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THEME ARTICLE

The Making of the Good Lay Summary Practice Guidance: A Multi-Stakeholder Document That Was Adopted Into Regulation – An Interview with Dr Ingrid Klingmann

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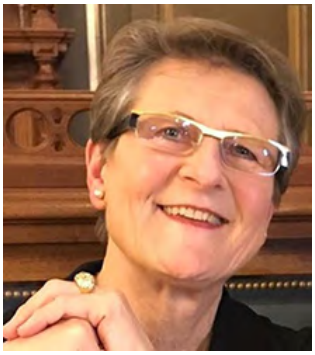
This interview describes how the Good Lay Summary Practice guidance (GLSP) came into existence. Its development had been initiated by a group of enthusiasts who wanted to provide guidance on how to plan, write, translate, and disseminate lay summaries and on how to best involve patients into the process. The GLSP is the result of a multi-stakeholder initiative with more than 60 contributing organizations, comprising patients, patient organizations, academic research networks, small and medium enterprises, and members from big pharmaceutical companies. The initiative collaborated over more than 3 years to arrive at a final guideline that was then accepted into regulation. Major steps were the development of an organizational structure consisting of a Core Management Team and 5 Task Forces that worked on the different topics, a large global public consultation of the draft document, and an intense discussion with the regulators in Europe. Dr Ingrid Klingmann, a physician, patient advocate, and cancer survivor, was at the helm of the Roadmap Initiative during the entire time and provides her insights on the challenges and results of this long and successful process.



Dr Ingrid Klingmann is a physician, patient advocate, and cancer survivor. She has been at the helm of the multi-stakeholder Good Lay Summary Practice (GLSP) Initiative that developed a guidance for writing lay summaries. Lay summaries are short documents understandable for the public that summarize the results of clinical trials. Lay summaries are now mandated for all clinical trials in the European Union (EU) based on European Clinical Trial Regulation (536/2014). They are also called Plain Language Trial Summaries, Patient Summaries, or Trial Result Summaries. Lay summaries are a novelty as they are the first regulatory documents that are meant to inform the public. Even more so, the GLSP Initiative was the first guidance that had been developed by a multi-stakeholder initiative that was then adopted as regulatory guidance. Some readers may be at odds with the use of the word 'lay' as for them it has a belittling connotation. However, as this is the official legal term in Europe, it has also been used in this article.

INTERVIEW

Schindler: Why did you and the European Forum for Good Clinical Practice (EFGCP) pick up the topic of lay summaries in 2018? At that time, several working groups had already been developing recommendations.

Klingmann: EFGCP had already been involved in the preparation of certain aspects of the European Clinical Trial Regulation. However, at that time there was no discussion on informing the public about the results of clinical trials. When the European Regulation was released in 2014, we were surprised to see the obligation to prepare lay summaries for all clinical trials. Apparently, this topic had been added very late to the legislation. The mandate to inform the public in a systematic way about the outcomes of clinical trials triggered a lot of interest and excitement, and EFGCP and the European Federation of Pharmaceutical Industries and Associations (EFPIA) decided to organize a workshop.

We wanted to clarify what it would mean for sponsors to prepare and disseminate lay summaries. During this first workshop in 2015, we became aware of the work of international collaborations such as Multi-Regional Clinical Trials (MRCT) and TransCelerate. It became clear that stakeholders would need more detailed guidance on the content and structure of lay summaries. When the European Expert Group issued their guidance on structure and content of lay summaries in 2017, we conducted another workshop

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during which we reviewed their guidance. We realized that it was not enough to know about the requirements and best approaches to present the content, but that an overall process for planning, preparation, translation, and dissemination was needed. Most importantly, producing lay summaries should involve patients in a systematic way. This aspect had not been included in existing guidances at the time. We had a very strong patient representation at this workshop, and they made it very clear that without patients, the process cannot be successful. As a conclusion from that workshop, EFGCP and EFPIA decided to create the "Roadmap Initiative to Good Lay Summary Practice" (the GLSP Initiative).

Schindler: What were the aims of the GLSP Initiative?

Klingmann: To bring together all the involved stakeholders—so, commercial and academic sponsors, patients, patient organizations, not-for-profit organizations, medical writers, lay language specialists, and translators. We wanted to involve all viewpoints and existing experience to jointly develop guidance on how to set up an overall lay summary process. We needed a bit of time to get our act together, but then our road map initiative was kicked off in 2019.

Schindler: What were the biggest challenges in getting the initiative off the ground and keeping it afloat?

Klingmann: Well, there were a lot of challenges. Firstly, we needed to give the initiative an organizational structure and we needed to identify the topics to work on. In total, we had over 60 organizations from Europe and the United States who participated in the initiative. To more efficiently manage the process an international Core Management Team was formed. Initially, after a lot of discussion, we settled on 5 task forces, each one led by a member of the Core Management Team and a patient or patient representative. The initial task forces were

1. Principles and processes of lay summary implementation beyond existing guidance.
2. Competencies required for development and translation of lay summaries.
3. Lay summary dissemination within and beyond the European Medicines Agency (EMA) Portal.
4. The issues of lay summary creation, translation, dissemination, and funding, particularly for academia and small and medium enterprises.
5. Suitable technology to reach patients, health care professionals, and the public including the development of lay summaries for trials in children.

It was difficult to get people to actively contribute to these different task forces. Participants were sometimes unaware that simply listening in was not going to help moving forward. The idea was to actively work out the content and to develop recommendations. Ultimately, we managed through a process of regular meetings, regular updates, and building up awareness in all the task forces to adhere to the timelines and to come up with proposals. In spring 2020, we had brought together a first draft of the GLSP that was then used in a very early discussion with the European Commission. They indicated that they were principally interested in collaborating toward a guidance and expressed that working on this aspect of transparency would be a good way to support the overall goals of the new European Clinical Trial Regulation. In line with the Core Management Team, the Commission supported the plan for a wide-spread public consultation on the draft in summer 2020. It was agreed to reconvene thereafter.

GLOSSARY

CTEG – the Commission Expert Group on Clinical Trials. They provide the Commission with advice and expertise on clinical trials in relation to the preparation and implementation of legislation and policy initiatives. The CTEG is part of the Directorate Sante and consists of delegates from all national authorities and ethics committees in Europe.

EFGCP – the European Forum for Good Clinical Practice. They are a not-for-profit organization established by and for those with an interest in the development of medicines and medical technologies.

EFPIA – the European Federation of Pharmaceutical Industries and Associations. They represent the biopharmaceutical industry operating in Europe.

European Commission – the executive branch of the European Union (EU). It operates as a cabinet government with 27 members (informally known as "Commissioners") headed by a president.

European Clinical Trial Regulation – the binding law that specifies the rules for conducting clinical trials throughout the EU.

MRCT – Multi-Regional Clinical Trials. They are a research and policy center that wants to identify and deliver ethical, actionable, and practical solutions for the global clinical trial enterprise.

TransCelerate Biopharma – a not-for-profit entity with a mission to collaborate across the global biopharmaceutical development community to identify, design, and facilitate solutions designed to drive the delivery of new medicines.

The GLSP draft was posted on the EFGCP website and disseminated by all Roadmap Members to their networks. We received a high number of comments on the structure and a lot of detailed recommendations from all stakeholders. And of course, like always, after such a public consultation, it takes time to consider and discuss and agree on the comments and write a revised draft. The workload associated with integrating the various comments and the preparation of a second draft was a major challenge for the initiative.

In addition, much to our surprise, one of the key messages was that the document that we had produced was far too complex and too long (about 100 pages), especially for academic sponsors and investigators, and that we would need a type of summary. In response to this, the team developed the idea of having a "Quick Guide," summarizing the principles and basic information, and a "Handbook" that contained the detailed guidance, recommendations, and experiences. And with that we went again to the European Commission. Keeping all stakeholders invested during the difficult discussions that ensued was a major challenge.

Schindler: Was it your idea to involve the European Commission at the draft stages?

Klingmann: Actually, it was an idea that was developed in the Core Management Team during one of our regular meetings. The team thought that the most effective way to support the implementation of good lay summary practice was a guidance that was issued by the regulators, ie, the European Commission. We believed that an official release and recognition would make it so much more powerful than when it was coming from a group of enthusiastic individuals who wanted to improve the world.

Schindler: In this long journey of the initiative, what were the moments of crisis? As a member of the Core Management Team, I remember a few. There were instances when it was difficult to keep the academic group engaged, and there were moments of distress when some colleagues in major pharmaceutical companies wanted to have some very specific points included. Most importantly, we had very critical discussions with the European Commission and the Clinical Trial Expert Group (CTEG).

Klingmann: Well, in fact, you listed them already quite correctly. I think the involvement of academia was an ongoing issue that came in different waves. Initially, it was difficult to get academia engaged at all because they were largely unaware of the new requirement. It became clear that the biggest issue for academia is that the writing of lay summaries is a very late-stage activity in a clinical trial. At that time, funding is often no longer available because conduct-related activities have subsided and given current funding procedures, writing a lay summary after the end of the project is not possible. Unfortunately, this situation is not solved. So, we agreed that we would also need to work with the large funding bodies to make them aware of the situation.

When we had submitted the revised draft GLSP to the European Commission, they forwarded it to the CTEG for comments and review. Because CTEG is a group of 54 representatives from national regulatory authorities and ethics committees of all European member states, we were afraid of receiving many comments and maybe even serious pushback. And, as expected, we received a substantial number of comments and a list of several topics with which they were not in agreement. One problem was that they insisted that the GLSP must primarily be a European document because it relates to the European Clinical Trial Regulation. So, the need for lay summaries for patients in international and global studies and the need of patients all over the world to have access to these lay summaries was not a priority for them. It was quite a tough discussion, and it was difficult to find agreement. Some representatives of global pharmaceutical companies were disappointed about this focus on the EU. However, building on the good will of all stakeholders, we were able to agree on a compromise.

The second topic that the European Commission absolutely did not want to go into was indirect dissemination—that is, dissemination of lay summaries via company or third-party websites. They felt that it was not appropriate to provide guidance in the GLSP because currently there is no broadly agreed standard for this type of dissemination. Also here, some representatives of large pharmaceutical companies were disappointed because they were hoping to get further guidance on how to disseminate lay summaries in a compliant way. In the Core Management Team, we agreed to tackle this topic again and work it out in full detail for another discussion with the regulators. This discussion in spring 2021 was one of the most critical moments when it was really unclear whether we would come to an agreed document.

Schindler: You really contributed a lot to steer the initiative through these crises and you skillfully managed the interaction with the regulators—your professionalism was truly important for the success of the initiative.

Klingmann: Well, many people contributed to this—not only me—and many members helped to overcome diffi-

cult moments. In addition, the Commission and CTEG had appreciated that this was a multi-stakeholder initiative with strong patient involvement. They were willing to accept that they could have not created something better. Whatever they would have done could only have been top down, and probably not as relevant and practical as the document that we have produced. Finding agreement on the various topics of concern was often difficult, but many members of the initiative and the Core Management Team contributed to a good outcome. Remember, we had 9 months of intense interaction between all the road map stakeholders and the European Commission to come to a final document.

Schindler: For me, one of the most fascinating things is that the GLSP is a bottom-up multi-stakeholder initiative that made it into law.

Klingmann: Yes, it is unique that an initiative that was started by a group of enthusiasts who wanted to provide clinical trial data in an understandable way was recognized by regulators and turned into an official guidance. The final document is posted on the EudraLex website, which is the place where all European laws are published. I believe it was of critical importance that the initiative was driven by a neutral body, and I am proud that EFGCP could serve in this capacity.

Another key factor was the ongoing substantial involvement of patients in the initiative. The role of patients was very practically worked out throughout the entire guideline without avoiding the complexities that this may create sometimes. So, it was not Big Pharma or academia who drove this guideline, but it was the balancing of all the efforts of the different stakeholder groups in an open and fair way. For academic research and for small and medium enterprises, it was important to be offered a stepwise approach of implementing the GLSP.

Schindler: You have been at the helm of the initiative for more than 3 years. What does it take on a personal level to make such an initiative successful?

Klingmann: First of all and foremost, it takes a lot of time and energy. I was working philanthropically for the initiative, and I still had to do my other work. During the intense phases, I had only very few weekends for myself. It requires a lot of energy to keep people engaged, which is sometimes difficult to muster. From time to time, I needed to give myself another push to advance the topic and to motivate the others and encourage them to deliver on the agreed topics. And of course, I was not alone in this. We were so lucky to have an exceptional group of dedicated individuals in the Core Management Team. Without their ongoing support and their critical input over several years, the initiative would have gotten nowhere. Also, I am very thankful for the ongoing support of all the members in the Task Forces and the entire initiative.

I believe we have a window of opportunity now to make the provision of lay summaries a part of the normal clinical trials process. With the COVID-19 crisis, there is so much interest in transparency and in the results of clinical studies. Our initiative will make those results more readily available for patients and the public.

Schindler: What are the next steps for the GLSP Initiative?

Klingmann: Most importantly we need to continue spreading the news about the availability of the GLSP to all parties that are potentially involved in the preparation of lay summaries. Webinars and workshops on a national level are planned. A next step could be to make the GLSP available in additional languages. The initiative is currently planning training programs for stakeholders and members of the public to learn about best practices in the preparation of lay summaries. And we will create an independent GLSP website that will become the central communication tool and repository for GLSP–related activities and content.

Another key issue we need to tackle is to encourage academic researchers to fulfill the obligation of writing lay summaries, especially because about 40% of all trials in Europe are conducted by academia. We need to continue the discussion with the European Commission, particularly the Directorate-General "Research and Innovation" that is providing funding for a lot of academic clinical research. In addition, we need to continue to inform national funding organizations about the requirement to write lay summaries and related resource needs. They need to change their requirements and their funding conditions to meet the costs associated with providing lay summaries.

We want to re-initiate the discussion with the regulators on the topic of indirect dissemination, ie, the option of sponsors to make lay summaries available on their websites. Although lay summaries are a European requirement, all patients in a global trial and the global public have the right to be informed about results regardless of their location. For this, we need to define the processes and develop an appropriate framework. And of course, the initiative should continue to provide a platform for best practices for example the provision of lay summaries for children.

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BIOS

Ingrid Klingmann, MD, PhD, FFPM, FBCPM

She is a physician specialized in clinical pharmacology with over 30 years of experience in different senior functions in the pharmaceutical industry focusing on clinical trial design, ethical, and regulatory aspects. She owns and manages a pharmaceutical development and site management support consulting company since January 2003 (Pharmaplex bv). The company creates networks of experienced specialists that work on diverse international projects such as drug development consulting, study management for pharmaceutical companies, teaching projects, and academic site support. Dr Klingmann is Chairwoman of the Board of the EFGCP. Based on her broad professional background, she facilitates the alignment between stakeholders in medicine development with the aim to develop patient-relevant treatments more efficiently.

Dr Klingmann is currently also Secretary of the European Federation of Exploratory Medicines and President of PharmaTrain Federation (EUFEMED), a not-for-profit organization focusing on global standardization and improvement of post-graduate training in medicine development. She teaches on topics like clinical research and regulatory affairs at the Universities of Bonn, Basel, and the Université Libre de Bruxelles.

Thomas M. Schindler, PhD

He is a biologist and linguist educated in Germany and the United Kingdom, holds a PhD in molecular physiology, and did postdoctoral research in the United Kingdom. He was the editor of popular science books in biology, geography, and astronomy. He then turned to medical writing and has over 25 years of experience in both medical affairs and regulatory medical writing, including the preparation of marketing authorization application dossiers in different jurisdictions. He founded, established, and led the medical writing function at Boehringer Ingelheim for almost 20 years, and he has recently focused on lay summaries, video creation, and AI-driven writing. He participated in the TransCelerate Return of Results work stream, is in the Core Management Team of the GLSP Initiative and has supported the development of the Patient-Focussed Medicine Development (PFMD) Plain Language Summary guidance. For many years, he is the editor of the statistics section, "Statistically Speaking," of the *AMWA Journal*.

FURTHER READING

Directorate-General for Health and Food Safety. *Good Lay Summary Practice Guidance*. European Commission; 2021. Accessed February 21, 2022. https://ec.europa.eu/health/latest-updates/good-lay-summary-practice-guidance-2021-10-04_en

European expert group. *Summaries of Clinical Trial Results for Laypersons: Recommendations of the Expert Group*. Version 2. Expert Group on Clinical Trials; 2018. Accessed February 21, 2022. https://ec.europa.eu/health/system/files/2020-02/2017_01_26_summaries_of_ct_results_for_laypersons_0.pdf

Aldinger C, Bierer BE, Collyar D, Li R, Myers L. *MRCT Center Return of Aggregate Results to Participants Guidance Document*. Version 3.1. Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard; 2017. Accessed February 21, 2022. https://mrctcenter.org/wp-content/uploads/2017/12/2017-12-07-MRCT-Return-of-Aggregate-Results-Guidance-Document-3.1.pdf

Schindler TM. Lay summaries of clinical study results. In: Hall G, DeTora L, eds. *Regulatory Writing: An Overview, Second Edition*. RAPS; 2020:265-277.

Brauburger K, Sroka-Saidi K, Schindler TM. New European clinical trial regulation: the requirement for lay summaries and its impact on medical communicators. *Amer Med Writers Assoc J*. 2015;30(2):60-63.