The eCOA Worst Case Scenario Survival Handbook

A handy guide for overcoming common challenges.

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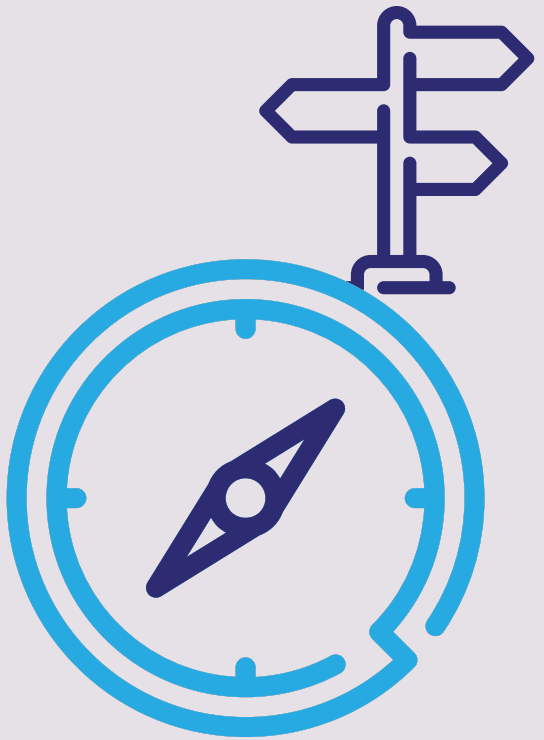

eCOA continues to evolve. There's no shortage of best practices and guidance for overcoming operational challenges, implementing new technology and meeting regulatory expectations.

Sometimes you need more than that. Our eCOA Worst Case Scenario Survival Handbook was built from YPrime's knowledge gained, lessons learned, and creative solutions used in overcoming unexpected disruptions in past work to keep projects on track, no matter what.

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When one of your eCOA devices fails in the field

Although uncommon, device failures can happen. Backup and recovery is an essential part of eCOA deployment planning. For eCOA devices, remote troubleshooting and other strategic methods offer ways to eliminate the possibility of lost or missed data.

Remote diagnostics allow helpdesk staff to provide deeper support to patients and sites 24 hours a day, 7 days a week, 365 days a year.

Consider the otherwise compliant patient whose data have been missing for the past 3 days: Using remote troubleshooting can speed resolution of device issues. Instead of labeling that patient as non-compliant, systems can determine network connectivity issues and force the device to send data. If a patient using a provisioned device drops out of a study, that device can be wiped clean remotely, once data have been synchronized.

Access to a web back up diary can be an alternative for users when an issue with the device cannot be resolved remotely, and a replacement device must be issued. Alerts are sent to study teams to encourage intervention and resolution with a replacement device as soon as possible, so that data entry may continue as intended.

For countries with longer import timelines, YPrime recommends sending extra devices with the initial shipment to an in-country depot, or a monitor to facilitate expedited provisioning of replacement devices as needed. When a resupply is needed, the current study build is synced to the device once it has been assigned to the site. This action will help avoid the risk of losing a patient due to logistical challenges.

These simple methods go a long way in effective risk management techniques because after all, a failure to plan is a plan to fail.

When managing eCOA devices is more than a full-time job

Let's face it, in the digital age, device management should be much more than a weekly static report that's obsolete by the time you receive it. For many eCOA managers, device management is akin to herding cats.

You need to know how many available devices are out there and where they are. That sounds simple enough, but complexity arises quickly in global studies. Some sites may stockpile devices in anticipation of ambitious patient enrollment goals. Then there are devices waiting to ship, in transit, or otherwise not usable. A device management portal streamlines the labyrinth of logistics required to keep track of eCOA devices. Real-time visibility means less waste and less time spent on device inventory management.

Once devices are assigned to participating sites within YPrime's eCOA platform, they can be tracked, managed, and replaced all in our web portal. This allows for transparent oversight of inventory. YPrime's device inventory management portal gives you the control to mitigate the risks experienced in legacy systems, and significantly improves the ease and efficiency of device management.

How to prepare for increased regulatory scrutiny

So first the good news. Regulatory agencies clearly recognize the value of eCOA for sponsors, sites and patients, and the superior data quality that eSource offers when compared to paper. The less-good news? As technology evolves, so has regulatory scrutiny of data integrity.

The single most important component of any system to ensure data integrity? End-to-end audit trails. However, audit trails can be complex, hard to map and even more challenging to interpret. With massive amounts of data, audit reports often resemble more of a data dump than a human readable format.

YPrime recommends a collaboration between sponsors and eCOA providers to build an audit trail report:

- Critical data points should be mutually agreed upon between sponsor and vendor during system development. Pre-defined formats of what the audit trail report should look like should also be decided at this stage.
- It's important for both parties to understand how this information may be reviewed during the life of the study and how it might be presented following its conclusion.
- Providers should make audit trail reports available in the web portal, with role-specific viewing rights, and the ability to view in real-time.
- Audit trail output can be used to perform periodic data integrity checks. At regular intervals, sponsors should proactively review audit trail data to identify anomalies or trends.
- Proactive data review should be one component of broader data integrity plan that's organization-specific. The plan should be documented so it may be presented to regulatory authorities at any time.
- Algorithms and programming that are applied to audit trail information should be defined to demonstrate oversight and minimize questionable actions.

A comprehensive audit trail should answer common regulatory inspector questions: *Who touched the data? Why? Can you reproduce it? Can you clearly show the chain of custody? Will the raw data produce the same conclusion?* The surest path to regulatory preparedness starts with full transparency.

When your pivotal study can't afford to miss any data

One of the central challenges of any study involving patient diaries is maintaining compliance. There's the question of when to act – right after the first missed entry, or the second or third? Then there's the question of whose job it is to monitor compliance. The CRO? CRA? Site staff?

eCOA features such as customizable email alerts and reminders can help study teams stay on top of patient compliance. However, these tools don't help if no one looks at the data or follows up on flagged issues. And some high-priority studies require more personalized attention, beyond your over-tasked clinical operations team.

When you need a reliable solution for pivotal studies that can't afford any missed data, look to YPrime's data monitoring services. This service combines automation and clinical expertise to ensure eCOA data collection compliance. An experienced eClinical analyst looks at eCOA data every day, using compliance thresholds and parameters set by you.

Analysts can raise questions to sites or CRAs before compliance issues warrant rescue actions or compromise your study's data integrity. In addition, they can mine the data for gaps, trends and anomalies. It's especially powerful when multiple sources of data are combined.

When a validated scale requires scrolling on eCOA device

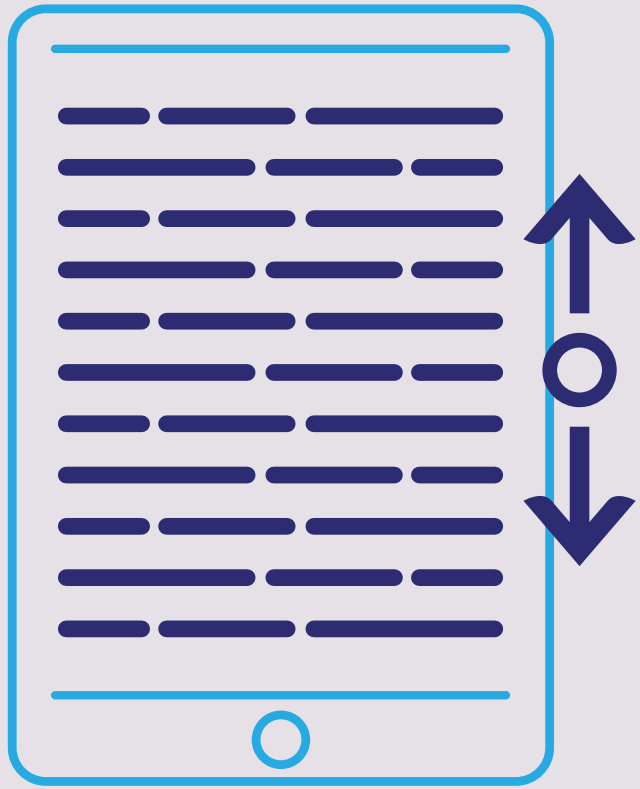
Scrolling is often frowned upon in eCOA deployment, and for good reason. It can lead to missed or incorrect data if a patient doesn't see all the available response options on a handheld screen.

However, it can be necessary when using a text-heavy validated scale. Smaller fonts are rarely an option, especially when you must scale to the longest-form language of participating countries in your trial. If it's long in English, think about how long it will be in German. Scrolling with controls is a better approach than splitting screens, because short-term memory challenges are a real phenomenon. In fact, when instructions are on one screen and questions and response options are on the next screen, many people lose context quickly and don't carry the instructions forward.

There are a handful of practical solutions for scrolling available, including:

- A "strategic" scroll – the patient is informed that scrolling is required, with an additional visual cue.
- The insertion of a pop-up box when the user clicks "next" to let the user know there are more response options while reminding the user to keep scrolling. Or disable the "next" button until the user has scrolled down to the bottom of the page
- A scroll bar that pops back and forth as a visual reminder of the scrolling option.

It's only a matter of time before technology advances introduce a better solution. In the meantime, regardless of the approach - cognitive debriefing and usability testing should be conducted to confirm the measurement properties aren't impacted by the visual changes.



When shipping timelines for some countries exceed development timelines

While shipping to domestic sites is usually straightforward and fast, a global study involving multiple countries has much longer lead times, due to import logistics and customs. This is especially prevalent in emerging clinical trial regions.

An app-based platform offers more flexibility with eCOA deployment than hard-coded devices, down to the device level.

YPrime's app-based eCOA platform allows for advanced shipment of hardware around the world. Sites can be ready from Day 1– even before the final solution is configured or ethics committee approval is obtained. When the build is complete and ethics committee approval is obtained, site staff can easily install the study-specific diary to the pre-installed generic app using a study-specific asset tag, via Wi-Fi or mobile connectivity.

Our app-based platform removes deployment of hardware from the critical path by shipping well in advance of need in time for investigator site initiation visits.

When multi-sourced data integration turns into data clarification form (DCF) hell

Many sponsors rely on a mix of research instruments and objective measures to quantify endpoint data as well as criteria for trial inclusion. While the integration of multiple data sources produces a comprehensive picture of disease activity, this method can present data management challenges.

Often, complex scoring algorithms and manual transcriptions of data result in the need to raise DCFs. If these discrepancies are not carefully monitored, many change requests may be raised at once – often shortly before pivotal milestones like database lock. This can lead to significant delays. Simple data corrections can take up to 5 days. A bolus of change requests may take weeks.

With YPrime's eCOA platform, you can save time associated with data modification processes and boost data quality by eliminating manual score calculations. Our solution allows for DCFs to be implemented instantaneously following approval. This helps you avoid backlogs, and removes the variable costs associated with DCFs.

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Will your eCOA data support endpoints for labeling claims?

Recent initiatives from the FDA demonstrate the growing influence of patient perspectives. Key considerations and recommendations on this extensively-discussed topic include:

- A high-quality trial begins with a well-articulated protocol, with critical study parameters.
- Safety and efficacy endpoints should be considered first, followed by a discussion of what technology is most appropriate, with consideration given to patient population, the setting and the end user.
- Sponsors should take advantage of pre-submission meetings with FDA. Get feedback on endpoints and what data you plan to collect. Critical stages of input include:
  - Pre IND/IDE
  - EOP II
  - Pre NDA/BLA/PMA submission
- Technology selections can make or break a marketing application. Technology must demonstrate compliance with applicable provisions in 21 CFR Parts 11, 56, 312, 314, 812, 814.
- Don't treat all data equally. This includes distinguishing the nature of data errors, and recognizing the impact on usability and the interpretation of results. Delineate between inaccurate vs. incomplete vs. missing.
- Migration from paper to e-formats must ensure there are no changes in content, and patients interpret and respond the same way regardless of mode. The migration process, however, is time-intensive, and rigorous when collecting evidence to support measurement equivalence. Recent evidence suggests duplicative tests for already-proven conclusions are unnecessary. For minor changes, the selection of eCOA solutions with a good user interface and user experience properties that have undergone usability testing may enable many instrument migrations to be accepted– without formal validation studies. In these cases, a structured expert screen review may be conducted instead.

How We Can Help You

In addition to our modern eCOA technology, YPrime brings a well-earned reputation for flexibility and problem-solving. If you have a challenge that doesn't quite fit the mold, contact us today. And we'll show you an effective way to deal with it.

Our mission is simple: To support our clients in the timely and accurate completion of innovative research that gets them to the next stage in their drug development projects.

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