

Roadmap Initiative to Good Lay Summary Practice

Communicating trial results to the general public – How patient engagement can work

Ingrid Klingmann, EFGCP, and Silvia Garcia, EFPIA

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Introduction to the Roadmap Initiative to Good Lay Summary Practice (GLSP)

- A **multi-stakeholder initiative with over 60 participating organisations** that started in March 2019 with the aim to establish a **recommendation** on best practices for the implementation & dissemination of Lay Summaries as per the requirements of the Clinical Trial Regulation
- **Global initiative** involving US partners to ensure consistency in biomedical research
- Building on **experience gained**, to complement the 2017 EU Recommendations

Some of our Roadmap Initiative Members



Definition of Lay Summary

Summary of results from a 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

Lay Summary Content According to Clinical Trial Regulation

- Clinical trial identification
- Name and contact details of the sponsor
- General information about the clinical trial
- Population of subjects (trial participants)
- Investigational medicinal product used
- Description of adverse reactions and their frequency
- Results of the clinical trial
- Indication if follow-up clinical trials are foreseen
- Indication of where additional information could be found

The Current Environment

- **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**

(EUPATI Guidance for patient involvement in industry-led medicines R&D)

Available Guidance

- **Recommendations of the Expert Group on Clinical Trials (CTEG)** for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use: “**Summaries of Clinical Trial Results for Laypersons**” (describes how to enable good content of a Lay Summary)
- **TransCelerate Biopharma Inc: “Layperson Summaries of Clinical Trials: An Implementation Guide”** (Draft 20Jan2017)
- **MRCT*: Return of Results Guidance Document (16Jul2016)**

*Multi-Regional Clinical Trial Center, Harvard University

Target Audience for Lay Summaries

- 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

Responsibility for Lay Summaries

It is the responsibility of the commercial or academic trial sponsor to ensure that the Lay Summary is developed, disseminated and submitted to the EU database within **the timelines required by applicable regulation**

Legal requirements for Lay Summaries are defined in the Clinical Trial Regulation for **interventional trials with a medicinal product**. But Good Lay Summary Practice recommends to develop and disseminate Lay Summaries for all clinical research projects

There is **no agreed process for the dissemination** of Lay Summaries **beyond the CTIS**

General Principles from the **CTEG** Recommendations

- 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
- Focus on **unambiguous, factual information**

General Principles from the **CTEG** Recommendations

- Ensure that no promotional content is included
- 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
- Follow health literacy and numeracy principles presented in these recommendations
- 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 possibility, it may enhance the final version

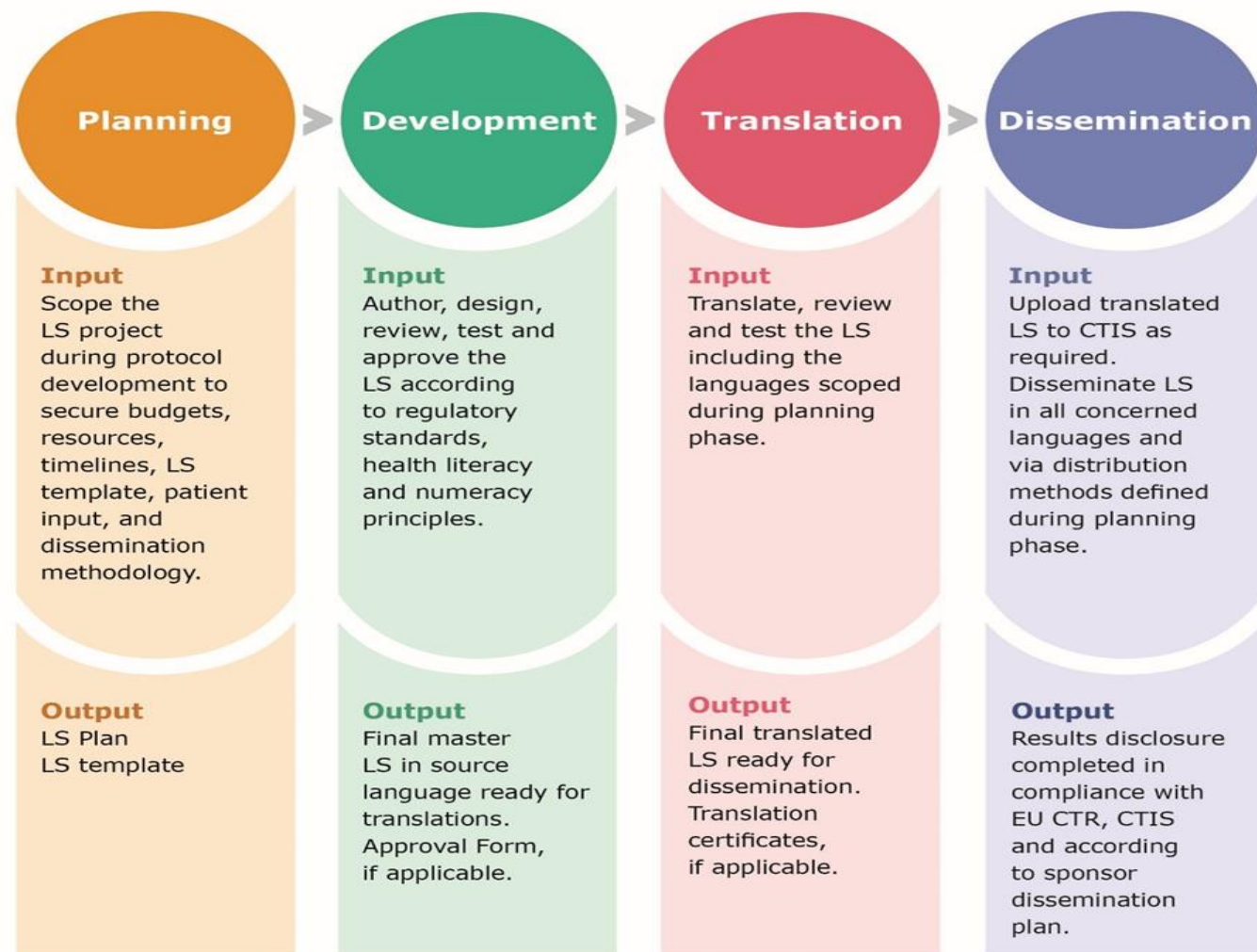
Scope and Intentions of the **GLSP** Recommendations

- Lay Summary 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 **Lay Summaries on paediatric trials** is recognised and addressed in this document, although highlighting the limited experience available so far

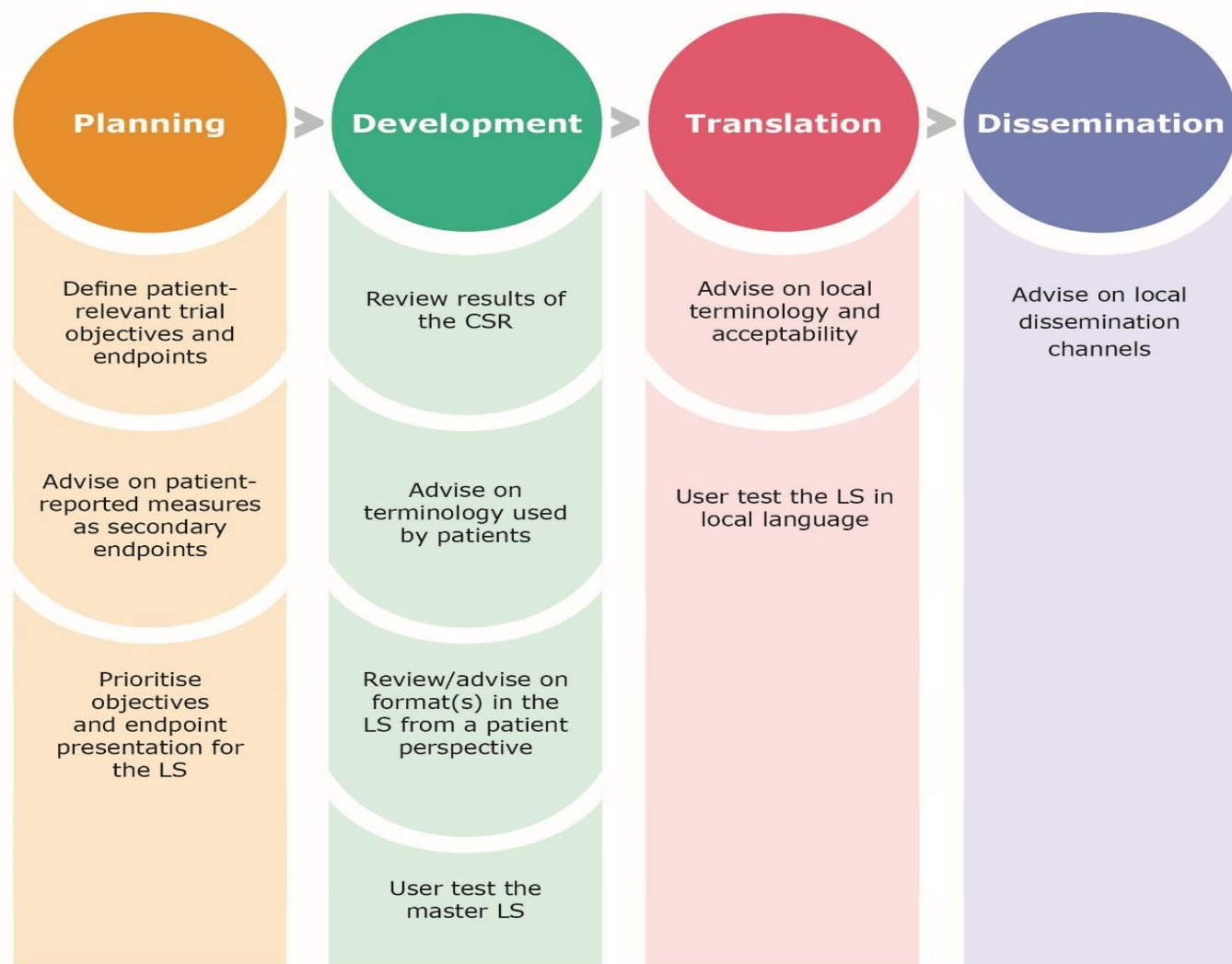
Scope and Intentions of the **GLSP** Recommendations

- 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** Lay Summaries **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

Flowchart of the Lay Summary Process



Patient Involvement during the Lay Summary Phases



Types of Patients in Patient Engagement Activities (EUPATI)

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

Timing and Type of Patient Involvement - Planning Phase

- Consultation regarding the planning, identification and prioritisation of patient-relevant outcomes and endpoints. Can be performed or contributed to by patient experts
- Consider integrating the perspectives of recently diagnosed persons with little knowledge about the disease, and persons who have lived with the disease for a long time and experienced its different stages, treatments and symptoms

Timing and Type of Patient Involvement - Planning Phase

- Consider obtaining insights of people who indirectly live with the disease like 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 Lay Summary

Timing and Type of Patient Involvement - Development Phase

- Co-authoring or consultation regarding terminology used by patients, format and presentation of the Lay Summaries. Can be performed by patient experts, patient advocates or patient organisation representatives
- Patient experts know 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

Timing and Type of Patient Involvement - Development Phase

- 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

Development Phase

| Health Literacy | |
|--|---|
| Principles | Examples and Elaboration |
| 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: <ul style="list-style-type: none"> • 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' |

Development Phase

| Numeracy | |
|---|--|
| Principles | Examples and Elaboration |
| Use visuals for interpretation of numbers | See Section 3.5 for examples |
| Use whole numbers | Round up to whole numbers if possible. '5' instead of '4.87' '1 in 1000' instead of '0.001' |
| Keep denominators and units consistent | "There is a 1 in 10 chance of nausea and a 2 in 10 chance of dizziness" instead of "There is a 1 in 10 chance of nausea and a 1 in 5 chance of dizziness" |
| Use percentages carefully | Not everyone understands percentages - but percentages can be better understood than absolute numbers. To help with percentages, numbers can be visually presented e.g. in a pie chart (see also Section 3.5 on 'Graphics'). Frequencies can be expressed as 'natural frequencies' e.g. '1 out of 10' instead of '10%'. |
| Use numerals rather than words for numbers | '2' instead of 'two' |
| Do not leave calculations to your reader | Basic maths is beyond many people - so do the calculations for them e.g. <ul style="list-style-type: none"> Do not present a body weight loss in %, do the math or show examples. Use simple units: '1 year' not '52 weeks'; 'half a glass of water' not '120 mL water' |

Development Phase

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

Timing and Type of Patient Involvement - Translation Phase

- Consultation regarding translations of Lay Summaries can be performed by patient experts or patient organisation representatives
- 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

Timing and Type of Patient Involvement - Dissemination Phase

- Consultation regarding dissemination of Lay Summaries can be performed by patient experts or patient organisation representatives
- 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

Dissemination Strategies

- Mandatory dissemination for clinical trials with IMPs: EMA's database "CTIS"
- Optional dissemination methods:



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.

Dissemination Strategies

- Technical and non-technical dissemination options:

| Technical | Non-Technical |
|--|--|
| <ul style="list-style-type: none"> • Email • Sponsor's investigator trial portal • Investigational site/clinic contains a patient portal • Sponsor website • Third-party website for trial participant LS registration and notification • Patient organisation website • Social media | <ul style="list-style-type: none"> • Print/postal service • Printed and handed to the trial participant • Face-to-face meeting between the trial participant and investigator |

Dissemination Strategies – Risks

- The trial participants may forget the URL which was provided at their last visit
- The trial participant's email address may change, and the third party is not informed by the trial participant
- 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
- The investigational site does not explain to the trial participants at their last visit where and when the LS will be available

Dissemination Strategies – Risk Mitigation

- 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

Good Lay Summary Practice (GLSP) – Public Consultation

- ◆ Launched: 01 July, 2020
- ◆ Deadline for comments: 14 September, 2020
- ◆ In total 40 organisations commented (industry, academia and patients), mainly from Europe and some consolidated their comments
- ◆ 35 sets of comments received*:
 - 20 from industry (19) and CRO (1) companies,
 - 1 from a patient group,
 - 13 from academic institutions (2 from USA) and not-for-profit organisations,
 - 1 from an individual.

*The industry cohort includes one comment that was a consolidation by 5 EFPIA companies and 1 academia comment came jointly from 2 different organisations.

General Comments:

While most respondents from industry, academia and the patient group welcomed the GLSP document and appreciated the level of guidance provided, there were similar comments from some industry and academia respondents:

- The GLSP document is too long, detailed and prescriptive
- The proposed level of patient engagement is not realistic, especially in academic trials
- The patient group was concerned about how the patient engagement recommendations would be enforced
- The requirements should be highlighted as CTR-related mandatory, good practice and nice to have. The so far missing Executive Summary should provide the GLSP principles highlighting the minimal requirements to fulfil
- Paediatric LS aspects should either get mentioned specifically in each chapter or get an own chapter

General Comments from Academia:

- IITs can never fulfil the requirements for skilled resources, translation and dissemination
- Involvement of patients (even different patients in planning and review of LS) currently not within available resources and budgets
- Make clear that the different skills beside the patient view can be enabled by one person
- It was questioned why user testing in PROs and LS is at the same level and that this is not requested for PIS/IC
- The need for comprehensive training in GLSP was stressed
- One nfp organisation requested that early phase clinical trials with healthy volunteers should be exempted from participant involvement due to the specific nature of the trials, their reporting timelines (30 months) and subject population
- The GLSP should also be valid for medical device trials

General Comments from Industry:

- The position of the GLSP in relation to existing guidance was questioned. It was suggested to refer to these and to just fill gaps.
- The format was challenged: should it be a recommendation with main text and annexes or a handbook or a high-level principles document? What is the role of the GLSP in general?
- Concern was expressed that the GLSP will not provide enough flexibilities in content and process, e.g., in case of changes in protocol and course of the trial or unexpected results
- The recommended presentation of safety results was questioned, AEs vs ADRs, etc.
- The need for enabling a single master LS for a global study was expressed, also in countries where national rules are defined (e.g., UK's HRA Transparency Strategy)
- The feasibility of the proposed patient engagement level to be enabled under the huge time constraints was questioned

Next steps:

- Consolidation of public consultation and CTEG comments and related adaptations in the GLSP Recommendations in October 2020
- Discussion with CTEG members on 7 October to discuss the CTEG feedback and potential next steps
- Finalisation of the document and approval from all involved stakeholders in November and beginning of December 2020
- Release and dissemination of the GLSP Recommendations by December 2020 / January 2021

Thank you
for your attention

