CLINPAL

Remote Study Webinar Follow-Up

Questions and Answers

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1 Introduction

This document provides responses to the questions asked during the remote clinical research webinar hosted by eClinicalHealth and Sanofi. Some related questions have been combined to avoid duplication.

The webinar recording is available **HERE.**

2 Questions and Answers

Question: Are there patient privacy matters to deal with?

Answer: Security and Privacy of patient data collected online is always a major concern. Not only because of the complex global Data Privacy landscape but also because in a fully remote study setting, data subjects (i.e., patients) are having an active involvement in the study by directly accessing and exchanging data with the online platform. In this setting patients can be seen more as informed collaborators with a central role to the successful conduct of the study rather than passive participants administered by the clinical site.

eClinicalHealth as provider of Clinpal™, a cloud-based solution for clinical research, complies with all regulatory expectations for software developers and service providers, with the requirements of the UK data protection act 1998 (and its amendments), the EU data protection directive (95/46 EC) and applicable local laws and regulations. eClinicalHealth is a registered data controller in the UK, and deeply committed to respect the privacy and protect any personal information submitted to and hosted on the Clinpal™ platform.

To ensure and promote compliance, eClinicalHealth has procedures and policies in place that are consistent with Good Clinical Practice (GCP) and the Health Insurance Portability and Accountability Act (HIPAA) standards for the protection of any personal data (personally identifiable information – PII, and personal health information - PHI) we collect, transmit or store.

Protection of personal data is facilitated not only in terms of compliance with legal frameworks but it is also secured through technological means. Clinpal was designed from the outset to protect patient privacy as a core principle of the system:

- Advanced mechanisms are in place for informing data subjects and for capturing their explicit consent for the data collection activity. These mechanisms are fully compliant with the applicable data privacy regulations and best practices in the area of data privacy.

- State of the art technical measures are in place to avoid misuse or accidental disclosure of personal and sensitive personal data (PII/PHI).

- An advanced and robust data security model is built in Clinpal that complies with GCP data blinding and confidentiality requirements This prevents users of certain roles from accessing personal data. (Patient's personal data is not accessible to the Sponsor).

eClinicalHealth maintains a high level of expertise in providing solutions for remote and traditional studies that are fully compliant with all the aspects of Data Privacy Regulations worldwide. eClinicalHealth can provide consultancy and support to the Sponsor to ensure adherence to the applicable regulations from both a technical and procedural perspective and compliance with mandatory notification and authorization requirements.

Question: How do you prevent fraud by patients and confirm their identity?

Answer: Most studies do have identity verification mechanisms such as physical site visits that can be used to confirm the patient's identity and other details. For completely remote studies, this needs more consideration. In VERKKO, the study materials were supplied to the patient's address and they had to go to the post office to pick them up and show their ID. This identity verification mechanism was approved in VERKKO as it was a very low-risk study. Studies with different risk profiles may require stronger mechanisms to verify the identity of the participants. There are several methods for this, including technology solutions where participant's identity can be confirmed using devices with cameras and the participant's ID. The candidate registration workflow can also include asking for contact information for the participant's primary care physician or a specialist who can confirm further medical details. Some countries have well established systems to confirm identification of individuals using mobile technology, ID card readers, and other such mechanisms. When there is a study design under consideration, eClinicalHealth can provide guidance and help implement a suitable identification mechanism to meet the needs of the study.

Question: Did the content of the patient-facing ICF video require many edits from IRB and was the video presented to IRB in audio visual or written format?

Answer: VERKKO did not actually use a video, but we have used videos in other studies using elements of remote research. As a best practice and in compliance to the FDA's draft guidance on the use of electronic informed consent – (Page 6/Line 220) which is related to the provision of a transcript of any audiovisual content to the patients, it is recommended that the IRB's are provided with a transcript of the video prior to production to get their feedback regarding the content. This saves money and time as the script can be more easily revised than video material. The visuals used in a video should be

made available to the IRB for review, but if the content is already pre-approved, it is much more likely that there will be no further revisions required.

Ref: Use of Electronic Informed Consent in Clinical Investigations – Q&A

Question: Was this study only done in Finland?

Answer: Yes, it was, mainly for practical reasons. The comparator study was also done in Finland and the study infrastructure (clinical site) was easily accessible in Finland. The fully remote study could have been done in other countries as well and many elements of remote research are already replicated in other countries. While not all countries are well suited for a fully remote research model, the eClinicalHealth team can advise further on best approaches for specific countries.

Question: What was the budget impact compared to the comparator? Was it increased or decreased?

Answer: Significant cost reductions were demonstrated with the approach taken with this study. These are summarized as follows;

- One virtual site with very low overheads
- No participant travel costs
- Reduced site burden leading to reduced costs at site
- Electronic Source data removing the requirement for source data verification
- Single system used which reduced setup and data reconciliation costs for a significantly lower total cost of ownership

The per-patient cost was significantly reduced even with such a small scale study. On a larger scale study, these reductions can be exponential.

One further potential cost reduction that was not used on Verkko is to use the existing glucose meters patients already have. In Verkko, we wanted to specifically test the use of the wirelessly connected devices, which were provisioned for the participants, along with a SIM card. This increased the costs. In other cases, to further reduce costs, the same methodology can be applied with the participants own devices. The trade off is the loss of truly real

time data capture and the convenience of fully automated synchronization of the measurements.

Question: Was a drug being tested in the trial?

Answer: No, VERKKO was a Non-Interventional Study involving a CE-marked device. The main objective was to assess a novel mechanism to conduct patient profiling for diabetics to understand their current treatment outcomes that could then be scaled up. All appropriate procedures including IRB / Ethics approval and systems validation were followed to ensure an accuracy comparison with drug studies. Studies that involve medicinal products will need to consider other factors to operate in a fully remote manner, however, many of the methods used remain applicable. Since the launch of Verkko, we have implemented remote research methods into a variety of studies that included a study drug. Some of the therapeutic areas we are using remote research methods in today include, obesity, cardiovascular, cystic fibrosis, respiratory, endocrinology, otolaryngology, and soon to launch in oncology.

Question: Did this study have lab collections using a lab?

Answer: No, this study did not use a lab. However, some our other Clinpal studies in cystic fibrosis for example, do use labs and this process can be built into the study workflow and data capture plans.

Question: How geographically diversely located were all these subjects?

Answer: All of the subjects were recruited within 50 kilometers from the diabetes clinic where the Investigator was located. This was done to retain the possibility of inviting some participants to visit the clinic in case an in-person visit was deemed necessary. In the end, it wasn't necessary for any study patient to physically visit the investigational site. In hindsight, our assessment is that we could have expanded the geography to the entire country and would have completed recruitment sooner.

Question: What types of challenges do you foresee with running a trial remotely with CNS patients, particularly patients with schizophrenia? What solutions could be used?

Answer: CNS studies with serious conditions often involve the study participants as well as their caregivers, or caregiver network. The challenges often lie with the participant's ability to adhere to the study protocol and this is where technology like Clinpal can help. Clinpal is a useful tool for caregivers and can keep the caregivers informed of upcoming study activities. With Clinpal, caregivers can also be notified of any compliance issues. Allowing some study procedures to occur at home, such as responding to patient diaries or questionnaires, can help with data quality and compliance. As an example, when the participants can complete assessments at their own pace in familiar surroundings some of the stress associated with site visits can be avoided. Home nursing is another option and Clinpal is the perfect tool to coordinate home nursing activities.

Question: Have you used Clinpal in many countries? What local considerations need to be taken into account?

Answer: Clinpal has been used in more than 30 countries and Clinpal studies include more than1,600 trial sites. As a patient-facing system, it is a requirement for the platform to support the local languages and Clinpal has support for virtually any language. The system can also be adapted to be compliant with local regulations and culture. For example, some countries do not allow the sponsor name or logos to be displayed anywhere. The system allows for country or language specific configurations, such as cultural adaptation of the virtual avatar or providing different study populations with an adapted landing page with different visuals.

Question: Which types of studies do you think would NOT be appropriate for a remote trial?

Answer: We believe that many of the methods demonstrated successfully with the VERKKO study are applicable to almost any type of study.

Phase I, and some hospital based, inpatient trials may not experience the cost benefits of remote research methods.

Pre-approval studies with an investigational product are sometimes more challenging in this aspect as they need a strong mechanism for patient

identification and the confirmation of their diagnosis, medical history and drug shipping.

The 'sweet spot' for remote trials are in large observational, real-world trials where the high degree of automation yields great efficiencies.

Question: If the trial is interventional rather than observational, how can your technologies help?

Answer:

eClinicalHealth has broad experience and is currently contracted to support studies in 30 countries, including work in Asia and Africa.

The Clinpal platform has been selected by several Pharmaceutical and Medical device companies to support small, medium and large scale clinical studies as well as for patient recruitment and patient engagement.

The majority of our work today is done for studies that only use elements of remote research and are not fully remote, like Verkko. Our experience includes the technology support for both observational and interventional studies.

For interventional studies, nearly all of the methods used in VERKKO are potentially suitable, including:

- site eLearning
- site start-up
- participant recruitment and retention
- patient education
- patient engagement via dashboard
- study reminders
- direct patient data capture
- eCRF's
- post-study follow-up.

The key to Clinpal is its ability to offer the appropriate configurable engagement to patients that assists them in their journey through a clinical trial.

Question: What is your experience with ePROs and how would you handle that in a remote trial setting?

Answer:

ePROs are included in several of our studies, including the remote VERKKO trial and we have worked with many validated scales like SF-36, IBDQ, etc. We can support ePROs either via the Clinpal app or via the adaptive Clinpal web interface. Both methods are suitable for a BYOD approach and utilize devices that the patients already have and are familiar with. The benefits of BYOD are many, including cost and time savings and keeping it more simple for sites and patients. Checking what devices patients have access to can be easily done in Clinpal as part of the screening process and a suitable device can be delivered to those that don't already have one. We call this the hybrid-BYOD approach. There is also the question about additional evidence required when a validated paper PRO is migrated to different electronic devices and we have developed a new methodology to address this. In summary, ePROs are included in many Clinpal studies and it is very feasible to include them in remote studies as well.

Question: How scalable is Clinpal? What is your largest study?

Answer:

Clinpal has been used in many different kinds of studies, ranging from very small studies of only 50 patients to very large registries. The largest Clinpal study is 10,000 patients and another one has 5,000 patients. Between these two trials there are over 1,000 study sites in 20+ countries. Clinpal has been engineered from the beginning to be a true cloud system, making it a robust and scalable solution to support large numbers of users and transactions. The cloud architecture also means that it's a zero IT-footprint system for our clients, which also allows for flexibility in our pricing model, making the use of the system financially feasible for different needs.

We want to again thank all of our webinar participants for your interest and great questions. As a next step, we recommend you to contact us and **request a demo** to see how Clinpal could be used to help you in your upcoming trials.