Build a Better Study: Six Must-Know EDC Guidelines

You've just been handed a protocol and asked to build it out in your EDC system. How can you make sure that the protocol is implemented in a way that maximizes efficiency and data quality? Getting the details right during the build phase paves the way for a smoother study, generates better data, and keeps stakeholders productive and happy throughout the process.

While each study protocol is unique and will have its own needs, there are six proven elements that consistently contribute to a successful build:

- Know your users
- Obsessively simplify
- Optimize workflows
- Right-size your eCRFs
- Leveraging functionality
- Embracing standardization

Let's dig into each guideline and look at examples of how it can impact your study's success

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Guideline #1: Know your users

As you build your study, consider how the system will be used by all the different stakeholders throughout the clinical trial process. These stakeholders may include data managers, investigators, coordinators, monitors, statisticians, external sponsors, and study participants. Let's briefly look at each of them to see how you might accommodate their needs.

Site users, such as research coordinators and investigators are on the front lines. These individuals are responsible for working directly with patients and entering data in the prescribed eCRFs. If the study uses electronic Patient Reported Outcomes (ePRO), they may also be training study participants on how to use this part of the system. Site users typically work in very busy environments (e.g. hospitals and clinics) and are juggling many tasks at once.

Meet site users where they are by making it incredibly easy for them to enter data. Be judicious with hard edit checks or other barriers that can create frustration. No critical thinking should be required.

Get sites to provide timely data by giving each site a dashboard showing them what's overdue and what's coming up. Rather than waiting for site users to come and check the dashboard, have the system automatically push this information via email.

Data managers are the power users of EDC software. Their job is to keep the data flowing at the highest quality and greatest efficiency possible. To do this, data managers need tools to ensure data accuracy and completeness. Throughout a study, they'll be looking at key metrics in order to uncover issues within the data. For example they need to know what forms are missing or incomplete, how well queries are being resolved, and how well sites are performing. They will spot and respond to overarching trends as well as discover issues with individual data items.

Fulfill data managers' needs by deploying smart edit checks and an overall user experience that promotes data quality at the point of capture. Limiting the burden of downstream data cleaning will also enhance the satisfaction of participating sites and enable a faster route to locking the final database.

Data manager's job is greatly simplified if all the data is in one place. For example, if ePRO data is in a separate database, this can greatly complicate the data manager's job.

Monitors typically have broad oversight responsibilities in regards to site compliance and, when it comes to EDC, they may be most interested in data points supporting primary and secondary endpoints as well as fields with safety implications. Monitors will likely require limited write access in the EDC as they will be issuing queries but not manipulating data.

Support your monitors' needs by giving them read-only access, reports that make it easy to identify potential problems at the site, and a dashboard-driven source data verification (SDV) workflow.

Statisticians need clinical data that they can easily analyze. And they may need it at multiple points throughout the study.

Consider the structure and content of the datasets your stats colleagues will require. Here are some questions you could ask your statistician:

- What data will you need and how often do you need it?
- How do you prefer to get the data? (e.g. direct access to EDC, auto-run exports, or API calls)
- What software will you be using to analyze it?
- Do you have any preferences or constraints when it comes to variable naming or length?
- Do you need the data to adhere to certain standards? (e.g. CDASH, STDM)
- How would you prefer to see repeating data structures (e.g. tall/skinny, sort/fat)?
- Do you have any preferences around how codelist values are represented?

The way you define your eCRFS and study events can often have an influence over how data are represented in exports. Also, make sure they review and approve variable names in advance. As a result, it's always a good idea to share some "sample" data sets with your statistician prior to finalizing the study configuration.

External sponsors will likely want a "window" into the study to be able to monitor progress. They are interested in bigger trends such as recruitment, site performance, as well as safety incidents. Typically, they are not interested in the nitty-gritty details, but may want to take a deep dive if necessary.

Meet sponsor needs through easy-to-read reports and dashboards showing metrics and visualizations on complete/incomplete eCRFs, query aging, AEs, SDV statuses, and much more. Offer read-only access to see what the data looks like, what the sites are seeing, and what the queries look like. The sponsor can drill up and down with the data as needed.

Patients have become active data contributors in clinical studies through the use of ePRO (electronic patient reported outcomes) technologies and the increasing virtualization of clinical trials. Patients place a premium on convenience and ease of use.

Focus on building a frictionless experience for participants. Allow them to interface with the study through their own device (smartphone, tablet, laptop, etc.). And don't tie them to one particular device. For this reason, native apps are often not an ideal approach for ePRO as they present many technical hurdles: the participant must successfully download and install the app on each device, their device must have adequate memory, and the app needs to be up-to-date and running when it needs to be. Don't assume that just because it's easy for you and me, it's going to be easy for your study's participants.

Participants should be able to get to the forms they need in as direct a manner as possible. Configure rules-based notifications to automatically send participants text messages and emails when data is required (e.g. diary entry, survey, etc.). Giving participants one-click access to their forms means they can click-and-go when they get these messages and don't have to fish around for their password.

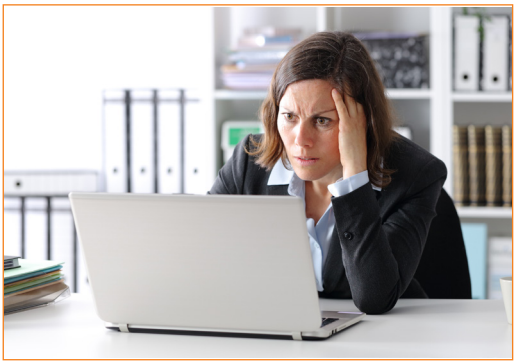
Keep in mind that some study participants may not be sufficiently capable of using technology (e.g., due to age or disability).

Consider offering a hybrid approach where these participants can use paper while others go electronic. ePRO doesn't necessarily have to be an all or nothing proposition.

Study Builders need to deploy studies quickly and in a manner that is optimized for all stakeholders. They need to be able to easily maintain the study's configuration in the face of inevitable change. The study builder needs a toolset that allows them to immediately see/test work in progress, share draft versions with stakeholders, capture feedback, and iterate quickly.

Even if a study is finely tuned when it first launches, protocols change and it is the job of the study designer to manage this change in a way that delivers against the new requirements while minimizing risk and disruption.

Meet study builders' needs by equipping them with build tools that are both powerful and easy, allowing them to quickly configure, test, and deploy changes to eCRFs without compromising the integrity of data already collected.



Guideline #2: Obsessively simplify

Less is often more, and this is especially true in clinical trials. It can be tempting to pack a study with unnecessary data fields and too much validation logic. Catering to every stakeholder requirement can feel like the right approach, but can have unintended consequences. An over-engineered study:

- Increases testing and training time
- Promotes bad data (users may enter incorrect values in order to satisfy a particularly unnecessary edit check or simply experience fatigue and get sloppy)
- Complicates inevitable study changes.

Don't be afraid to challenge your colleagues on how much data to collect. While some may feel the need to squeeze out every data point conceivably possible, it is important to recognize that each variable has its own costly lifecycle (building, testing, training, collecting, verifying, cleaning, and analyzing). Therefore, just because you can capture something doesn't mean you should capture it. To simplify your study:

- Make deliberate decisions about what data is essential and what is not.
- Ask only necessary questions, and in the order they need to be asked.
- Make the data entry process easy with minimal barriers and nothing superfluous.

For example, consider eligibility. Simplify the process of determining participant eligibility by asking disqualifying questions first. This prevents users from spending time collecting unnecessary data on ineligible participants.

When it comes to long picklists (e.g. lists of medications, diagnoses, etc.), let users dynamically search/filter the list without having to scroll through everything.

Strategically use show/hide logic so end-users only need to focus on what's relevant. We recommend avoiding an excessive amount of dynamic show/hide questions by setting certain data items as required or optional.

Guideline #3: Design intuitive data collection workflows

Thinking critically about the data collection workflows can help site users deliver better data, faster. Conversely, poor workflow leads to frustration and, in a worst-case scenario, missing information.

Good EDC study design creates a smooth experience for site users by aligning with existing site workflows. Bear in mind that in a multi-site study, individual sites will likely have pre-existing differing ways of doing things. Be careful about enforcing a specific order to data entry unless it is truly necessary. Instead, give sites flexibility to complete eCRFs in any order when possible. Make it easy to provide readily available information (such as demographics and medical history) before requiring more esoteric data. The study design should easily dovetail with how a site already collects patient information in the course of their normal clinical workflow.

Study designers can reinforce intuitive workflows by:

- Offering clear sets of instructions right inside the eCRFs
- Including hyperlinks to reference material or other resources
- Using bulleted lists
- Formulating unambiguous questions
- Embedding instructional videos

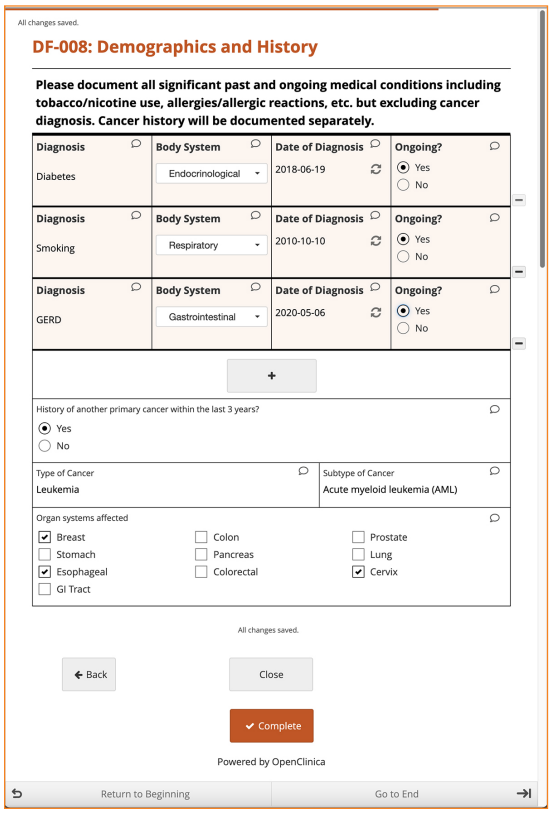
Another way to ensure a fluid workflow is using hard edit checks judiciously. Hard edit checks, or edit checks that prevent the user from moving forward or saving data unless specified criteria are met, are often misused. A hard edit check could result in the unintended consequence of the user feeling forced to enter a false value in order to be able to proceed.

It is important to validate data as it's entered, but consider making the vast majority of edit checks soft as opposed to hard. A soft check should let the user proceed, while flagging the unmet condition for future follow-up.

Timing is another key element of good workflow design. Good study design asks for the right information at the right time in the workflow. For example, a patient's blood labs may be part of a particular event definition, suggesting it might be appropriate to import the lab data at this point in the EDC system. However, in reality, lab analysis results may not be available until a future visit. Users may become confused if they repeatedly encounter validation checks or rules requiring information that is not yet available to them.

Additionally, an expected data field that is missing can lead to misrepresentation of the overall form or event status—or even provide an incorrect indication of the patient's actual status in the study. In most EDC systems, the missing lab result from the example above would prevent the baseline visit from reaching a completed status. In this setting, it would be difficult to distinguish a delayed result versus missing data, so it would make sense to put the lab form in its own event.

If possible, have some of your sites review and provide feedback prior to going live to ensure the study uses a logical sequence of events and that eCRF questions are clear with rules and error warnings that cannot be misconstrued.



Guideline #4: Right-size your eCRFs

In today's digital world you should expect that your end-users will employ computing devices spanning a wide spectrum of screen sizes and shapes, from large high-resolution monitors to small smartphone screens. An EDC system that has a responsive UI means that page elements will dynamically adjust to fit the user's screen while retaining their function and usability.

Consider form length. When designing eCRFs, it is important to keep your forms and their pages/sections short.

Long forms can function as hurdles to data entry and if scrolling is required (either horizontally or vertically), the user may not see everything on the page. This is particularly important for ePRO forms, which are often being filled out by patients using smartphones. If the patient cannot see all of the choices, or excessive scrolling is required, it will be more challenging to ensure complete and accurate data.

Conversely, form sections that are too short can be frustrating to use, lack sufficient context, and require unnecessary clicks. Place applicable sections together and design forms with the end-user—and their preferred device—in mind.

Finally, consider repeating item groups as a way to present forms compactly, while remaining extensible. If you have a form containing a set of five questions that might repeat up to say, ten times, rather than creating 50 individual fields, create five fields and allow the user to add additional records as needed—assuming your EDC system supports this functionality.

Guideline #5: Optimize system functionality

The only way to truly maximize the benefits of your EDC system is to understand its full capabilities. Only then can you unleash the full power of whatever system you are using for any clinical trial. Here are some features to potentially leverage in your next study.

Dynamic logic: It would be hard to overstate the power of dynamic logic. When used correctly, it adds useful personalization, resulting in greater efficiency and momentum to data collection. Use dynamic logic in order to present the user with only options that are applicable to their scenario. For example, it wouldn't show pregnancy test questions if the participant is male.

Dynamic defaults: Like dynamic logic, you can increase data capture efficiency by setting default values, and allowing the user to edit them. For example, if you are tracking vitals every 15 minutes into rows of a repeating item group, you could have each row default with a time value that is 15 minutes post the value in the row before. Of course, you should be careful about using defaults for particularly critical fields that you want the user to really scrutinize, or where the default value has a good chance of not representing the actual value.

Reuse data: Let's say a study captures height in Visit #1 and needs to calculate the participant's BMI in Visit # 2. In Visit #2, rather than asking for the height value again, the form should be able to compute the BMI using the previously captured value. There may be other cases where the site needs to reference certain demographic information on a form. If that information was previously collected, then logic can read it into a note on the current form for convenient access.

Auto-calculations: If your EDC system supports auto-calculations, you can use this feature to minimize user effort and increase data accuracy. This feature works well in data fields that require scoring. For example, the glomerular filtration rate (GFR) is a common way to assess kidney function, and uses race, sex, serum creatine, and age as inputs:

$$141 \times (SCr/0.9)^{-0.411} \times 0.993^{age}$$

The above exponent (-0.411) and constant (141) are taken from a table of values based on race and age group. There is a fair amount of complexity here. If sites are forced to compute the GFR, they face an increased burden and a strong likelihood of error. If the GFR is instead calculated centrally by a study team member, there is a substantial delay getting your hands on what might be an essential data point. Look for your EDC system to eliminate user burden and produce this data point accurately and automatically in real-time.

Of course, make sure any such system-calculated data point is set as read-only/non-editable to prevent any accidental updates. While the input values could be edited, the calculated final score (in this example) should not be.

Auto-notifications: Setting up automated email notifications can be a great way to deliver time-sensitive information without relying on data extracts or reports.

For example:

- The pathologist can receive an email when there is a new image to review.
- The safety committee can receive an email every time a serious adverse event is recorded.
- A research coordinator can receive an email when a query requires their attention
- Participants can receive text messages with a link to a survey, or to remind them to take their medication

Email alias/distribution lists are a great feature to use for continuity of communication within the study team. For example: safety@yourtrial.xyz. As people come and go from the project, their email addresses change. Email aliases, however, can be permanent and "repointed" as needed. Using email aliases can save you from having to update the EDC system when a team member is no longer working on the study.

Guideline #6: Standardize

Most organizations conduct multiple studies, and most EDC technology offers the ability to easily reuse eCRFs, edits checks, and other assets for new studies. Therefore, it's a great idea to adopt standards that facilitate this reuse and help "future-proof" your investment.

Such standardization should include specific naming conventions for your data variables. It's also a good idea to create a well-curated library of forms and fields categorized by domain so that they can easily be recombined into new "standardized" forms. Here are some examples of the types of content that could be standardized for your studies:

- Adverse events
- Concomitant medications
- Common treatments
- Demographics
- Diary information
- Injury details
- Labs
- Medical history
- Vital signs
- ...and other content specific to your therapeutic area

If your studies will be used in regulatory submissions, you should incorporate CDISC[1] standards, in particular CDASH[2]. CDASH provides a standardized way of describing your study data. It is also linked to another CDISC standard called STDM, which is used in data submissions to the FDA. Configuring your form items to align with CDASH standards and naming conventions enables faster transformation of the data to SDTM or ADaM, and eases the data submission process. Ask your EDC vendor if they have prefabricated CDASH eCRFs to help you get a head start on building your study.

As users become familiar with your core standardized forms they will require less training, deliver more consistent data, and do so more quickly. Standardization also facilitates interoperability and shareability and reduces overall study build time.

As you build new forms, do so with an eye towards standards. If you take the extra step of having it reviewed and pre-approved for various uses, you'll be one step closer to supercharging your next study.

Wrap-up

E-clinical study designers often find their attention commandeered by tight timelines, frequent requests for fixes, and seemingly endless revisions. It can be a real challenge to create unique solutions for complicated requirements while optimizing system functionality. By leveraging the six guidelines described above, you can build a study design that will support a productive clinical trial—and hopefully lay the groundwork for many more trials to come!

[1] CDISC: Clinical Data Interchange Standards Consortium. CDISC is a non-profit organization that has established standards to support the acquisition, exchange, submission and archive of clinical research data and metadata. See http://www.cdisc.org.

[2] CDASH: Clinical Data Acquisition Standards Harmonization. CDASH establishes a standard way to collect data consistently across studies and sponsors so that data collection formats and structures provide clear traceability of submission data into the Study Data Tabulation Model (SDTM), delivering more transparency to regulators and others who conduct data review. See https://www.cdisc.org/standards/foundational/cdash

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