numeracy (www.healthliteracymissouri.org)


A synthesis of health literacy principles used to create health information that is better aligned with the skills and abilities of those using that information.


MRCT Return of Results Guidance Document, Version 2.1, July 13 2016 – Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard. MRCT Return of Results Toolkit, Version 2.2, July 2016 – Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard.


For more information:

- [http://www.plainenglish.co.uk/free-guides.html](http://www.plainenglish.co.uk/free-guides.html)
- [www.plainlanguage.gov](http://www.plainlanguage.gov)
- The Centers for Disease Control and Prevention (CDC) has developed extensive health literacy resources including links to free training and an assessment tool:
  - Overview: [http://www.cdc.gov/healthliteracy/](http://www.cdc.gov/healthliteracy/)
  - Free online training: [http://www.cdc.gov/healthliteracy/gettraining.html](http://www.cdc.gov/healthliteracy/gettraining.html)
- Annex 1-3 (Templates) of the EU Expert Group Recommendation to be included.

Annex 1 - Templates with example wording

Annex V of the EU Clinical Trials Regulation contains 10 elements that must be included in the summary of the results of the clinical trial for lay persons:

1. Clinical trial identification
2. Name and contact of sponsor
3. General information about the clinical trial
4. Population of subjects
5. Investigational medicinal product used
6. Description of adverse reactions and their frequency
7. Overall results of the clinical trial
8. Comments on the outcome of the clinical trial
9. Indication if follow up clinical trials are foreseen
10. Indication where additional information could be found

This document provides detailed guidance on the information that could be provided for each of these ten elements. The template below has substituted the ten elements with user friendly equivalent headings. Sponsors should cover all ten elements but can, if they wish, combine categories where this makes sense. For example, some sponsors might wish to combine section 3.1 (where the trial was conducted) with 4.1 (the number of subjects included in the trial). Sponsors may also decide to change the order of the headings if they feel this is appropriate and add sub-headings to help reader find and understand the information provided.

The use of suggested wording is not mandatory but a consistent approach with a familiar layout is likely to make the summaries more accessible to the lay person. Sponsors should pick and choose those sections of text that they think might be of use. Suggested text is provided in blue.

### 1. Study name

- This section should refer to the phase of the trial (see "ICH Harmonised Tripartite Guideline General Considerations For Clinical Trials E8: General Considerations for Clinical Trials" for descriptions of trial phases) and specify...
the fact that this trial is only one study in an overall drug development process or process for understanding how treatments can be improved. Some trials take place outside of the four phases and the rationale for these trials should be explained, for example, long term safety study, pragmatic trials of existing licensed products etc.

Example Language:
Researchers look at the results of many studies to understand which drugs work and how they work. It takes lots of people in many studies all around the world to advance medical science. This summary only shows the results from this one study. Other studies may find different results.

### 1.1. Study name
- It is important that the title is specific to the trial so that it can be directly linked with other information included within the EU database.
- If the full title is lengthy and/or complicated then also provide a shorter and/or simpler lay title upfront followed by the full title. A short title alone may lead to confusion with other similar studies. Avoid technical terms and explain them further down in the document if necessary. The title should focus on the basic aim of the study.

### 1.2. Protocol number

### 1.3. EU Trial number

### 1.4. Other identifiers
- Other identifiers refer to EudraCT number, WHO ICTRP number, US NCT number, ISRCTN number if available, etc.

### 1.5 Abstract
Inclusion of an abstract is not mandatory but will help the reader identify whether they wish to read the whole summary. Give a very short description of the trial including:

- Purpose of the study
- What was tested: the intervention and any comparators, the Phase of the trial where applicable
- People taking part in this trial: including total number of participants across x countries
- Topline results: Simple description of the result of the primary endpoint
- Safety: overall statement about the safety findings in the study.

For example:

**ABSTRACT:**

Purpose of the study: To see if [medicine x] prevents the development of type 1 diabetes in children with a high risk of getting this disease.

What was tested: [Medicine x] was compared to (placebo) in a Phase 2 trial. In a Phase 2 study a new treatment is tested in a small number of patients [amend as appropriate].

People taking part: 350 children aged 7 to 16 years at high risk of developing diabetes took part in this trial across 3 countries.
Results: [Medicine x] did not prevent the development of type 1 diabetes in high risk children. Safety: In this study, researchers found that [Medicine x] had more side effects than placebo

<table>
<thead>
<tr>
<th>2. Who sponsored this study?</th>
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<tbody>
<tr>
<td>- Give the name of the organization, and how to contact (not a specific person in most cases).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. General information about the clinical trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1. Where was the study done?</td>
</tr>
<tr>
<td>- The countries in which the trial took place i.e. where participants were recruited.</td>
</tr>
<tr>
<td>For example:</td>
</tr>
<tr>
<td>This trial took place in the following countries:</td>
</tr>
<tr>
<td>o France</td>
</tr>
<tr>
<td>o Belgium</td>
</tr>
<tr>
<td>o Germany</td>
</tr>
<tr>
<td>o USA</td>
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<tr>
<td>o Canada</td>
</tr>
<tr>
<td>o China</td>
</tr>
<tr>
<td>o Japan</td>
</tr>
<tr>
<td>o South Africa</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3.2. When was this study done?</th>
</tr>
</thead>
<tbody>
<tr>
<td>- The overall trial start and end dates. For example:</td>
</tr>
<tr>
<td>1. This trial started in December 2014 and ended in March 2017.</td>
</tr>
<tr>
<td>- Where a clinical trial has had to close early, the information included in the summary should explain the reason for this, for example, evidence of lack of efficacy, safety events, poor recruitment etc.</td>
</tr>
<tr>
<td>- Sponsors may want to specify follow up periods here for some longer trials.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3.3. What was the main objective of this study?</th>
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</thead>
<tbody>
<tr>
<td>This section should specify:</td>
</tr>
<tr>
<td>- The purpose of the trial (for example, finding a safe dose, comparing treatments, etc.) / why the trial was carried out.</td>
</tr>
<tr>
<td>- Why the comparator was chosen, for example, the comparator is regarded as standard treatment for this condition.</td>
</tr>
<tr>
<td>- Any critical changes made during the study. For example, if the dosage used was changed or if the trial stopped early due to efficacy or side effects this should be noted.</td>
</tr>
<tr>
<td>- Avoid the use of unfamiliar abbreviations, acronyms and medical terms, for example “RCT” for Randomised Controlled Trial. Explain the concept simply. If you wish to use a medical term, use it in brackets after the simple explanation.</td>
</tr>
</tbody>
</table>

Suggested wording for different phases of clinical trials:

**Phase 1:**
In this study, researchers looked at how this drug works in the human body. Researchers did medical tests on men and women before and after they took the drug. The researchers wanted to know if there were:

- Any chemical changes in blood or urine, and
- Any unwanted side effects of the drug

This trial did not test if the drug helps to improve health. [Patients/healthy volunteers] took part in this study.

**Phase 2 trial:**
In a Phase 2 study a new treatment is tested in a small number of patients [amend as appropriate]. In this study, researchers gave medicine X to patients with diabetes to find out if medicine X lowered the amount of sugar in their blood.

**Phase 3 trial:**
In a Phase 3 study a new treatment is tested in a large number of patients [amend as appropriate]. In this study, researchers compared the test medicine to the standard treatment used for [disease/condition] or placebo (identical looking tablets but with no medicine in them).

**Phase 4 trial:**
This trial was carried out after the new treatment had been approved for use (meaning that the treatment can already be prescribed by doctors). Researchers looked at the effect of the new treatments in a larger number of people.

**Randomisation:**
People with diabetes were put into 2 groups by chance (randomised) to reduce differences between the groups. Putting people into groups by chance helps to make the 2 groups equal. Reducing differences between the groups in this way, makes the comparison between the groups fairer.

**Blinding:**
[If the trial was double-blinded, also add the following wording] This trial was also “double-blinded”. This means that neither patients nor doctors knew who was given which treatment/drug. This was done to make sure that the trial results were not influenced in any way.

[If the trial was single-blinded, use the following words] This trial was single-blind. This means that the patient did not know who was given which treatment they were given but the doctor did know.

[If not randomised, list how many patients/people were in each group, and how this was determined.]

**4. What patients/people were included in this study?**

4.1. The number of subjects included in the trial by country both within and outside of the EU
For example:
This trial included (specific population to whom this applies, including healthy volunteers and patients as appropriate]

The trial was run in the following [list country (ies) that enrolled patients]. In each country [name the country] (#) people were enrolled in this study. If there are a lot of countries involved, it may be easier to present this data in a table or pie chart. It may be helpful to
combine the requirement under section 3.1 with those of this section presenting both together rather than separately.

### 4.2. Age group and gender breakdown
- Provide basic breakdown of participants by age and gender in the trial as a whole
Consider including a simple graphic that helps the reader understand the study.

### 4.3 Inclusion and exclusion criteria
- The number of inclusion and exclusion criteria can vary substantially, and long lists of technical criteria can be very difficult to understand. It is suggested that when there are large numbers of inclusion and exclusion criteria, the sponsor should only list the most important inclusion and exclusion criteria - and draw attention to those criteria that have the most impact on the population to be studied.
- If possible, sponsors should include references to age, gender, diagnosis, indication, disease stage or severity as this will help define the scope of the trial (for example, 'very severe chronic obstructive lung disease')
- Sponsors should also avoid using technical terms that lay persons might struggle to understand. For example, 'myocardial infarction' would be better described as a 'heart attack'. Explain the concept simply. If you wish to use the medical term, use it in brackets after the simple explanation.
- Care should be taken not to provide information that might inadvertently identify specific individuals who have taken part. Particular care should be taken in trials for rare diseases where the number of potential participants will be relatively small.

### 5. Which medicines [or vaccines] were studied?
- This should include naming of the trial medicine (and comparator(s)) as used in the protocol and trial registration.
- For early phase trials it might not be possible to refer to a specific name and will need to use the internal compound code instead.
- If a placebo was used in the trial, this should be stated clearly and the term 'placebo' explained. See the description above in section 3.
- Randomisation and blinding arrangements should be described.

### 6. What were the side effects?
Sponsors should note that the lay summary calls for a description of adverse reactions whereas the technical summary refers to adverse events. This difference is intentional and means that text should not be simply copied across from one section to another. Whilst it is not always possible to establish an exact causal relationship between the investigational medicinal product and the adverse events in a single study, the sponsor should define 'adverse reactions' as those adverse events where the investigator has indicated that there is a possible causal relationship between the event and the investigational medicinal product.
- Consider using a simple term, such as "side effects" to refer to adverse reactions, explaining how 'side effects' are defined for the purpose of the lay summary.
• Serious adverse reactions need to be listed first, followed by other common adverse reactions listed by frequency (starting with the most frequent) and using a clearly communicated ‘cut-off’ where needed.
• Frequencies should be given in numerical terms as well as percentages (X out of X patients [x%]) following the principles of numeracy. Where specific adverse reactions coincide with endpoints, this should be stated.
• The number of serious adverse reactions including fatal adverse reactions should be clearly stated together with any adverse reactions that have led to the early closure of the trial or the withdrawal of patients. The classification of serious adverse reactions should be explained (for example, "reactions that are life threatening or require the individual to have to go hospital").
• Include clinical laboratory changes only if they are useful/clinically relevant.
• MedDRA (Medical Dictionary for Regulatory Activities) terms, or other similar terminology as appropriate, should be translated into lay language where necessary. This might mean using the preferred term and a lowest level term as a plain language descriptor.

Suggested wording to describe adverse reactions (also known as side effects) is as follows:

Side effects are unwanted medical events (such as a headache) that happen during the study and are reported because the trial doctor (investigator) believes the side effects were related to the treatments in the trial. Not all the people (people/patients) in this trial had side effects.

Serious and common side effects are listed here.

(List the serious adverse reactions and most prevalent other adverse reactions for each trial drug(s) tested (excluding the serious in the latter section to avoid duplication). If possible, compare the number of people who had each event by dose level.) Where the adverse reaction profile is similar for both the intervention and the comparable arm(s) the sponsor should only have to list the adverse reactions once indicating the numbers in each arm of the study.

(Plainly state any objectives or statistically valid endpoints that dealt directly with adverse reactions.)

Side effects [in Group A] included:

(List the serious and most prevalent (excluding the serious) adverse reactions. Apply numeracy and health literacy principles.)

(Minimise acronyms/medical terms and explain any that are used.)

Side effects [in Group B] included:

Side effects [in Group C] included:

More side effects were seen in Group C than in Group B. Because so many side effects were seen in Group C, no higher doses were tested.

7. What were the overall results of the study?

This section should describe each of the trial arms including the name of the drug (generic only) as well as the outcomes (both positive and negative), using text and graphics where appropriate, including:

• A general high level statement summarising the overall results and their implications without using promotional language (See neutral language guidance in Annex 2).
• Information on whether the trial completed as planned, or was stopped and for what reason.
• The primary endpoint(s) and results by trial arm which were pre-specified by the statistical analysis plan as a primary endpoint.
• Additional safety data important to the overall results of the trial.
• Sponsors should reference the complete list of outcomes based on all endpoints available in the technical results summary for each clinical trial in the EU database including patient relevant secondary endpoints.

Describing numerical concepts to a lay audience can be difficult and sponsors should follow the following guidance:

• Outcomes should be described using numeracy (x out of xx people [xx%]) and plain language principles.
• Refrain from using technical terms such as 'number needed to treat', 'odds ratio', 'confidence interval' etc. If technical terms are included, then they need to be explained in simple language.
• If reference is made to numerical differences that are not statistically significant, this should be explained to the reader. For example:

  2. Group A had lower blood sugar levels than Group B but the difference between the groups is likely to be by chance rather than a difference caused by the treatment.
• Further guidance on providing numerical information can be found at www.healthliteracymissouri.org/.

The following table lists common clinical trial endpoints in simple language. Terms are defined with general descriptions, followed by examples of simple, plain language that can be used in summaries of clinical trial results for laypersons. Please select those examples that relate to the type of outcome in your trial.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Original description of the type of endpoint</th>
<th>Example of desirable simple, plain language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>A composite endpoint, as the primary endpoint, combines multiple outcomes (for example, death, getting sick again (relapse), and serious event) and test results into one measure of how well the drug/therapy/device works. This is useful when there are many different outcomes that can happen during a trial. This can also be called a combined or multi-part endpoint.</td>
<td>“The XXX trial measured [patients/people] to see if those in Group A (ABC treatment) or Group B (XYZ treatment) lived longer, had fewer heart attacks, or fewer hospital visits for heart failure. These outcomes were measured together (combined) because each one is quite rare. Researchers also wanted to see if the drug worked in patients who had all 3 conditions. The trial found that there was no change in the number of outcomes for [patients/people] in Group A or Group B.”</td>
</tr>
<tr>
<td>Dose Escalation</td>
<td>Dose escalation is sometimes used in phase 1 studies to measure safety. People in the trial start with a low dose of the medicine (drug). If that dose does not cause safety problems, then more people are given a higher dose until there are too many safety issues. The highest dose that is tolerated is called the maximum tolerated dose (MTD).</td>
<td>“This trial was undertaken to find the highest [dose/amount] of treatment that people could safely take [or use] without having severe side effects.”</td>
</tr>
</tbody>
</table>
**Mortality / Overall Survival**

The goal of this trial was to see if Treatment ABC or Treatment XYZ helped patients with [disease/condition] to live longer.

"This trial compared patients in Group A (Treatment ABC) to those in Group B (Treatment XYZ) to see who lived longer.

If there was no effect –

"Patients in both groups lived about the same amount of time, no matter what treatment they got."

If there was an effect (statistically significant) –

"The times given below refer to the average amount of time that [patients/people] in this study lived.

Some [patients/people] lived for a shorter time and some lived longer.

People in Group A (ABC treatment) lived about 15 months.

People in Group B (XYZ treatment) lived about 12 months.

This means that people in Group A (ABC treatment) lived about 3 months longer than people in Group B."

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**Morbidity**

Morbidity endpoints are those that measure the severity of disease, or when the patient experiences a new disease or illness.

"People with diabetes were put into 2 groups by chance (randomised) to reduce differences between the groups.

Group A received drug X, Group B followed a diet and exercise program. All people were followed over time to test the health of their heart and blood system, including stroke, high blood pressure and heart disease.

**EFFECT** – After x years both groups had similar health conditions and outcomes. There was no difference in the health of the heart for patients in Group A (drug X) compared to patients in Group B (diet and exercise)."

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**Non-Inferiority**

Non-inferiority endpoints are designed to show that a new treatment or drug is not worse than the control (or other comparison drug) by a pre-specified amount (also termed the non-inferiority margin). Efficacy can, in fact, be worse if there are other benefits (for example, fewer side effects).

"Non-inferiority studies are conducted when it is not possible to compare the new treatment with an established treatment. In a non-inferiority trial, it is expected that the new treatment would work as well or almost as well as, the existing treatment but might have other advantages such as fewer side effects or offer a better quality of life."
This trial showed that insulin A (Group A) was not different or at least not worse than standard insulin therapy (Group B) in lowering the blood sugar level in Type 1 diabetic patients. Patients in Group B had fewer side effects of upset stomach and feeling sick (nausea) than those in Group A.

**Patient-Reported Outcomes**

This trial asked patients about their [list the main purpose of the questionnaire: for example, symptoms, activity level, quality of life, income and/or happiness] and if the measurement changed based on whether a patient got A or B.

The primary endpoint is less XXX based on the YYY scale. This scale measures ZZZ and how this changes over time.

“Patients answered questions to measure pain, stiffness, and how well they could climb stairs, stand or bend over. Questions were asked during each trial visit.

About 2 in 4 people (50%) in Group A had less knee pain.

About 1 in 4 people (25%) in Group B had less knee pain.

This means that fewer patients in Group A had knee pain than patients in Group B (Drug B/placebo).

The incidence endpoint tells how many new cases of XXX occurred over a given period of time.

“Women who had a bone fracture after they stopped having their monthly periods (menopause) were put into 2 groups by chance (randomised) to reduce differences between groups. The trial was carried out using two different groups because no one knew if one treatment was better than another.

1. In 20 women (5%) in Group A (bisphosphonates) had a break in their back bone (vertebrae).

2. In 20 women (10%) in Group B (X Treatment) had a break in their back bone (vertebrae).

Fewer patients in Group A had a break in their back bone.”

Progression-free survival endpoints measure how much time it takes from the beginning of starting a drug/therapy/device until a patient has a sign that the disease has progressed/spread/got worse.

The goal of this trial is to measure whether people given drug XXX had longer PFS than those that did not get drug XXX.

“Patients in this trial were assigned to 2 groups by chance (randomised). This was done because no one knew if one treatment was better than another.

The goal of the study was to measure the size of each breast cancer tumour to see if it had shrunk, stayed the same, or grew in a 1 year period.

56 in 100 patients (56%) in Group A (ABC treatment) had tumours that stayed the same, while 12 in 100 patients (12%) had tumours
Surrogate markers may be used instead of a clear endpoint (for example, overall survival) when it is hard to measure the outcome or the trial would take too long to complete. Surrogate markers measure participants’ level of X over time. Doctors believe that measuring this level of X may show how severe the disease is or how likely something is to happen in the future.

The main goal of this trial was to see if drug A lowered pressure in the eye (called intraocular pressure).

Higher eye pressure could mean that vision may be lost faster than with lower eye pressure.

This trial found that people in Group A (drug A) had lower eye pressure at the end of the trial than at the beginning.

People in Group B (placebo) had no change in their eye pressure over the course of the study.

Eye pressure may be linked to how much vision is lost due to glaucoma [define the disease]. This is not yet known.”
Findings from this trial will be used [add general next steps to this sentence to help explain context. Suggestions include:]

- in other studies to learn whether [patients/people] are helped by this drug
- in other studies to compare this drug with other treatments for [patients with condition/disease]
- to seek approval for using the treatment for [patients with condition/disease].

<table>
<thead>
<tr>
<th>9. Are there plans for further studies?</th>
</tr>
</thead>
<tbody>
<tr>
<td>This section should explain whether other related trials are ongoing already or provide public domain information about related trials. For example:</td>
</tr>
<tr>
<td>- Clinical trials with Drug X are ongoing and further trials are planned</td>
</tr>
<tr>
<td>- Further clinical trials with Drug X are planned</td>
</tr>
<tr>
<td>- No further clinical trials with Drug X are planned at the current time.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10. Where can I find more information about this study?</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Provide links to helpful websites with further information such as industry based websites as well as university websites and others.</td>
</tr>
<tr>
<td>- Care should be taken to avoid readers being unnecessarily exposed to any promotional language either on the linked pages or pages that readers might be exposed to in the process of accessing the relevant pages.</td>
</tr>
<tr>
<td>- Provide links to other generic sites of related interest such as other clinical trial registries, European Clinical Trials Register (EU CTR), the Cochrane Library etc.</td>
</tr>
</tbody>
</table>

Suggested wording might be:

To learn more about this study, you can find more detailed information on this website (EU database)
- [include link to technical summary].

More information may also be available by going to

(list relevant websites that may have further information about this trial etc if appropriate).

You can also find more details about this trial at:

(List all applicable citations and websites that are not listed in clinicaltrials.gov or EudraCT. This can include resources as well as articles).

For general information about clinical trials, go to: [Below are some suggested sites. List appropriate sites whilst taking care not to overwhelm readers with links]

- http://www.testingtreatments.org
- https://www.clinicaltrials.gov/ct2/about-studies/learn
- http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm
Annex 2 - Neutral language guidance in describing results

Sponsors, as well as individuals and groups, who intend to communicate summary results to trial participants and the public are sometimes concerned that the language used might be considered unduly positive, promotional, or serve a marketing purpose.

Below we offer terms to avoid and terms to consider that reflect objective, neutral descriptions of trial results. The first column in the table below lists possible statements that might be considered promotional. The second column with blue text suggests neutral language that provides neutral and objective information.

<table>
<thead>
<tr>
<th>Examples of Promotional Language</th>
<th>Neutral Language - Consider this</th>
</tr>
</thead>
<tbody>
<tr>
<td>This trial proved</td>
<td>This trial found that This does not mean that everyone in that group had these results.</td>
</tr>
<tr>
<td>This trial proved that using &lt;drug A&gt; to prevent &lt;disease/condition&gt; is effective.</td>
<td>This trial found that people with &lt;disease/condition&gt; who received or were treated with &lt;drug A&gt; had &lt;primary endpoint&gt;.</td>
</tr>
<tr>
<td>The combination treatment of &lt;drug A and B&gt; may also help &lt;a different disease/condition than what was/was not studied elsewhere&gt; as observed in new small studies.</td>
<td>When &lt;drug A and B&gt; are used together, people in this trial had &lt;study endpoint&gt;. The drugs may be helpful in other diseases/conditions, but this was not studied here. Further studies in &lt;disease/condition&gt;will be needed.</td>
</tr>
<tr>
<td>This means that &lt;drug A&gt; is better than &lt;drug B&gt;.</td>
<td>In this study, people who took &lt;drug A&gt; had more &lt;study endpoint&gt; than some people who took &lt;drug B&gt;.</td>
</tr>
<tr>
<td>&lt;drug A&gt; works better than &lt;drug B&gt;, but some people didn’t tolerate it as well.</td>
<td>In this study, more people who took &lt;drug A&gt; had &lt;trial endpoint&gt; than those who took &lt;drug B&gt;. But they also had more side effects that may have interfered with their daily lives, &lt;list specific adverse reactions&gt;.</td>
</tr>
</tbody>
</table>

Examples of Promotional Language

<drug A> is better tolerated than <drug B>.

Neutral Language - Consider this

People taking <drug A> lived longer after they had <therapy> for <disease/condition>, even with more adverse reactions.

People who took <drug A> lived longer than those that took <drug B>. The patients who took <drug A> also had more side effects.

While the combined treatment of <drug A and B> did not extend life over <drug A> alone, people felt better and lived longer with the combined treatment.

People in both groups had the same kind of results (outcomes). People who took the combined treatment <drug A and B> had milder side effects <list specific adverse reactions> but did not live longer.

Trial groups had the same results. More studies are provided after acceptance for publication in a peer reviewed journal.

There was no effect in the treatment groups/there was no difference between the groups.

People in group <1> were able to tolerate the highest dose of <drug A> so more studies will be done.

People in group 1 were able to take the highest dose of drug A without side effects so more studies will be carried out with drug A.
Annex 3 - Examples of readability tests by country

Dutch

The Leesindex was developed by Brouwer in 1963 and is a modified version of the Flesch Reading Ease Score (see below).

English

Using Microsoft Word, writers can test the readability of writing in English by using the Flesch Reading Ease Test or the Flesch-Kincaid Grade Level Test based on counting syllables and sentence length. This can be helpful in multi-country studies where summaries are first drafted in English and then translated into other languages. The Flesch Reading Ease Test assesses readability on a scale from 1 to 100. The higher the Flesch Reading Ease test score, the easier the text is to read. Anything that scores 70 and above is easy to read.

The Flesch-Kincaid Grade Level Test uses an algorithm that includes both the number of syllables per word, as well as average sentence length and transforms the test score into a school grade equivalent based on the U.S. school grading system. An ideal reading grade level is 6th grade, which is close to the literacy level of the general population. Even if the writer cannot achieve this, strive to get as close to this as possible.

French

Kandel & Moles Modified Flesch Reading Ease has been adapted for French Texts. The Kandel & Moles scale scale ranges from 0 to 100 and scores of 60 to 100 indicate text, which is normal or easy to read. Text that scores below 60 is regarded as difficult to read.

German

There are a wide range of readability tools available for the German language. The Flesh Reading Ease Index has been adapted for the German language. This was done by keeping the original scale and newly calculating the word factor, taking into account the greater length of German words. (REF: Amstad T. Wie verstaendlich sind unsere Zeitungen, Universitaet Zuerich. Dissertation 1978). Text that scores 80 and above is defined as easy to read.

A more recent and frequently used tool is the Hohenheim Comprehensibility Index which operates on a scale from 0 (totally incomprehensible) to 20 (very comprehensible). The Index is generated with the support of a computer program for automatic text analysis (TextLab). The analysis takes into account the length of sentences and words, use of nested sentence, proportion of abstract terms. An easy to read text should have a score of 17 and up.

Italian

The GULPEASE formula is the first readability formula directly adjusted on the Italian language and considers two linguistic variables: the length of the word (in letters and no longer in syllables) and the length of the sentence compared to the number of letters (see Lucisano-Piemontese,1988, and Lucisano, 1992).

The formula is the following:

$$89 + \frac{300 \times (n^\circ \text{of sentences}) - 10 \times (n^\circ \text{of letters})}{\text{number of words}}$$
The GULPEASE index (Lucisano and Piemontese, 1988) is seen as a suitable alternative tool for assessing readability of the Italian language. The GULPEASE index takes into account the length of a word in characters rather than in syllables, which proved to be more reliable for assessing the readability of Italian texts. The index ranges from 0 (lowest readability) to 100 (maximum readability).

**Spanish**

The Huerta Reading Ease, developed by Fernandez-Huerta, is a Modified Flesch Reading Ease for Spanish text. In this test, scores range from 0 to a 100 – a 100 represents the greatest ease of reading. A text with a result of <30 is considered very difficult, whereas a score of 70 is considered appropriate for adults.

In 2008 Barrio-Cantalejo et al proposed the use of the new Inflesz scale, which is a modification of both these scales for a more appropriate assessment of texts in Spanish. On this scale, a score of 55 marks the cut-off between a text that is accessible or not to an average person. “Normal” is defined as a score of between 55 and 65, “very difficult”, between 0 and 40, and “somewhat difficult”, between 40 and 55. Among the higher scores, “quite easy” is indicated by a score of 65 to 80 and “very easy” by a score above 80.

**Swedish**

LIX (The Lasbarhets index Swedish Readability Formula) is a readability measure to calculate the difficulty of reading a foreign text. The Lix Formula was developed by Swedish scholar Carl-Hugo Björnsson in 1968 and revised in 1983. As with other readability tools, LIX is based on a combination of word and sentence length. However LIX assesses word length by estimating the percentage of words with more than six letters. Scores below 40 are regarded as easy and scores of 50 and above indicate text that is difficult to read.
Appendix 3: Planning, Development, Translation and Dissemination of Lay Summaries

Planning Patient Involvement

The collaboration between commercial 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 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.

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.\textsuperscript{33}

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.\textsuperscript{34}

**Compensation of Patients and Public Contributors**

1. 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.

2. If the patient is requested to travel within the agreed frame of collaboration, the sponsor should organise the trip and cover the 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.

**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.

The Thank You Letter should be provided as soon as possible after achieving patient input with information about the timing and channels of dissemination of the final LS.
Table 3.1: Table of Estimated Effort for Lay Summary Production According to Trial Complexity

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

Adverse Reactions and Safety Information

Element 6: Description of Adverse Reactions and Their Frequency

Annex V of EU CTR 536/2014 specifies that a “description of adverse reactions and their frequency” should be included in the LS. The EU Expert Group expands on this, acknowledging an intentional difference in the adverse reaction information presented in the LS compared with the adverse event information presented in the technical summary. The intended audiences of these two summaries differ. While recognising that it is not always possible to establish an exact causal relationship within a single clinical trial, the EU Expert Group recommendations state that the sponsor should define adverse reactions as those adverse events for which the investigator has indicated that there is at least a possible causal relationship between the event and the investigational medicinal product. The recommendations suggest that a simple term such as “side effects” could be used to refer to adverse reactions. However, terms such as “side effect” and “adverse reaction” described in the product label may be confused with the adverse drug reactions (ADRs) occurring in a clinical trial (see Table 3. below). 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, including those that are life threatening, result in death, are medically important, cause significant or lasting disability or require hospital care also need to be explained in plain language.
A further difference between the LS and technical summaries is the sequence of information. The EU Expert Group recommends 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. However, listing non-serious adverse reactions independently represents another difference versus publicly available technical summaries, in which the total numbers of all adverse events are listed regardless of seriousness.

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. Depending on trial design, discontinuation of trial treatment does not always result in participant withdrawal. 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. General or non-scientific readers may misinterpret adverse events as definite side effects; providing information on adverse events that have had some level of causality assessment is likely to provide a more accurate perception of the safety profile. Moreover, long lists that include unrelated events could be potentially misleading and alarming to a non-technical readership.

The reader should not be expected to make analytical judgements based on the relative incidence of events versus a placebo group. Likewise, 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 as noted in Table 3.2. These clarifications could be applied as standard language for LS, for example within template text.
### Table 3.2: Cautions Related to Description of Adverse Reactions: Considerations for Development of Standard Lay Summary Template Language

<table>
<thead>
<tr>
<th>Caution</th>
<th>Considerations for developing a standard LS template</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential confusion regarding “side effects” or “adverse reactions”</td>
<td>• Sponsors may consider prefixing the term with “possible”: “possible side effect” or “possible adverse reaction.”</td>
</tr>
<tr>
<td>described in the prescribing information/product label for approved</td>
<td>• Clear, plain language definition of what is meant by “adverse reaction” (or equivalent term used) for the purpose of the LS.</td>
</tr>
<tr>
<td>products</td>
<td>• 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.</td>
</tr>
<tr>
<td></td>
<td>• Other wording to explain that the assignment of causality is not definite.</td>
</tr>
<tr>
<td></td>
<td>• Explanation that other studies may have different findings.</td>
</tr>
<tr>
<td>Potential confusion with respect to:</td>
<td>• Explanation that the results may be presented differently elsewhere.</td>
</tr>
<tr>
<td>• Differences in numbers presented in other publicly available technical</td>
<td></td>
</tr>
<tr>
<td>documents (although there will also be unavoidable differences in</td>
<td></td>
</tr>
<tr>
<td>terminology due to translation into plain language)</td>
<td></td>
</tr>
<tr>
<td>• Information provided to trial participants in the informed consent</td>
<td></td>
</tr>
<tr>
<td>document</td>
<td></td>
</tr>
</tbody>
</table>

Regarding other safety information from the trial, the EU Expert Group recommends 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. Therefore, the GLSP may apply to important trends in safety measures within treatment groups. The Multi-Regional Clinical Trials (MRCT) Draft Food and Drug Administration (FDA) Guidance on Provision of Plain Language Summaries advises that additional safety data important to the overall results of the trial may be included so long as inclusion is balanced and there is reasonable justification. Clearly, this is subjective, and likely to be a clinical safety judgement based on the results, but sponsors should aim to adopt a consistent approach across trials as far as possible.

### Presentation of the Safety Information

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 (see section 3.4). 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.

Both the EU Expert Group and the MRCT Draft FDA Guidance on Provision of Plain Language Summaries 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.

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 if 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 the following statement: "The trial doctor did not know whether a participant was receiving the investigational treatment or placebo at the time of judging whether an event might have been a possible adverse reaction." 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. As discussed in section 2.7 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. Notwithstanding design-specific considerations, it is anticipated that the general principles for content and presentation described above will apply to all LS.
## Examples of General Phrases

### Table 3.3: General Phrases

<table>
<thead>
<tr>
<th>Term or concept and what the phrase may contain.</th>
<th>Lay language examples</th>
</tr>
</thead>
</table>
| 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.  
   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.  
   The purpose of the clinical trial was to look at how well the medicine works and how safe it is.  
   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.  
   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.  
   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.  
   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>.  
   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.  
   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. |
<p>| 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. |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Randomisation</td>
<td>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.</td>
</tr>
<tr>
<td>9</td>
<td>Arm of the study</td>
<td>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.)</td>
</tr>
<tr>
<td>10</td>
<td>Multi-arm</td>
<td>This is a multi-arm study. In this study, each of the four (3, 5, 6) different groups of patients received a different treatment.</td>
</tr>
<tr>
<td>11</td>
<td>Multi-stage</td>
<td>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.</td>
</tr>
<tr>
<td>12</td>
<td>Approved vs non-approved product (investigational product)</td>
<td>Treatment A is already approved for use by authorities. Doctors can prescribe the Medicine A to treat &lt;disease/condition&gt;. Treatment A is not yet approved by authorities to treat &lt;disease/condition&gt;. Treatment A is already approved by authorities to treat &lt;disease/condition X&gt;. Researchers now wants to see how well it works to treat &lt;disease/condition Y&gt;.</td>
</tr>
<tr>
<td>13</td>
<td>Placebo</td>
<td>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.</td>
</tr>
<tr>
<td>14</td>
<td>Purpose of blinding</td>
<td>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. 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.</td>
</tr>
<tr>
<td>15</td>
<td>Open-label treatment</td>
<td>Patients were either taking Medicine A or Medicine B. In all cases both the patients and the doctor knew which medicine they were taking</td>
</tr>
<tr>
<td>16</td>
<td>Differences in the numbers of randomised and treated participants.</td>
<td>In this study, xx men and women agreed to take part. Of these, only yy people took the medicine.</td>
</tr>
<tr>
<td>17</td>
<td>Statistical power – explaining the lack of power</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Good Lay Summary Practice</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----------------------------</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Adverse reaction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>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. 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. We have only shown those adverse reactions which happened in more than 1 in 5 people in the study.</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Serious adverse reactions (SAR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Adverse reaction of special interest</td>
<td></td>
</tr>
<tr>
<td></td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Endpoints</td>
<td></td>
</tr>
<tr>
<td></td>
<td>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. 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.</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>2nd endpoints</td>
<td></td>
</tr>
<tr>
<td></td>
<td>This trial also collected info about heart attack and stroke. 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. 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.</td>
<td></td>
</tr>
</tbody>
</table>
### Good Lay Summary Practice

| 23 | Patient reported outcomes and HRQoL | The study also collected information on outcomes directly from patients. These outcomes were:  
- pain, breathing, fatigue (symptoms)  
- how well patients were able to walk/move (physical functioning)  
- mood, coping (psychological state)  
- ability to go to school, work, take part in community (social functioning)  
- quality of their daily lives with the treatment  
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.  
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>.  
In this study, researchers found/studied <describe the study outcome and how it will help patients and researchers>.  
Findings from this study will be used: <select the most applicable from below or add text as appropriate for study>  
- in other studies to learn how <generic drug or device name> may help people.  
- in other studies to compare <generic drug or device name> with other treatments/medicine/medical tools for <disease/condition>.  
- to combine <generic drug or device name> with other treatments in people with <disease/condition>.  
- to seek approval for using <generic drug or device name> to treat people with <disease/condition>.  
- to further study the safety/efficacy of <generic drug name>.  
- to further improve the most effective use of <generic drug name>. |
## User Testing

### Table 3.4: User Testing Steps

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

### Table 3.5: Child Development, Comprehension and Learning by Age Group

<table>
<thead>
<tr>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comprehension</strong></td>
<td>Use interesting words and phrases. Use evidence from text when discussing. Use glossaries to check meaning of words. Able to identify details that support main messages. Learn to justify inferences with evidence. Develop understanding of concepts. Able to make simple comparisons. Begin to understand mutual dependence, and that people have different experiences and views.</td>
<td>Able to apply known concepts to new theoretical understanding. Have a clear understanding of distinction between facts and fiction and the way they are presented. Able to handle complex information and make comparisons. Able to comprehend complexity/coherence/inference in what they experience, read and are being told. Have strong (own) sense of right and wrong, good and bad.</td>
</tr>
<tr>
<td><strong>Learning strategies</strong></td>
<td>Learn through storytelling and find it easier to engage with topics and issues they can make personal or emotional connections to (egocentric perspective).</td>
<td>Learn through personal experience and basic theoretical thinking, especially if interlinked. Learn by mirroring other children of the same age. Belonging to a group is becoming important. Highly influenced by peer groups. Focus on themselves and belonging to a group. Family support seems not important. May want to challenge rules and recommendations.</td>
</tr>
<tr>
<td><strong>Scientific understanding</strong></td>
<td>Objects are made of specific materials. There are different kinds of materials. Objects have certain properties: weight, length, area, and volume. Properties can be described, compared and measured. (Observable properties: colours, hardness, flexibility, fluidity, solid forms). Measurements are more reliable than common-sense impressions. Measurement involves comparison. Ideas can be evaluated through observation and measurement. Instruments, such as microscopes, can extend our ability to observe and measure.</td>
<td>Solids, liquids, and air are forms of matter and share general properties. There can be invisible pieces of matter (too small to see). Combining two or more materials can produce a product with properties different from those of the initial materials. Measurements can be more or less precise. Sources of measurement error can be examined and quantified. 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. The properties of materials are determined by the nature, arrangement, and motion of the molecules that they are made of. In chemical changes new substances are formed as atoms are rearranged into new molecules. The atoms themselves remain intact. In physical changes, molecules change arrangement and/or motion but remain intact, so the chemical substance remains the same.</td>
</tr>
</tbody>
</table>
## Numbers and maths

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6 years</td>
<td>Able to count to 100. Understand ⅓ and ¼ of a part or of a group.</td>
</tr>
<tr>
<td>7-8 years</td>
<td>Understand and work with numbers up to 1000. Understand simple fractions: (2/5 = 4/10).</td>
</tr>
<tr>
<td>9-10 years</td>
<td>Learn basic percentages. Understand and work with negative numbers. Round numbers to nearest 10, 100 and 1000. Understand and work with decimals. Round decimals to nearest whole number.</td>
</tr>
<tr>
<td>Work with ratio, proportion and percentages. Round to nearest 10,000,000. Understand basic ratio, scale factors, and equations. Understand unequal sharing and grouping. Work with infographics: pie-charts, 2D-diagrams: column, line and bar-charts.</td>
<td></td>
</tr>
</tbody>
</table>

## Grammar

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6 years</td>
<td>Read one syllable words. Use (read) capital letters and punctuation. Use (read) common exception words.</td>
</tr>
<tr>
<td>7-8 years</td>
<td>Read one or two-syllable words that they can decode already but with a prefix or suffix added on. Use (read) simple sentences made of main clauses.</td>
</tr>
<tr>
<td>Understand verbs to describe relationships of time and cause. Understand expanded noun phrases to convey complicated information concisely. Understand relative clauses: who, which, where, when, whose, that or with an implied relative pronoun. Understand commas to clarify meaning or avoid ambiguity. Understand the use of a colon or bullet points to introduce a list.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 3.6: Recommendations for Paediatric Lay Summary Content

<table>
<thead>
<tr>
<th>Background knowledge</th>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Write at relevant level of knowledge about/experience with disease and intervention – this will vary according to the trial and the patient group.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perspective</th>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Write from a group perspective including a limited number of people and how their different contributions helped researchers create new knowledge.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Write at population level.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Representativeness</th>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use a limited number of people or characters:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child, or boy and girl Doctor or nurse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent(s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Make sure to reflect diversity of race, gender, ethnicity, class, disability and age.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe main characters and their connection to a larger group of maybe 10 or 20 children.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Make sure to reflect diversity of race, gender, ethnicity, class, disability and age.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>May be easier to follow the study-flow and procedures when writing about specific characters.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present variations at population level.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Storyboard</th>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start:</strong> Introduce characters. Present disease characteristics, relevant symptoms and how this affects the child. Frame the child as a unique contributor to research.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Middle:</strong> Describe trial-related actions, procedures and the child’s experiences incl. side effects.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>End:</strong> What the child learned, achieved, succeeded in – and what researchers learned. Acknowledge the child’s contributions as part of the ‘research-team’.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Story</th>
<th>Age ≤ 8 years</th>
<th>Age 9-11 years</th>
<th>Age 12-15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use familiar words to explain what happened / was done. Reflect the child’s point of view. Describe:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• who were involved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• tool</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• purpose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focus on what the child did during procedure/trial. Less on doctor’s actions or scientific explanations. Avoid time shifts, and changes in point of view. Choose content or stories with straightforward and time-reflecting descriptions that are easy to follow.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflect child’s independence from parents in a narrative if applicable to the trial.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More children can be included in the narrative/story to show what different participants did or if they experienced different effects.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Describe how the treatment works/is expected to work in the body. Describe the effect on the disease/symptom and how the child reacted – if any changes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence</td>
<td>Describe/show what the participant took/had, how often and for how long. Example: &quot;The child took two pills each morning for 28 days&quot;.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects</td>
<td>Describe/show how the side effect made the child feel and how often. Include causation. 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. E.g.: &quot;The pill made the boy feel dizzy for 2-3 minutes&quot;, rather than &quot;Dizziness occurred&quot;.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbers and scaling</td>
<td>Use small denominators that are closer to &quot;plausible&quot; group sizes in human society (x/20). Show percentages as infographics.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equality between participants</td>
<td>Make sure that all participants are described as &quot;heroes and &quot;important contributors&quot;. Include children who took part in a control group, placebo group, group with negative results etc.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 3.7: Recommendations for Paediatric Lay Summary Lay-out and Design

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

### Table 3.8: Step-by-Step Translation Process

<table>
<thead>
<tr>
<th>Step</th>
<th>Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Planning</td>
<td>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.</td>
</tr>
<tr>
<td>2. Forward translation</td>
<td>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.</td>
</tr>
<tr>
<td>3. Back translation</td>
<td>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.</td>
</tr>
<tr>
<td>4. Comparative review</td>
<td>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.</td>
</tr>
<tr>
<td>5. Final Quality Assurance inspection</td>
<td>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.</td>
</tr>
<tr>
<td>6. Delivery and certification</td>
<td>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.</td>
</tr>
</tbody>
</table>
### Technical Distribution Methods

#### Table 3.9: Technical Distribution Methods: Benefits and Risks

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

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

| LS is posted by the sponsor on a **third-party public website.** | The trial participants receive a card from the investigational site at their PLV notifying them of the third-party public website.  
Option of the trial participant to self-register for an email notification when the LS is posted on the third-party managed public website.  
Option of the third-party website to contain an “opt in or opt out” by the trial participant before viewing the LS  
Metrics are easily obtained.  
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.  
The investigational site does not notify the trial participant at their PLV explaining where and when the LS will be available.  
The third-party website is not available in local languages.  
The trial participant may forget the URL, which was provided at their PLV.  
The trial participant does not have access to the internet.  
The trial participant’s email address may change, and the third party is not informed by the trial participant.  
Blind/illiterate trial participants may not be able to access the portal autonomously.  
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.  
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.  
Distribution method reaches public sector with or interested in the disease.  
May facilitate participation interest in future research. | The sponsor has no contact with Patient Advocacy networks.  
Incomplete notification of global, regional, local patient organisations.  
The patient organisation shuts down (no website).  
The patient organisation publishes the LS rather than providing the link to a sponsor or third-party public website.  
There is a risk the LS viewer thinks the patient organisations could address any questions about the LS.  
Blind/illiterate trial participants may not be able to access the portal autonomously.  
The patient organisation may ask for sponsor funding, increasing development costs. |

2116 IEC = Independent Ethics Committee; IRB = Institutional Review Board; PLV = Participant’s Last Visit.  
2118
### Non-Technical Distribution Methods

**Table 1.10: Non-Technical Distribution Methods: Benefits and Risks**

<table>
<thead>
<tr>
<th>Distribution method</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct methods</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A face-to-face meeting is scheduled and conducted by the investigational site(s) with the trial participant.</td>
<td>Alleviates potential investigator concern on how to simplify technical results for review with trial participants. Facilitates the investigator discussion with the trial participant about the overall results, individual results and the medicine which the trial participant received. Trial participants can ask questions/obtain dialogue.</td>
<td>There is no guarantee that the investigational site(s) will conduct a face-to-face review of the LS with the trial participant. The trial participant may opt out of a face-to-face meeting with the investigator. The investigational site budgets may increase.</td>
</tr>
<tr>
<td><strong>Indirect methods</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mailed via postal service from the investigational site to the trial participant.</td>
<td>More rapid distribution than awaiting a scheduled face-to-face meeting with the investigational site. Some LS research indicates that trial participants prefer postal notification.</td>
<td>Investigational site does not mail the LS to the trial participants. Trial participants may move and not leaving a forwarding postal address. Risk of misinterpretation of the LS by the trial participant receiving the LS via postal service without explanation from the trial investigator. Blind/illiterate trial participants may not be able to access the portal autonomously. Investigational site budgets will increase.</td>
</tr>
</tbody>
</table>
Appendix 4: List of Glossaries

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

Drug Discovery Glossary
University of Oxford
http://davies.chem.ox.ac.uk/Data/Sites/31/downloadable-files/drug-discovery-glossary-v2.pdf

Drugs@FDA Glossary of 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.

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.

European Medicines Agency (EMA) Glossary
This glossary gives definitions for the main regulatory terms used on this website and in EMA documents.

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, Spanish, Polish and Russian.
https://www.eupati.eu/glossary/

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.
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 have 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


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/
Good Lay Summary Practice

2211 National Institute for Health Research (NIHR) Involve - Jargon Buster
2212 Portal with interactive search glossary. The glossary contains definitions of terms commonly
2213 used in public involvement in health research.
2214 https://www.invo.org.uk/resource-centre/jargon-buster/

2215 Pharma-IQ Glossary
2216 A glossary of keywords, acronyms and general terminology used in day-to-day professional
2217 work, compiled by Pharma IQ
2218 https://www.pharma-iq.com/glossary

2219 Plain Language Medical Dictionary - University of Michigan Taubman Health Sciences
2220 Library
2221 Portal with interactive search glossary for medical terms in plain language, contains 1,100 terms
2222 in English.
2223 https://www.lib.umich.edu/plain-language-dictionary

2224 R&D Chemicals Glossary
2225 This is a glossary of terms and abbreviations used in the drug discovery industry.
2226 https://www.rdchemicals.com/glossary.html

2227 World Health Organization (WHO) Glossary
2228 https://www.who.int/ictrp/glossary/en/
Appendix 5: Other Guidance References

General Guidance on Lay Summaries

European Patient Forum (EPF) Position: Clinical Trial Results – Communication of the Lay Summary
March 2015

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://www.regulations.gov/contentStreamer?documentId=FDA-2017-D-5478-0001&attachmentNumber=1&contentType=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

Summaries of Clinical Trial Results for Laypersons.

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.

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
Guidance on Patient Involvement

EUPATI Guidance for Patient Involvement in Industry-led Medicines R&D

The guidance document 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.eupati.eu/guidance-patient-involvement/](https://www.eupati.eu/guidance-patient-involvement/)

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](https://www.avac.org/good-participatory-practice)

INVOLVE Briefing Notes for Researchers

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](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](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/](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](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
https://www.jstor.org/stable/40013635?seq=1


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

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.

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/