TriTiCon Articles

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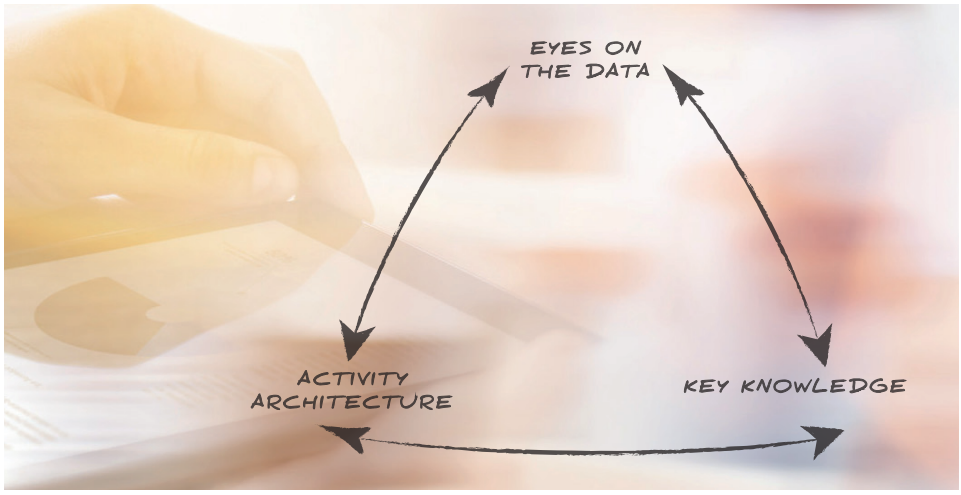

Getting Started – Strategy and Foundation

The number of systems and standards under the 'eClinical' umbrella is long and can be quite overwhelming: Think EDC, IRT, ePRO, SCE, Safety system CDISC, SDTM, eTMF, E2B and many more.

So, where do you start? In the previous article, we discussed the implementation of an eClinical framework and how important it is to make your own informed and active decisions. In this article, we will look at the overall approach, the steps you should take to make the first informed decisions, how to define a strategy and finally, how to establish the initial technical foundation.

We will start with understanding the fundamental considerations and requirements to ensure you get the right foundation: the data you need, data that is ready for future use and data that meets regulatory requirements. Subsequently, we will discuss the very first technical components and processes you need to have in place: standards and delivery definitions, secure data storage and control and oversight processes.

In the next article we will look more at "front end" systems (EDC/eCRF, ePRO, IRT, eTMF etc.), both from a sourcing and an internal implementation perspective.

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About these articles

This is the second article in TriTiCon's series on eClinical solutions and implementations.

The eClinical environment can be thought of as a process and system framework for the electronic conduct of clinical trials and the handling of clinical trial data (and documents). Although this article is written primarily for small or midsize companies who are starting to build an eClinical framework, the same approach is taken in large companies and when updating existing frameworks.

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Trials are temporary – ***data is forever***

Activity architecture first – then systems architecture

All you need is (access to) – ***a little bit of key knowledge***

Standards – ***an enabler,*** not a constraint

Keep (store) it ***safe***

Oversee – not overdo.

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Getting Started

Strategy and Focus

As for any strategy, you should start with the end in mind. What do you need to achieve? Where do you want to be (and what do you want to have achieved) in the next one, three or five years? Regardless of the timeframe, you will undoubtedly want the trial results obtained to be trustworthy, collected and handled according to regulatory expectations. You will also want the data generated to be valid, structured and documented ready for submission (or ready for due diligence from a potential buyer or partner).

To achieve these fundamental objectives, you need to focus on three essential aspects:

- Keep your eyes on the ball (data)
- Establish an overall activity architecture – who does what and where?
- Ensure (access to) key knowledge.

Combining these three simple components provides the very basis for a data handling and eClinical strategy. Once in place, the focus can move to the actual sourcing of services and selection of systems.

1: Keep your eyes on the ball: Trials are temporary – data is forever

In the early stages of starting a company or with a new product in the pipeline, the focus is primarily on trial execution: getting trials started and patients recruited. That's where most of your money and resources go and what drives the timelines. And of course, execution *is* important. However, it's important to keep in mind that trials are transient; they are temporary. It is the **accumulated data** that matters in the end. The data is the evidence revealing the value of your product and it's the data that will determine future funding, partnering or out-licensing of the product in the development stage. It is also the foundation for a future submission. From a regulatory perspective, you, as the sponsor, have a responsibility to ensure that the data is accurately recorded and reported, *even* if you fully outsource your trials.

Three crucial requirements for data handling:

1) Make sure the **trial data** is collected in a **compliant structure** and with the **required documentation**. The type of data collected is primarily driven by objectives and the protocol. However, it is also important to consider how the data will be used in the future, e.g. pooling with other trials and submission to the regulatory authorities. The advice is simple: Follow CDSIC standards from the beginning. The Clinical Data Interchange Standards Consortium (CDISC) is not only a technical data concept for data specialists, it is also a best practice and quality driver for CRF design and an expectation from the FDA for how data is submitted in the end. Ensuring that your CRF and data are CDSIC compliant from the start and that the required documentation is included, supports submission and readiness. Furthermore, it increases the value of your data for a potential buyer.

2) Ensure that the data is **collected and handled in a compliant manner** and that all involved systems are validated. It might not be innovative, interesting or the most fun part of clinical development, but it *is* a requirement. Without it, your data might be rejected and in the worst-case scenario, the entire trial deemed worthless. It is vital *not* to assume that your CRO or provider has it all in order. As a sponsor you must ensure it is and have the evidence to document this.

3) Ensure **proper storage** of both **data and documentation**. If you source your trials, ensure you get all you need back from the vendor (visit www.triticon.com/resources for a checklist on what should be submitted together with the data). Store the data in a versioned, secure and controlled (ensure no one can modify the data) manner with backed-up files, together with documentation describing the data. Data *must* be available in data-files, not only as pdf tables or as an appendix to the trial report. This might all sound very basic and obvious, but unfortunately, the essentials are frequently missing.

2: Activity, sourcing and systems architecture – in that order!

Before you even start considering systems, regardless of whether you are fully outsourcing your trials or looking to buy and implement systems yourself, you need to first understand the activity architecture, i.e. what needs to be done and by whom?

After this follows the decision regarding the best way of splitting tasks between internal resources and different external roles and providers, along with the best way of splitting tasks between systems.

These considerations will impact your sourcing model which can be very different depending on the type of product, the therapeutic area and the company stage and business strategy. The systems you do or do not need in your trials will also impact the sourcing model (more on sourcing models in upcoming articles).

As discussed in the first article in this series, there is no 'best way' for which systems to use. There are some basic categories of systems, but companies, therapeutic areas and types of sites differ. There are increasing numbers of superior systems available on the market, and systems are becoming progressively more flexible and module-based, meaning that there are several ways to 'cut the cake'.

This should not be a massive project. We're not suggesting you overcomplicate things or re-invent the wheel. But it *does* require some dedicated thought as the challenge arises to forget parts of what you thought you knew and re-think aspects to reveal new facts and understanding.

This exercise might not make a huge difference to the end result, but it will likely reduce the list of systems you thought you needed by half, and furthermore the list of what the vendor recommends you need the systems to do, by another half. This will result in saving substantial amounts of time and money along with decreasing the risk involved. It might also significantly reduce site burden (as well as CRA and other trial users' burden) by decreasing the number of systems they need to use, or by reducing the number of jumps between systems, thus eliminating redundancy.

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3: (Access to) Key knowledge

The third component is the key knowledge you need – as a sponsor – to ensure that the data handling, sourcing and systems (discussed above) are accurately chosen and managed. If you have a full in-house organization, you should already have this readily available. However, as regulatory and business requirements are changing, technology develops and so too do trial design and medical science. What worked yesterday or at another company might not work in your current situation, there may be new opportunities for doing something different and better.

Even if you are sourcing the whole trial to vendors (a full service or a multitude of different providers), you still need to ensure you have the key knowledge "on your side" to manage the sourcing. You need to select the right vendors, scope the work, define workorders, negotiate prizing, make pivotal decisions and check deliverables. There are regulatory requirements for oversight of your providers, and from a business perspective, there is money and time to save plus issues to avoid.

Building the foundation

In the first steps towards an eClinical environment, you don't need to start with buying and implementing a lot of expensive and complex technology. In fact, none at all. What you need is a simple foundation for standards management, data storage and oversight. It is perfectly fine to start with a very simple version of things but is critical to get the major components correct from the start.

Standards management: Define standards for your data deliveries

There are specific tools available for managing CRFs and data standards, but in the beginning Word and/or Excel will do just fine. Standards are important for much more than data structure including areas like documentation, outputs (Tables, Listings and figures) and not least, standards for which data you want to collect. This includes things such as TA specific or industry standards (Cancers AE grading, which instruments you want to use for HEOR etc.). You can find an overview of standard areas here: www.triticon.com/resources.

The important thing is to actively define what data you want and write it down. Not every single detail is required from the beginning, but it is vital to start with the key elements such as the type of compound, the indication and the endpoints/clinical development plan. Of course, you might want to use a provider or choose other advisory input, but at the end of the day, you, as the sponsor, are closest to your development program and thereby have the greatest understanding of what you need.

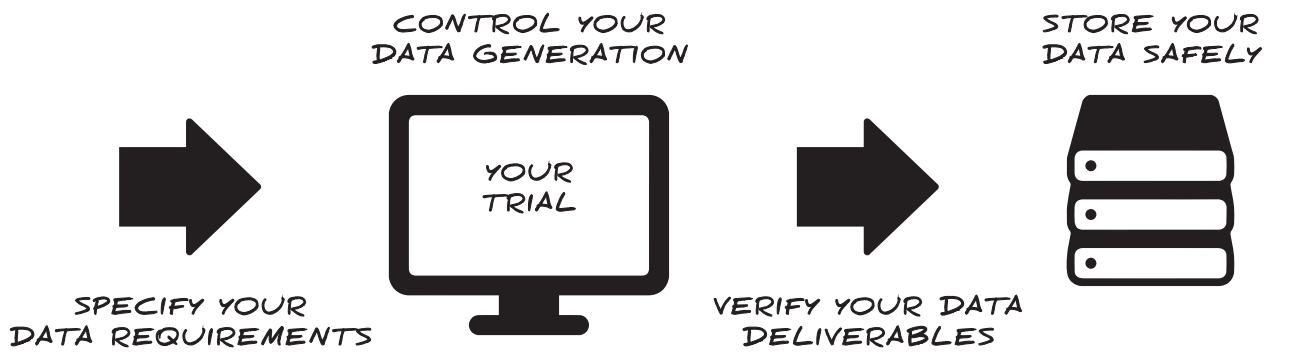
Start with statements and references and gradually enrich these with details such as specific variables or classifications. When the level of detail grows, lists can be formatted as tables and moved to excel. In the long run, you can potentially consider using a dedicated tool for managing your standards.

A very useful tool here is a standards compliance checker: a program that checks data against formal CDISC rules for structure and content of actual delivered data-sets (which is also what the FDA does if you send them data and is most likely one of the first things a potential buyer would do in a due diligence). You can get this in-house (probably the smallest, cheapest and easiest tool you will ever get, though a bit on the technical side), or if you source your trial, simply request that your vendor runs the checks and addresses any issues found. Small solution: big value.

Data Storage

Even more critical, and slightly more complicated, is the controlled storage of your data and associated documentation. There are some truly advanced systems on the market for data storage (and for managing statistical processing of the data). These are true heavyweight systems to buy and implement, and the solutions on the market all come with their challenges. We will discuss these further in upcoming articles, but as long as you are storing data, you can (luckily) get a very long way with a basic file-server, as long as you (by process and basic technology) ensure the following:

- Security: For external threats and hardware failure (with back-up and disaster recovery capabilities).
- Access control: Access must be controlled with documentation on who has had access to data over time, including proof that no one has modified any of the data.



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- Version control/traceability/reproducibility: There must be a clear 'line of sight' from statements in reports and submission back to data and programs so that results can be reproduced, i.e. you cannot overwrite data, and you must document who took which program and applied it to which data to produce a certain output or result.
- GxP compliant provider: with defined working procedures (Quality Management System/SOPs) that can handle and allow audits and inspections.

In a nutshell, if you don't have in-house IT capabilities, your best bet is to source your storage to a CRO or GxP established IT partner/provider who can support you with the above requirements. There are various online providers implementing storage services at practically no cost. Technically most of these are safe and stable, but it can be difficult to get documentation of their procedures and details about audits/inspections that have been carried out.

Sponsor control and oversight

So now you have your data, it is CDISC compliant and safely stored. Unfortunately, it does not end there.

You must also have evidence that it was collected and handled correctly. There are very strict regulatory requirements for systems validation, risk management and oversight when it comes to the collection and handling of the clinical data. Therefore, you must have the following two activities in place:

- Audit (preferably before selection) documenting that you have ensured quality processes and compliance for data and systems handling.
- Oversight of the ongoing trial execution documented activities to ensure quality and compliance by your vendors.

Even if you fully outsource your trials, you as the sponsor, still have full responsibility of the clinical trial. If you run the trial in-house, the tasks and processes are still the same, but the "label" is changed to internal quality assurance work. As usual, if it is not documented, it didn't happen.

As for standards, this is not (yet) about systems: it is about getting the fundamental requirements and needs right, guided by a small number of precisely developed processes and documents.

Summary

It would be understandable if these questions and decisions about systems and data, technology vendors and data structure felt a little like 'technical detail overload'. Fair enough! Data standards and system validation will definitely not revolutionize the way you develop your product, and are mistakenly often associated with larger trials, or for use later in a trial. They are however critical, since mishandling of the data may not only result in a decrease in the value of your product to a potential buyer or partner, though may also result in incompliance and possible rejection of your data by the authorities.

Managing your data in the right way doesn't have to be a huge exercise or investment. It is simply about starting with the basics, getting your focus and strategy right and having the understanding and knowledge to source or implement the right services and systems. Since regulatory focus and expectations are increasing, it is important to remember that even if you source, you must have control and ensure oversight and validation.

There are three components you need to have in-house: 1) standards management – know what you need; specify what you want; verify that you have got it, 2) store the data in a safe and controlled way, and 3) ensure validation and compliance in how 1) and 2) are being done. Using a file server with programs such as Excel and Word together with small toolkits and processes, will enable you to reach the first step and set the foundation for more comprehensive system implementations.

In the next eClinical article, we will look more concretely at systems such as eCRF/EDC, ePRO and IRT amongst others, and discuss different models for sourcing both services and systems.

About TriTiCon

TriTiCon provides expert consultancy for Clinical Data Processes and Systems. When establishing solutions for the handling of clinical data, TriTiCon will help you all the way from initiating the process to end-user training.

TriTiCon combines the 3 Tiers of Subject Matter Expertise, Strategic Understanding and Project Management to fit the needs of each specific situation or stage of a project.

TriTiCon is not a CRO but can help you manage your clinical trial set-up and execution, and can support you with everything from vendor selection and contracting, through set-up, operations and oversight.

Author: Anders Martin

Editor: Emily Jensen

It is not rocket science! It is simply about ensuring all the details are in place.

5 essentials for handling your data:

1. Follow CDISC and other industry standards from the start for CRF design as well as for data and documentation. It is not only a regulatory expectation, but also a best practice and quality driver.
2. Ensure compliant data handling (from a regulatory perspective, but also consider data privacy and other legislations).
3. Data is needed as data – i.e. in data files, not as pdf or tables & listings.
4. Data is not enough – the associated documentation and analysis programs are also required.
5. Keep your data safe – store it in a controlled environment with documented and traceable access control, back-up and adequate security.

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