eCOA BACK-UP STRATEGIES

No longer the "what if" situation: today's reality and eCOA back-up strategies. How to ensure they are adapted?

October 2020

kayentis

Dedicated to eCOA & Patient Engagement

There have always been, and there will probably continue to be, situations where an eCOA back-up strategy is necessary. The reasons that justify implementing a back-up strategy include, among others, device failure or loss, the risk for the device to be forgotten by a patient when travelling, or lack of connectivity.

At the moment, the over-riding reason for a robust back-up strategy is the ongoing pandemic we are living through currently. This has generated the need for eCOA back-up strategies to be implemented very quickly. This has been required to cover situations where either patients were unable to go to sites or sites were unable to maintain on-site visits.

Choosing the right eCOA back-up solution can become a challenging exercise, as there are several aspects to consider; what are the key criteria to properly select an eCOA back-up strategy?

THANKS

We invited a small, diverse group of experts to discuss the complexity of eCOA back-up strategies and address the clinical teams' expectations during an online workshop. The workshop discussions and best practice recommendations are reflected in this whitepaper.

This session was hosted by Jean-Michel Combe, Strategic Marketing Director at Kayentis.

We warmly thank all the participants for their active contribution to this session.

CONTENTS

PATIENTS FIRST!

Patient burden must remain as low as possible.

This is a key criterion for most clinical trial stakeholders that was not debated during this workshop. The solution must be quick and easy to set-up, not only for the site but also for the patient who is the first one to pay the price if the solution fails or the device is broken.

> ***"Patients are often compliant and diligent, they are willing to complete their questionnaires or e-diaries, but situations like the pandemic have prevented them from being as compliant as they wanted to be"***

The solution being low-cost was not considered to be an important selection criterion, reinforcing the idea that patient burden is more important in the clinical trial strategic decision-making process.

"Patients are often compliant and diligent, they are willing to complete their questionnaires or e-diaries, but situations like the pandemic have prevented them from being as compliant as they wanted to be" said a Global Trial Director from a large pharma organization.

The type of patient population adds complexities to the choice of a robust back-up solution

"Patients age groups and health conditions, as well as patients' agility with technology add another layer of complexity in the selection of the back-up strategy" acknowledged a Global Trial Director from a global pharma organization. A robust solution could be seen as one that

can be easily used by all types of patient population. Such a solution would achieve a high compliance rate in any context, which can vary widely according to patients preferences and technology ability. How do we resolve this variability?

Some patients may prefer a BYOD approach to use as a back-up while others may prefer a web-based approach, or a replacement device. This disparity does not facilitate the selection of a patient-centric universal back-up option.

Variability does not sit only in patients behavior and acceptance of the different solutions, but in sites' acceptability and their experience with the use of technological solutions.

> ***"Patients age groups and health conditions, as well as patients' agility with technology add another layer of complexity in the selection of the back-up strategy"***

A lot will come with confidence and trust, so if sites are well trained and if the CRAs and eCOA vendor teams spend the necessary time to pragmatically train and educate the site's staff, the likelihood of successfully cascading the training to the patients will be high.

Training programs are evolving, they are now more and more focused, accessible and pragmatic. Although there is still room for improvement, the industry is moving in the right direction.

However, the data quality should never be compromised by the ease of use and satisfaction for patients.

DATA QUALITY SHOULD NEVER BE COMPROMISED

"One could consider that in order to lower the patient burden you could throw them a piece of paper to fill in, but that would be dangerous" said an eCOA System Manager from a global CRO.

Despite the complexity of eCOA systems, it is important to try and avoid paper. The benefits of an electronic system versus a paper system have been demonstrated. Paper being made available as a back-up on site could represent an easy default option that would probably be popular with site staff if they are not very familiar with technology, but this would be a risky approach.

> ***"One could consider that in order to lower the patient burden you could throw them a piece of paper to fill in, but that would be dangerous"***

That's an interesting point... but how can one be sure to always reconcile patient comfort with data quality? With quality comes robustness, and so what exactly is a robust eCOA back-up solution?

- **A solution that would ensure data integrity.** Implementing a back-up option means introducing another method of data collection, which leads to discussion regarding the equivalence between the two methods. A large amount of articles have been published on equivalence between different methods of data collection. It seems that the scientific community is generally in agreement that electronic data collection methods are likely to be equivalent when only minimal changes are made, which does not not adversely

affect the overall comprehension and use of the eCOA solution by the users https://bit.ly/2EmSnBV and https://bit.ly/2FPCULE.

- **A solution that would be Quality Assurance certified,** so that all data collected via the back-up option would have the same high-quality standards, including full audit trails, as if they were collected via the original eCOA solution.
- **A solution that would cover various situations,** from a broken device up to a pandemic such as COVID-19. The current crisis has taught us that we cannot anticipate everything, and so we need a solution as robust and as flexible as possible. *"Experience has shown that every single study needs - at some point - a back-up strategy"* recognized a Systems Implementation Leader from a large pharma organization.

> ***"Experience has shown that every single study needs - at some point - a back-up strategy"***

- **A solution that could not be challenged by any regulatory agency.** Industry is evolving fast and the pandemic is acting as a catalyst to digital evolution and implementation of new ways of collecting data. However, we all know that the regulatory bodies do not evolve at the same pace, and the whole industry needs to make sure that introducing innovative and, potentially, multiple data collection methods into a study report do not lead to the data being refused by agencies.
- **A solution that would include a robust deployment strategy.** The best solution could be selected, but if it is not well implemented it won't succeed. As in every project with complex operational aspects, the back-up deployment strategy must be well defined and processed. *"The technical option has to be robust - that's a given - but it seems to me that a robust eCOA back-up strategy encompasses a solid deployment strategy as well"* described an eCOA System Manager from a large international CRO. So, whichever the option itself, it the operational implementation is not well thought and planned the eCOA back-up solution won't be robust enough.

100% EQUIVALENCE SHOULD BE GUARANTEED

The vast majority of this expert group agreed that 100% equivalence should always be guaranteed.

A back-up option is necessary only because the primary eCOA solution may sometimes fail, and every effort should be made to avoid having to use a back-up solution. If implemented, the back-up solution should be as equivalent to the primary solution as possible, so that both solutions can be "considered as one".

What does equivalence mean exactly to the numerous clinical trial stakeholders?

- For patients, equivalence means that they can read, understand, and answer the questions the same way. But this is not how equivalence will be perceived by other stakeholders: for example, a data manager may not consider two eCOA solutions to be equivalent if one generates more edit checks than the other, although the two may be considered to be equivalent from the patient perspective. And from the clinician's perspective, the perception of equivalence will be driven by the presence or absence of bias in the way the data were collected, which again is a different perception.
- From a questionnaire perspective, equivalence between two displays or devices may not always be guaranteed for every single questionnaire. The fact that a patient is likely to understand and provide the same outcome when using a tablet or a web solution

does not guarantee that it will be the same with a handheld device, specifically for long and demanding questionnaires where keeping the patient's attention will be more difficult.

- In considering the eCOA back-up strategy that they will put in place, clinical teams should discuss equivalence and align on what it means to them and what they expect. The potential ambiguity in the meaning of equivalence should be removed early in the process.

"It all depends on what we're using the data for"

- The study purpose must be considered when defining equivalence requirement. Equivalence is a concept that must be discussed and defined ahead in the study set-up activities, according to the specifics of the study and the protocol. Whilst complete equivalence is certainly required in a pivotal phase 3 clinical trial, would it be really needed in an early phase study designed to progress to the next stage of the clinical development?

"It all depends on what we're using the data for" concluded an eCOA System Manager from an international CRO organization.

WHAT ABOUT PATIENT INTERVIEWS, WHICH HAVE BEEN IMPLEMENTED BY SEVERAL SPONSORS TO FACE THE COVID-19 PANDEMIC?

COVID-19 changed the world seemingly overnight. We went from "business as usual" to the "new normal" at warp speed. We all had to adapt at an unprecedented pace and find easy although still suitable alternatives to keep clinical trials up and running.

Phone interviews appeared to have the advantages of being

- fast to implement
- affordable
- a reasonably undisruptive contingency option to face this unprecedented situation
- allowing for some flexibility in the data transcription method.

This solution has been implemented for several ongoing clinical trials where alternatives such as BYOD or Web back-up were not an option, and has been perceived as an easy default solution to support sites and patients navigating trough the complexity generated by the pandemic.

However, phone interviews also have drawbacks such as:

- uncertainty of regulatory acceptance,
- risk of introducing interview bias,
- disappearance of the advantages of self-completed questionnaires, that may discourage patients to provide honest responses,
- licensing discussions that are required when the questionnaire method is changed,
- could require sites that were already under pressure to find more time to schedule and conduct the telephone interviews.

So, although interviews represented an easy contingency option whilst the world was facing an unprecedented crisis, they have drawbacks that have been discussed at the level of the C-Path- PRO Consortium. Very quickly after the beginning of the pandemic, this committee worked as assessing the risk and mitigation strategies for the collection of patient-reported outcome data through clinical sites. It thoroughly described the pros and cons of the different contingency options that could be implemented during the pandemic for a study protocol that originally required patients to complete measures in person during a site visit (https://bit.ly/2GjU8R9).

Selecting and implementing an eCOA back-up strategy that addresses all clinical team expectations is a challenge. Making sure that the patient is kept at the heart of this decision without jeopardizing data integrity will be key to the success of an eCOA back-up strategy. Maintaining the right level of equivalence in data collection methods will also be critical as we face unprecedented times of acceleration of the digitalization of clinical trials.

Focused on eCOA back-up strategies, this white paper transcribes the discussion that was held during one in a series of 4 workshops about eCOA complexities held by Kayentis in 2020.

WORKSHOP CONTRIBUTORS

- Clinical trials and eCOA experts from the pharmaceutical industry and from CROs

WORKSHOP MODERATOR

- Jean-Michel Combe, Strategic Marketing Director at Kayentis

AUTHORS

- Estelle Haenel, Kayentis Medical Director
- Andrea Murison, Kayentis Business Development Director

eCOA COMPLEXITIES WHITE PAPERS

#1 eCOA training: How can we improve the sites' and patients' experience?

#2 How to anticipate eCOA complexities in multi-year studies & develop best practice to support sites?

#3 No longer the "what if" situation: today's reality and eCOA back-up strategies: how to make sure they are adapted?

#4 eCOA set-up: how to anticipate eCOA complexities and ensure a successful launch

Panacee - November 2020

kayentis

Dedicated to eCOA & Patient Engagement