PLAYBOOK

Managing Change in Clinical Trials

A data management playbook

OpenClinica

Overview

The need to manage change in clinical trials is unavoidable. With so many moving parts, preparing for the unexpected and improving efficiencies is a necessary practice. In addition to moving parts, a multitude of stakeholders, each with different and often conflicting priorities, make managing change even more challenging. Stakeholders such as CROs, clinical data managers, clinical research coordinators, clinical operations, IRBs, IT, security, privacy and compliance have different approaches to managing clinical trials and aren't always prepared for change.

Change requires people to do things in new ways to either meet unexpected roadblocks or to improve upon the way existing tasks are carried out. Learning to do things in a new way takes time and effort. When teams make this kind of process investment, people can't focus 100% on their core functions. This in turn can cause bottlenecks and delays which drive up costs. The stakes increase further if patient outcomes are impacted.

But it doesn't need to be this hard. Planning for change related to the single most critical and thorny element of clinical trials – the data to support the therapy submission – can save substantial time, money, and resources in the short and long run.

A foreword from our co-founder and chief operating officer, Ben Baumann

Thank you for your interest in our playbook! Based on our 15+ years managing data—and change—in clinical trials, we've created this data management playbook to help you tackle change when the time comes. This eBook discusses data management challenges faced in clinical trials and offers a proven pathway for change management.

Clinical trial ecosystems are complex and data lives in many different places. If one area of the ecosystem is disrupted, the impact ripples outward to cause data management bottlenecks, missed deadlines, safety compromises, errors, etc., eventually delaying the ability to bring therapies to market quickly and effectively.

Central to successfully managing change is managing risk. Successful change management begins before change is introduced – by taking time to understand stakeholder requirements, anticipate potential issues, and ensure these are supported by your processes, systems, and good communication. This fuller context allows you to better anticipate and prepare for change.

Start with Stakeholders

In a clinical trial, people are your most important asset, and the single greatest determinant to successfully managing change. Start by identifying each stakeholder, their role in the study, and what they need. This will help make the study more predictable and help reduce risk and need for change. Key stakeholders include:

RESEARCH COORDINATORS

Clinical Research Coordinators (CRCs) are largely tasked with implementing protocols every day at each study site. They are the people who ultimately collect and deliver the data. CRC workloads can vary greatly, with some working on multiple studies for multiple sponsors across multiple systems. Often, they must collate data from disparate sources, generate their own source records, then manually enter the data into your electronic data capture (EDC) system. All of this creates bottlenecks in getting finalized data. The easier sponsors, CROs and site leadership can make their responsibilities, the more efficient your trial will be.

INVESTIGATORS

Investigators sign-off on the data. Like CRCs, they face increasing workloads. Making data review and signing easier for them and their staff will help keep your trial on schedule.

PATIENTS

The whole reason why we do clinical research is for patients. Today, patients frequently contribute directly to the trial database. Remove whatever barriers you can to make their data sharing frictionless.

DATA SCIENTISTS

Data scientists, including statisticians, process the data generated in your trial. These stakeholders often have pre-built tooling such as SAS programs and data ingestion/aggregation tools. Before your study starts, make sure they can access data in the format and structure they require.

DATA MANAGERS

Data managers are responsible for ensuring smooth flow of quality data. They need tools for checking, reviewing, and identifying bottlenecks before they become real problems. They also need to coordinate and manage many of the other stakeholders. Giving them the ability to easily monitor the study's data processing pipelines and facilitate actionable communication with disparate stakeholders is essential.

STUDY PROGRAMMERS

This role is usually carried out by technical personnel. But modern tools make it possible for people without specialized, technical training to configure complex studies. The ability to quickly and reliably modify the study (update forms, logic, workflows, sites, etc.) mid-study are essential for these stakeholders to do their part in successfully managing change.

MONITORS

Monitors assess data quality, review protocol compliance, and spot anomalies. This work is usually labor-intensive, stressful and slow. Providing dash-boards and automated alerts improves their ability to review and verify data in a focused manner to ensure protocol adherence, data quality and safety.

IT

Cloud-based software makes systems more manage-able for your IT group. However, as more data sources and systems are added to your trial, your IT team may be tasked with increased integrations, which can be challenging.

It's important to involve stakeholders during the planning stages of a study. Working with stakeholders early to understand their requirements and get feedback on proposed system interfaces, workflows and forms increases your chances of a successful study start. Throughout the study, practice frequent communication, solicit feedback and set/adjust expectations as necessary.

People are a great catalyst for change if they're well prepared and included from the start. This is especially true if the change will ultimately help them do their work faster and more efficiently. The size of your team and team dynamics is important here. If you have a large team, you will likely have greater differentiation of responsibilities which will also correspond to how each teammate is expected to use your e-clinical systems. On the other hand, if you have a small team with one data manager, you may combine multiple roles into one, and/or require more support from vendors.

Read this case study to learn how one data manager achieved what usually requires a large team to execute.

Human capital needs often change as the study goes on. Having the right amount of people power at the start does not mean you'll have it in the middle or end. Do you have a back-up plan if a clinical data manager leaves mid-study? What about turnover at sites? How about other critical personnel? With some studies running for several years and with growing labor shortages, planning for personnel changes should be part of your change management strategy.

Finally, consider making a list of risks that could impact each stakeholder and assess it periodically. Involving your staff in the assessment provides invaluable input and buy-in for change. Ask your team about the challenges they consistently face. Where are they spending chunks of their time? Where are the bottlenecks? As part of your management toolkit, a simple list can help you better anticipate possible change and more effectively set expectations among your colleagues. If you want to be more formal and quantitative about assessing risk, consider a full-blown risk assessment matrix.

Now, let's dig into some of the common types of change in clinical trials and ways they can be effectively managed.

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CHALLENGE

Mid-study Changes

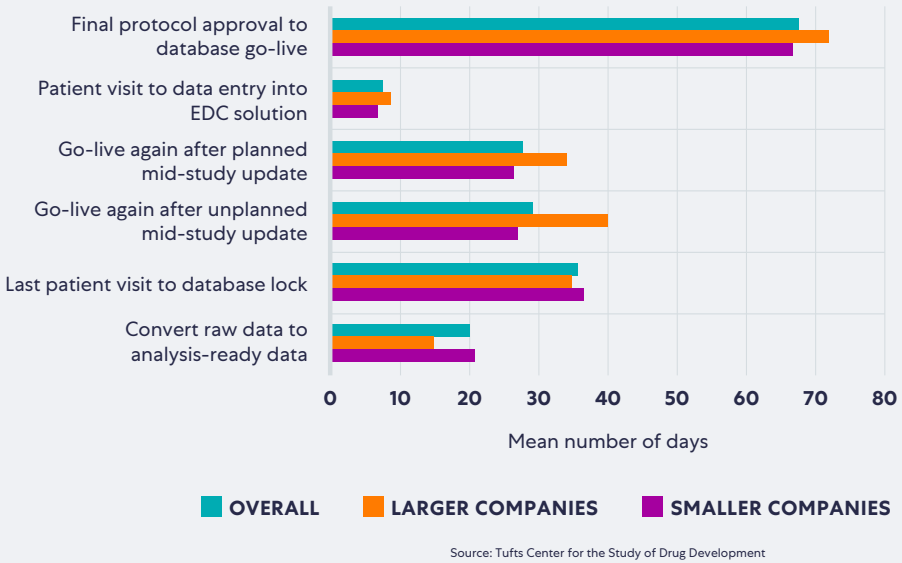
According to a 2021 report by Tufts Center for the Study of Drug Development (CSDD), of 194 global drug discovery companies surveyed:

56.5% said planned updates to Electronic Data Capture (EDC) systems or protocols were their biggest data management challenge

48.4% said unplanned updates were their biggest issue

Additionally, the study found each mid-study change added an average of 30 days to clinical trial timelines. Although avoiding mid-study changes is the ideal approach, this isn't realistically possible. Whether planned, or unplanned, change happens. And poorly managed change can impact data and ability to bring therapies to market.

Key Data Management Time Points



Source: Tufts Center for the Study of Drug Development

Let's look at three of the most common types of mid-study changes and how you can successfully manage them

CHANGES TO FORM DESIGN

For example, a change in eligibility requirements or new data required per protocol.

- If you're relying on an outside vendor to update your EDC system, form design changes can take a long time, especially if they involve change orders with a set cycle time. However, many modern systems include study design tools that can be used without any specialized technical expertise, affording you greater control.
- You shouldn't necessarily have to wait for every local IRB to approve a protocol amendment before deploying the corresponding changes. Consider rolling out new forms site-by-site as individual IRB approvals are secured.
- When deploying a new version of a form, think about the data collected on previous versions. Will you use the new version from that point forward or apply changes retroactively to data already collected?

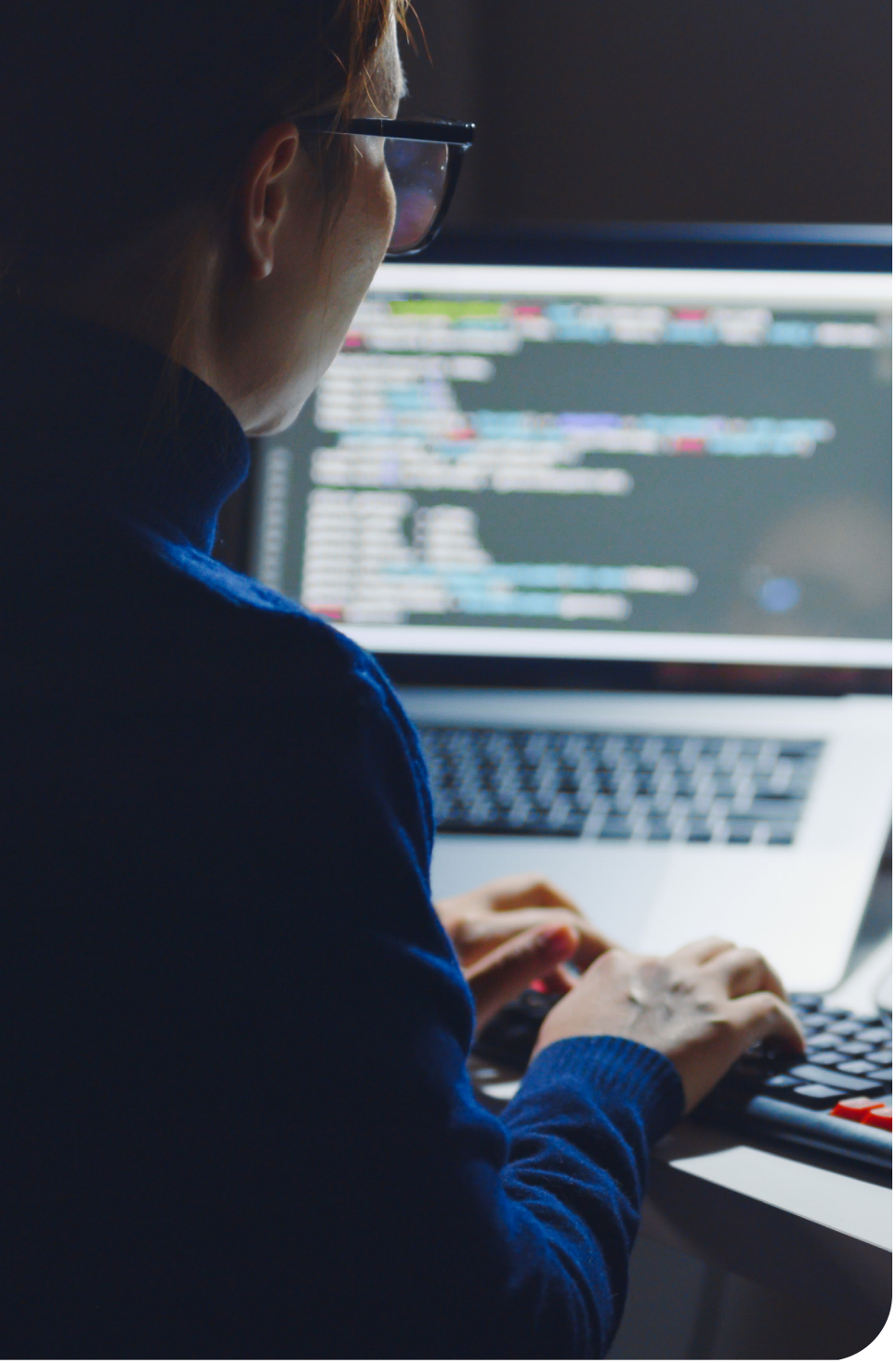
CHANGES TO WORKFLOW

If you're not clearly defining workflow processes and responsibilities at the start of a clinical trial or if the trial parameters change, you must address gaps or overlaps in tasks and find new resources to complete the study or risk overtaxing existing staff. Retraining may also be required, requiring additional time and expense. To minimize mid-study changes:

- Think of ways the system can "pull" the user through the protocol when building out your study. Minimize cognitive burden by making events and forms available to the user only as they are needed.
- Remember, an electronic case report form (eCRF) can be more than simply a vessel to receive data. It can incorporate decision aids, videos, notes, links to resources, and other helpful documentation.
- Leverage rules-based notifications (on-screen, email, SMS) to remind users of action steps and deadlines.
- Evaluate systems for optimal user experience. Don't let training become a crutch. Instead, build your study initially under the presumption that training end-users isn't possible. This will force you to think through and shape the user experience in the most effective way and make it easy for you to streamline the eventual training.

CHANGES IN SITE MEMBERSHIP

Adding new trial sites, especially virtual or decentralized sites mid-study, is increasingly common. Consider and plan for how you will add remote visits, mobile clinician services, enable EHR data pulls or conduct e-consent. Certain procedures may require learning how to administer a test remotely or connect and use a required measurement device. Onboarding sites one at a time allows you to iteratively improve the process for a better overall result at the end of the day with lower risk along the way.



CHALLENGE

Technology Updates

Software can change to meet evolving needs. Whether you are bringing in a new application, updating/modifying an existing one or building integrations across systems, the impact of these changes is often substantial. Having a plan for technology challenges is important, especially if these changes occur mid-study.

Some changes may be initiated by you, while others may be imposed upon you. Cloud-based software-as-a-service has become the predominant model for delivering clinical research software. The cloud offers many advantages including faster release cycles, greater responsiveness to fixes and increased reliability. However, these changes are pushed to all vendor customers, sometimes with little or no notice.

To manage technology updates:

- Request and ensure you receive sufficient advance notice of software updates, with the appropriate level of detail to properly assess impact and prepare for change.
- Understand which new features you must initiate (via a publishing workflow) vs. those initiated by the vendor that will automatically appear to end users.
- Request a pre-release sandbox environment for independent exploration and early testing with your specific study design.

CHALLENGE

Launching New Studies

As data managers, we are often tasked with standing up new studies in the software we use. These study configuration responsibilities have their own change management implications. For example, the ability to easily reuse components such as forms and rules built for a prior study provides a jump start on your new study, ensuring a smooth and on-time launch. A centrally curated library of case report forms ensures ease of data analysis and the ability to re-use collected data in other, similar studies.

Standardizing forms creates greater familiarity with sites and participants. This familiarity reduces training needs, cuts down on queries, and helps you get better data, faster.

User acceptance testing (UAT) can often be a change management bottleneck to launching a study. UAT is too often run as a serial process in which individual rounds have sequential phases for running a large suite of tests. After all testing, feedback is implemented. This cycle can repeat countless times. Consider an interactive approach to UAT in which study designers observe users testing the system live and apply fixes/changes in real time. This approach improves the final format by only changing what demonstrably needs to change and eliminates this common change management slow-down.

Forms have an outsized impact on the overall quality of your study. Form experience has a direct impact on downstream data review, data cleaning and time to lock. As a result, good form design helps manage risk and mitigate the impact of change.

Learn more about creating a great form experience for your users.[1]

1. And not every data point needs to be hand entered into a form nowadays. OpenClinica Unite makes it possible to pre-populate eCRFs with existing data from medical records systems. Automating this function reduces manual transcription that falls to busy Clinical Research Coordinators (CRCs) and other members of the site's clinical trial team.

CHALLENGE

The Unknown and the Unexpected

If there's an adage that resonates with battle-hardened trialists, it's "expect the unexpected." Trials will take unexpected twists and turns, and it is important to identify issues before they blossom into full blown change management problems.

A key to sussing out issues lies in analyzing the data and how it's flowing. Analytics tools help keep a pulse on your data flow, specifically through:

- Automated alerts for possible safety events,
- Identification of potential training issues,
- Detection of study configuration problems,
- Improved security (for example, detecting unauthorized login attempts).

To fully deliver on these capabilities, ensure your analytics tool provides unfettered access to all your data (clinical data, operational metadata, audit log data, etc.), makes it easy to ask questions from this data (queries), and sends proactive alerts.

It's impossible to anticipate every possible issue that may arise.

However, below are a few common categories of events with potentially far-reaching consequences.

ISSUE AREA	HOW TO MANAGE
Regulatory compliance issues - such as HIPAA, GDPR, ICH, GCP, FDA, MHRA.	• Regional data hosting • Data protection agreements • Data transfer agreements • Validation documentation
Data loss - Could be due to unexpected failures in hardware, IT networks, hacker, software bugs etc.	• Auto-save eCRF data • Redundancy • Limited SPOFs • Good DR test RPO/RTO
Monitoring findings - Site not using instrument properly; not following protocol.	• Real-time analytics with alerts • Built-in documentation and training
Recruitment issues - While studies often kick-off with a high degree of confidence that enrollment targets and timelines will be met, more often than not these things slip.	• Easy to add and onboard new sites • Ability to recruit patients in a siteless, or "site-lite" manner (self-registration, remote visits, patient-initiated data sharing of their EHR to auto-populate study forms).

Standards and Procedures to Facilitate Change Management

Understanding the potential challenges is one aspect to facilitating change management; the other is to implement standard operating procedures for your company.

TECHNOLOGY STANDARDS

Adopting **standards that create structured data to promote interoperability has many benefits**, including reducing unnecessary duplication of clinical testing. Working with an EDC provider committed to both understanding healthcare needs specific to data management and adopting interoperability standards to create efficiencies can speed up trials.

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM (CDISC)

CDISC, the leading data standards body for clinical research, partnered with OpenClinica to pre-create electronic Case Report Forms (eCRFs) from the CDISC portal into OpenClinica's EDC content library. Researchers can now leverage the eCRFs and easily adopt CDISC standards while capturing data for their studies. Implementing CDISC standards allows data to be structured more effectively, which simplifies downstream data analysis and submission. Further, the collaboration allows the academic community to reap the many benefits of connecting real-world evidence (RWD) to CDISC standards, including improvement in data sharing, cross-study analysis, and meta-analysis of data. **Read more**.

STANDARD OPERATING PROCEDURES (SOPS)

SOPs create a foundation on which you can prepare technology, people, and processes for optimal success. SOPs are invaluable to have in place when change is necessary because roles and responsibilities are clear, and time isn't wasted clarifying confusion.

SOPs are crucial to quality management as they define the document processes and procedures to be followed, the roles/ people who should follow them, and the foundation of quality management systems. In addition to defining and documenting roles and responsibilities, we recommend that the SOP template you develop includes SOP release/distribution requirements and version control.

Well-defined SOPs ensure that all parties involved in the clinical trial understand the clinical data management documentation methods and processes, and that data are consistently recorded and analyzed. How you create your SOPs is up to you and will vary based on your unique needs.

We highly recommend the following data-specific SOPs to enable compliance and to speed change management.

DATA ENTRY, RECEIPT, AND HANDLING

Data entry should address general guidelines, which will vary depending on your study. You might need to address how to input scientific symbols, for example. You should define all the different means by which data may be received and all of the methods by which the data will be received including electronic patient reported outcomes (ePRO), imports, web services, and paper.

DATABASE SECURITY

Create an SOP to describe the requirements, methods, and tests to ensure your database is secure, including username/ password requirements, password expiration, means for resetting passwords, how system/study access is granted/revoked, roles and role-based access.

DATA EXTRACTION AND VALIDATION

It's important to define the process for extracting data and the method for verifying that the extracted data matches the data that was entered into the system.

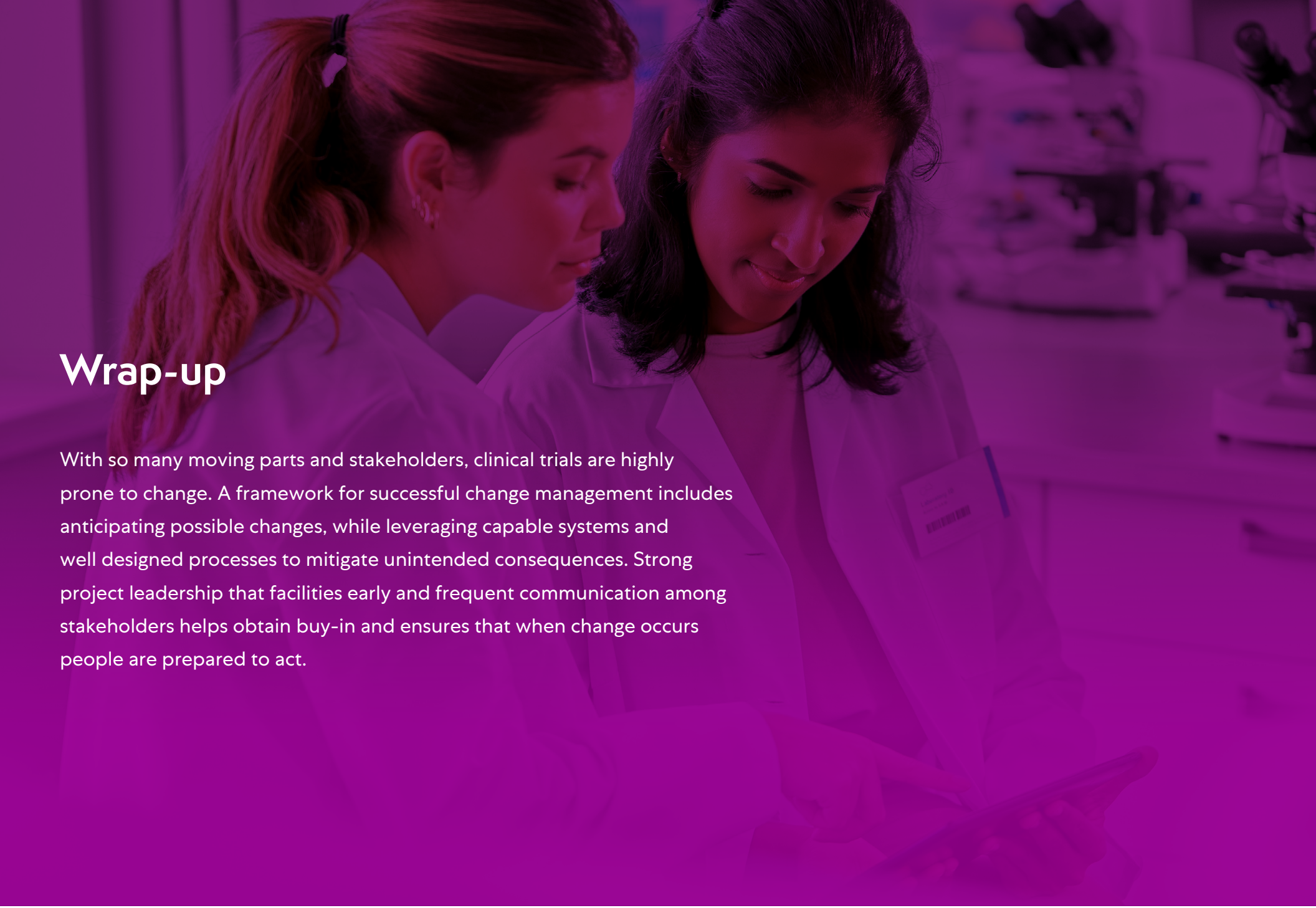
DATA RETENTION AND ARCHIVAL

A critical aspect of data management is defining the data retention, archival, and retrieval process. For databases man aged by external sources, define the process for accessing the database throughout the defined retention period. This should include the clinical data, eCRFs, and discrepancies/resolutions.

DATA VALIDATION

Validation is critical and can also be easily conducted in a cloud-based environment. Vendor support is vital. Work with your software partner(s) to ensure your validation measures make clinical data management a breeze for all stakeholders. As part of this step, define the process for transferring data to other systems and the method for verifying transferred data matches the data entered into the original system.

You can find a detailed SOP checklist here.



Wrap-up

With so many moving parts and stakeholders, clinical trials are highly prone to change. A framework for successful change management includes anticipating possible changes, while leveraging capable systems and well designed processes to mitigate unintended consequences. Strong project leadership that facilities early and frequent communication among stakeholders helps obtain buy-in and ensures that when change occurs people are prepared to act.

Additional Resources

Clinical Data Management Case Study

OpenClinica case study details the benefits of creating structured data according to standards that promote interoperability and the significant time savings that can be achieved with automated software.

Risk Assessment Matrix

Guide describes the value of creating a risk assessment matrix to help keep complicated projects on track. Includes tips for creating a matrix plus recommendations for project management software.

2021 CSDD Report

Survey of global data management professionals reports the average number of mid-study trial delays, the average time taken to get studies back on track, and the resulting delays in trial closeout.

The Ultimate eCRF Design Guide

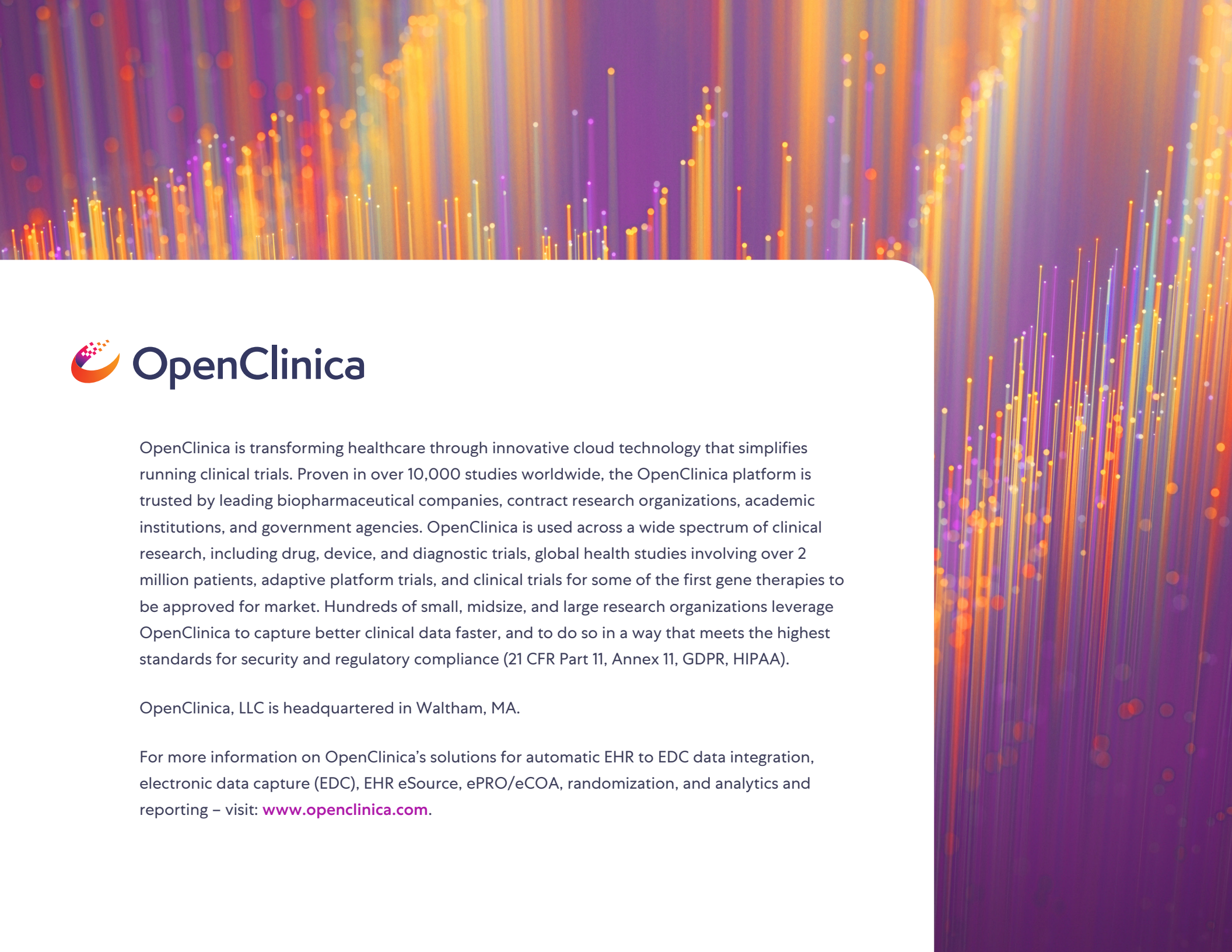
OpenClinica shares best practices for designing forms that speed time to capture data, enable the widest possible integration, facilitate robust and rapid analysis and make regulatory submissions smoother.

CDISC and OpenClinica Collaboration

Collaboration enables academic institutions and researchers to leverage eCRFs from the CDISC eCRF Portal to easily adopt CDISC Standards while capturing RWD data for their studies.

Suggested SOPs for Electronic Data Capture

OpenClinica shares a list of Data Management SOPs for Electronic Data Capture along with descriptions and definitions. Suggestions represent a minimum set of procedures.



OpenClinica

OpenClinica is transforming healthcare through innovative cloud technology that simplifies running clinical trials. Proven in over 10,000 studies worldwide, the OpenClinica platform is trusted by leading biopharmaceutical companies, contract research organizations, academic institutions, and government agencies. OpenClinica is used across a wide spectrum of clinical research, including drug, device, and diagnostic trials, global health studies involving over 2 million patients, adaptive platform trials, and clinical trials for some of the first gene therapies to be approved for market. Hundreds of small, midsize, and large research organizations leverage OpenClinica to capture better clinical data faster, and to do so in a way that meets the highest standards for security and regulatory compliance (21 CFR Part 11, Annex 11, GDPR, HIPAA).

OpenClinica, LLC is headquartered in Waltham, MA.

For more information on OpenClinica's solutions for automatic EHR to EDC data integration, electronic data capture (EDC), EHR eSource, ePRO/eCOA, randomization, and analytics and reporting – visit: **www.openclinica.com**.