Selecting EDC Systems and Services: From theory to practice

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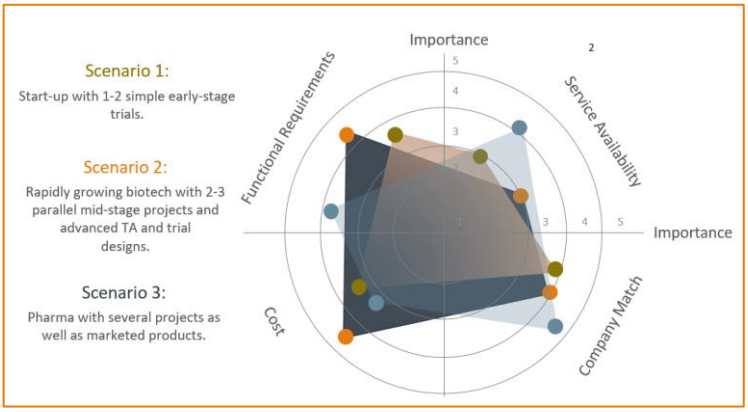

About TriTiCon

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.

Introduction & Recap

How do I select an EDC system? Should I select and own an EDC system in the first place? How do I source EDC system services? Where is the EDC market going?

In the first three articles in this series, we worked our way from looking at the very start of managing eClinical systems - mindset and approach (article 1) through to strategy and fundamentals (article 2). We have argued for why you need to start with your own company's current situation as a foundation, we advised on strategic focus on your data, and we suggested starting with the three fundamental elements of (compliance with) standards, proper data storage and oversight – all supported by (access to) key knowledge.

In article 3, we discussed system decisions and selection methodology. In this article we apply what we have learned to what potentially is the most central of the eClinical Systems – EDC . When and why (or not) you should own (control) the EDC system used in your trials, which key (macro) criteria you should you consider, and finally, what the service models and system market look like. We also give our "2 cent" prediction for how this market will develop in 2020 and beyond.

Own or Source EDC?

The benefits of ownership

The EDC system sits at the very core of trial execution and spans a multitude of processes. It is used by several different functional roles and is most likely the system where the highest number of man-hours are put in during your trial. Configuring the system to optimize how it supports the processes will have a considerable positive impact and can significantly reduce workloads for site and CRAs, amongst others. Furthermore, the trial-by-trial set up is a central component and the efficiencies and quality gains from using a good standards-library are substantial. These benefits accelerate with complex therapeutic areas, trial designs and trial-settings.

Another advantage from owning your EDC is that you can choose to have different vendors providing different services, such as study build. The value of this is that all vendors and trials will be using your library, shortening timelines and driving cross-trial consistency and quality.

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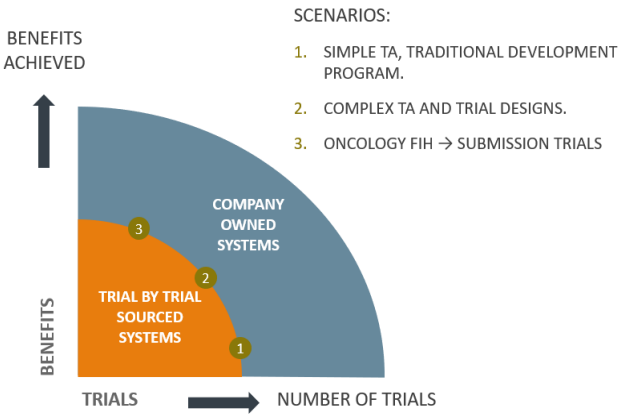

Figure 1:
Breaking point for moving to owned EDC for different types of companies and TAs

> ***Note:***
>
> *If your strategy is to fully outsource, trial-by-trial, it will of course limit the above-mentioned advantages and process optimization benefits and you will be looking to use the (different) CROs' processes and systems. At the same time, you will likely experience increased trial-by-trial differences and different ways of operating. As always, it is about identifying what is most important in your own situation and understanding as well as managing the downsides of your choices.*

The number of trials

Given the potentially significant benefits, ownership should be considered quite early.

If you only have a few small trials (phase I), you can easily live with cross-trial inconsistencies and there are limited efficiencies to gain. These trials are normally quite simple, limited in volume (man hours) and "stand-alone" in your submission. But quite soon the advantages gained from having a library (for CRF pages, checks, reports, data extracts/integration components), process optimization (users-roles, status-levels,) and "one way" of working, starts to pay off. In most cases the tipping-point is somewhere around 2-3 parallel trials (which are in phase II) or alternatively when several projects have been started at the same time.

However, if you are working in more complex fields, for example with adaptive first-in-human trials being converted to full efficacy-trials (something we see more and more in oncology and some rare diseases), you might reach the benefit tipping-point for ownership (or at least full control and an active choice of the system your CRO is using) already from trial one.

> ***Note:***
>
> *There is high regulatory focus on ensuring that systems are kept in a validated state. In recent years, it is my experience that this focus has shifted from system functionality and front-end validation to areas like hosting security, back-up processes and systems development processes. As a sponsor you must ensure these things are in place, even if you fully source to a CRO who in-turn sources the system from a provider.*

EDC benefits typically accelerate when you reach 2-3 parallel trials

The burden of ownership

Managing an EDC system is a substantial undertaking. You need special expertise, processes and man-hours to manage validation, upgrades, hosting, configuration, libraries and for trial-build. It is therefore not surprising that most companies choose to source both hosting and management of the system, in a model where the system vendor hosts and the vendor or a CRO manages the installations and builds the trials. Ownership does not mean that you have to change this model: you can (and in most cases should) source *both* of these services.

But ownership, does require a certain level of knowledge, procedures and resources, i.e., it *does* come with a degree of internal overhead. *However*, if you source trial-by-trial, you still need a similar set of competences for qualification and oversight for each trial (or for each provider). Therefore, it is the same type of competences, similar processes and the same level of resources that is required – and it is required in both cases (in both cases you can insource this expertise).

As a result, the overall burden for you as a sponsor is very much the same, whether you own or whether you source trial-by-trial.

The burden of ownership is not necessarily higher than the burden of qualification and oversight

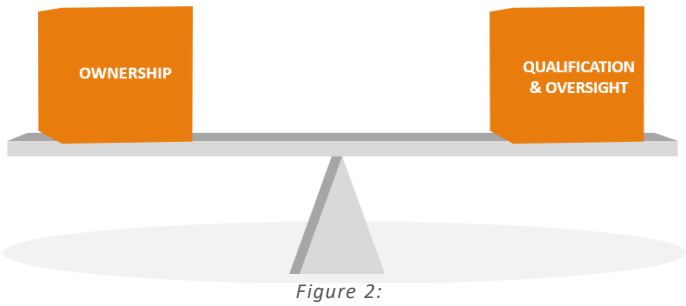

Figure 2:
The burden of ownership vs. the burden of qualification and oversight for EDC systems

Costs (and contractual conditions)

The simple answer: You save money by owning. If you choose to use the same system on a set of trials, you will most likely get a much better deal with a company agreement directly with the provider compared to choosing trial-by-trial licensing as a pass through from your CRO. The savings in direct license cost can be significant (we typically see 10-30% savings) and contractual conditions and flexibility can also be highly beneficial (and result in additional savings).

5 benefits to owning an EDC system:

1. Leverage standards to drive quality, cross-trial consistency, decrease trial set-up timelines and resource consumptions.
2. Configure systems to optimize process support and quality: process support will drive quality and efficiency.
3. Establish more interchanges of data such as meta-data to drive the status, metrics and oversight, safety-system integrations etc.
4. Independency from your CRO: If you own your platform you can change CRO or have different CROs working on your platform. You can use the same standards and configurations but have flexibility when choosing a service provider, thereby optimizing pricing, TA expertise, choosing to bundle with clinical services etc.).
5. Get a better deal: Better process and contract conditions on a company contract when compared to a trial-by-trial contact (via a CRO).

5 situations when you might not want to own your own EDC system:

1. Your company is currently only executing a "single-trial", i.e., there will be no cross-trial consistency or scaling benefits.
2. You have a "trial-by-trial" sourcing and execution strategy, i.e., there is no obvious case for cross-trial systems or processes.
3. You have a full-service sourcing strategy, i.e., you drive the required benefits, costs and negotiations etc. through vendor management and oversight.
4. You run simple and independent trials, i.e., the benefits do not outweigh the burden of ownership.
5. You do not have access to the required capabilities (resources, knowledge), i.e., you cannot "invest" in the ownership to achieve these benefits.

System or service?

For EDC it is mostly a combination. As discussed above, managing your EDC system is one thing, but owning an EDC also comes with a substantial trial delivery activity: **Trial build** (CRFs with logics and checks, reports, possibly integrations and other more advanced components).

How you source is very much a strategic decision (but with high impact on which type of system and category of service provider you will be looking for), so let us look at five main sourcing models (see Table 1).

Regardless of which model you choose you need to select a combination of services and systems as a combined decision. In other words, the combination of the two must be included in your macro-criteria.

Full-service outsourcing	Use a full service CRO: They use *their* EDC system, configured to match *their* processes. Easy and straight forward! But - you are limiting the potential benefits from using different CROs systems. Remember you still have a validation and compliance qualification/oversight responsibility (as a sponsor) for how the system is developed, hosted and managed. Here the system and service capabilities become part of the CRO selection criteria.
EDC System and trial build sourcing	Source EDC and trial build to one or more preferred providers. You can look for a more specialised EDC and trial build vendor, using the system you prefer. You can influence configuration and leverage standards to a certain degree, but not fully. In this model, you are combining several vendors in different ways on different trials and will most likely need to look for a "common way" and a "common system,". This will drive you towards widely used system(s).
EDC Provider as Vendor	The EDC provider manages the system and builds your trial. You can choose between more systems and the same solution for all trials but are dependent on the vendor having the resources and expertise you need. Furthermore, the Clinical CROs might not be used to the system you have chosen, and their process will not be "mapped" to the way the system works, therefore you get some overhead or inefficiencies from this gap.
FSP-Model	A vendor is "your department" for EDC System management and trial delivery (and most often also data management). You own and are more involved in design and libraries but have a vendor as system experts and managers for actually building standards, technical components and the trial itself. In this scenario, the *service availability* becomes a key part of your system selection. This will drive you towards widely used system(s).
Full-in house	You manage the system yourself, build the trials and are not dependent on trial-level services. (Note: You can of course use the system providers professional services /support).

Table 1: Main sourcing models

Selection

EDC Macro criteria - What is important for you?

So, what should you choose? Medidata as everyone else? Or Veeva who seem to be the new black in clinical trials? Well, if you read article 1, you know the answer – it depends!

The system undoubtedly needs to do what *you* need it to do, and an EDC system does *a lot*. You can easily list hundreds of detailed technical requirements on what the system should do, then compare and score different systems ability to meet them.

But to be honest, data management, including EDC, is a commodity. There may be key functionalities that are critical for you, but equally important and more differentiating are other key considerations such as company match, TA specific knowledge, service availability, the development state of the system and how established the CRO and sites are (see Figure 3 for an example of criteria categories).

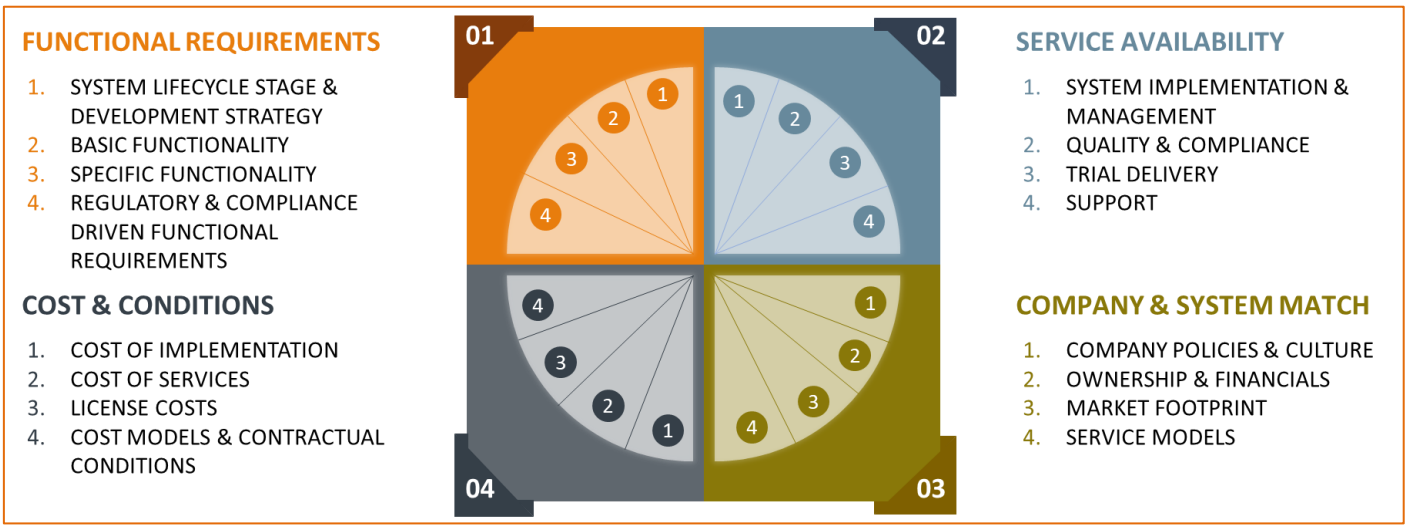

Figure 3: Example of EDC system and service requirement categories

So, the first step is to identify your key requirements and "must haves" driven by matching your company, strategy, pipeline and people on a macro level. There is no use in buying the perfect system that can do everything you need it to do, then realizing you can't actually buy the services you need to make it run (for example study build).

For all systems it is important to consider the entire user-community when looking at defining what is most important. As we have discussed, EDC systems are used by a multitude of roles and CRAs together with site users probably represent more than 90% of the usage of the whole system.

The result is – again – your own, but let's outline some typical (simplified) examples (Figure 4).

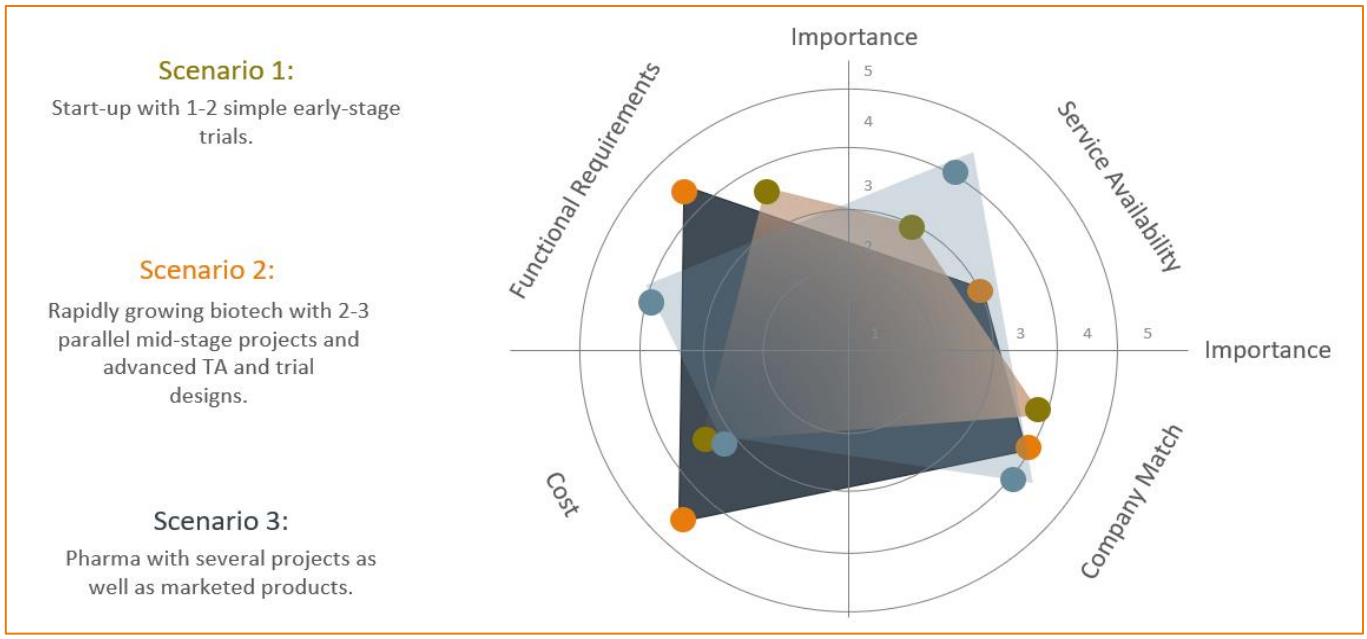

Figure 4 – Macro criteria examples

Market Overview - EDC system categories

Once you know your macro-criteria, it's time to map them to system types and service options. Let's look at an overview of the EDC system market split in five main categories (read about additional considerations for each system category at TriTiCon.com/Resources).

Category 1. **The Big One(s)**	This segment is characterized by having a wide set of modules to cover more than EDC plus advanced configurations and functionalities to adapt to client process requirements and specific trial requirements. This part of the market has been dominated by Medidata (Rave) and Oracle (Inform) for more than a decade. These systems thereby do not only now have the "largest" span of functionality and configurability but they also have the largest share on the market and the largest footprint when it comes to qualified service providers, site and CRO experience etc. With Oracle falling behind, Medidata currently is the one dominating player in this category (and the entire market).
Category 2. **The Mid-Tier Ones**	The mid-tier (in terms of functionality depth and module-span) for example OmniComm (Anju), BioClinica, DATATRAK and xClinica, have really struggled to break-through onto the market and challenge the giants. Their primary clients are CROs who need a cheaper, lighter alternative to Medidata, but who need more than the "small ones" can deliver.
Category 3. **The Small Ones**	This is a growing segment of basic, but very capable, EDC systems, focused on eCRF (and ePRO). Some of these providers have started adding more modules to their products, but most of them are primarily focusing on EDC with the strategy "Doing it one way - but doing it good." With the development of back-end technology, it is easier than ever to develop neat and nice systems and user interfaces – and to update your software with additional features and enhancements. Therefore, these systems often feel modern and are simple and intuitive for the end user. This category is by far the largest in terms of the number of providers and include providers like Medrio, Viedoc, ClinicalInk, TrialOnLine, Castor, Encapsia , just to mention a few. Although many of these providers are growing, successful and stable, each one has quite a limited market-share. In this category I also place the proprietary home-developed systems many CROs have offer as an alternative.
Category 4. **The Core + Custom Ones**	This segment includes a quite low number of providers, who have a core system and then works with additional custom components that can be developed or "tweaked" for you a as client or even for a specific trial. Often these providers work as "your own development department" and are able both to custom fit the individual trial that extra little bit, for example developing additional modules the way you want them. TargetHealth and Replior are examples in this category.
Category 5. **Open Source**	Open-source systems such as OpenClinica (open-source version) and RedCap are similar to the category 4 (Core + Custom) in that they also have a core and a number of customizable components. The different being that these are developed by an open community and not a specific provider. Open-source systems have had limited use in GxP clinical development due to validation considerations. However, open-source is not the same as uncontrolled. You can control and validate an opensource system as well. The most widely used opensource systems – OpenClinica and RedCap - have been used in thousands of trials.

Differentiating areas

Functionality

All the systems can do the basic data entry forms, checks and query handling. Areas where we start seeing a difference is in **complex set-ups** which have a lot of dynamics and dependencies, advanced checks, differences in status levels and more dynamic data review rules. Here we start seeing a difference between category 1, 2 and 3. Category 4 can do more or less all you need it to do, as the provider develops or modifies per your requests, but it comes with an overhead on your side and additional cost.

Additional functions: For example, ePRO (see next article), SAE handling, protocol deviation handling, scans and imaging. Here we typically see more "yes or no": the system either has it or it doesn't. This can be a helpful and easy way of filtering out options based on what you truly need (again, using your macro-criteria). If you are truly looking to get it "your own way", you are down to category 4: the core + custom, where you have the provider build in the tweaks you need.

Burden of ownership

As a rule of thumb, the smaller the provider, the greater the responsibility on you to ensure all aspects of compliance and validation are in order, meaning that category 1 has the lowest burden and category 4 and 5 the highest. However, as category 1 is more advanced, the system management burden is heavier for these systems, and if you only need a basic system, you can save this effort.

Services

The more they are used (larger footprint), the better the serviced availability. Generally, the system providers want to develop and provide systems, not build trials (even if they a professional services group, this is their main focus in most cases). So, if you are dependent on services (a certain level of capacity being available, global coverage, specific TA expertise etc.,) this will drive you towards the large footprint systems available in category 1 and 2.

Cost

The most expensive systems (type 1) differ approximately by a factor of 10 when compared to the cheapest (type 3). Type 2 and 4 are somewhere in between, with type 4 having a higher "moving" part, depending on what you need to have developed for you.

Selection scenarios

The start-up

A full-service, small or mid-size CRO, using a smaller and cheaper category 2 or 3 system. Preferably with proven experience in the specific TA and with submission ready data deliverables. Ensuring that system validation and hosting are fulfilling requirements need to be part of selection and qualification, and delivery of complete and submission-(and thereby due diligence) ready data deliverables are recommended to be included in the scope of services. Thereby you are keeping costs-down, minimizing the use of internal resources and have a single accountable provider.

The growing biotech

A mid-size FSP provider using an "owned" big or possibly mid-size (category 1 or 2) system for ensuring capacity, cross trial consistency and efficiencies, combined with the required functionality. Further advantages are the service provider flexibility and that clinical users at CROs and users at sites are familiar with these systems.

On the downside are costs, but the FSP model and your own system-contract will allow for negotiation of costs and conditions for both systems and services, as well as efficiency gains from standards and cross-trial re-use which will decrease cost over time.

The established pharma

A full-service CRO is an option, but the EDC is self-owned. Alternatively, internal trial build and system management, but the trend is towards outsourcing as for many other areas. The EDC System has a large footprint, i.e., category 1 or possibly 2. Based on volume (more trials, more money spent) your influence increases with regards to both (larger) full service CROs and the system provider, and the mutual benefits of aligned processes, organizations and system - set-ups increase.

You still need to keep an eye on consistency across trials, ensure you get efficiency gains from re-use and standards, and not least ensure TA-specific knowledge and the stability of team at the CRO (and knowledge sharing) across trials. Alternatively, choose an FPS provider to drive up the match to your organization and processes, TA and system expertise.

Looking forward: my 2 cents for 2021: Clash of the titans

When it comes to the EDC system market, I think 2021 will see the real (at least start of) clash of the titans. Not between Medidata and Oracle, as Oracle is not only struggling but also seems to be losing interest, but between Medidata and Veeva. Compared to other EDC competitors in the small and mid-size category who are primarily EDC and data capture companies and are trying to grow from there, Veeva comes from an enormous success on the document-based systems (not only in clinical development) and CTMS space. They are coming from another angle with more or less exploding access to the clients, a brand-new core platform and money to spend. From their success, Veeva are in a unique position to break Medidata's dominance in this segment and establish themselves as a key player in the EDC space.

However, even if basic EDC is becoming a commodity, you don't build a full suite of EDC and EDC-related modules overnight. In my view, the main constraint for Veeva, service providers, system experts, CROs will limit the possible pace of take-up. You can scale system hosting in hours and you can develop with features in weeks, but you don't get service providers and knowledge spread at the same pace. Medidata on the other hand has this enormous footprint, you can always get the services and the knowledge, and the Medidata-suite can "do it all" (well, some things better than other things). I think the biggest challenge for Medidata is that the back-bone is becoming old, and it gets increasingly difficult to keep the development pace.

Inevitably people will sooner or later want to try something new (also in our business). Of course, Medidata is trying to mitigate this by transitioning architecture and developing new front ends, and they are doing a pretty good job with it. The question is if it will be enough.

One key thing that Medidata has, and that Veeva can hardly get in the short term, is data. As we know, for good and for bad, data is knowledge, data is power and data is very, very valuable. So, the non-system factor, how much can Medidata package systems with data-driven value and thereby "boost" their offering (or even turn it upside down) will be a key factor for the outcome. What about the others? Well, I think mid-size (category 2) will continue to be limited to the (primarily mid-size) CRO market.

They will trade market shares a bit and some of this share will probably go to Veeva, but I don't think we will see any big changes.

The small size (category 3) will continue to be better for the right things and will probably eat a bit of the share from larger providers (although the overall market will continue to grow). I do think we will see more flexible offerings from mid-size and large CROs for start-ups and smaller companies, as well as for FSP providers, some of it based on smaller and cheaper systems.

A challenge here is increased regulatory focus, and the small providers must ensure they have system development and hosting in order.

Summary

EDC is maybe not the most difficult, but probably the most comprehensive clinical system selection you will make. The system spans many processes and user-groups of which must be considered, as well as the market-landscape and the link to sourcing strategy and service availability. All of this in addition to technical requirements, both for functionality, hosting and security.

Collection of clinical trial data is a transient activity (see articles 1 and 3), but EDC system selection will have a long-term impact due to the associated establishment of processes, standards, services and knowledge.

It is important to remember that if needs be, you can change the system. If your standards and storage are in order, there is no data or submission driven requirements tying you to the same EDC system through your company development or development program (remember that trials are temporary, data is forever). Things change, you change and so do service providers and system options.

If you find you need to change system and/or service provider, there will be a process effort and most likely a cost, but "technically" there are no major issues (between trials that is; changing EDC in an ongoing trial is a whole other discussion - please contact us if you want to discuss this, case specific).

Remember to consider macro criteria that are specific for you. Are you going to source? Can you get the service you need? How complex are your trials and processes? Can the systems in play support your needs? How much is cost a factor? Macro-criteria will quite efficiently guide both key decisions such as whether to own or not and which sourcing model you will use, as well getting you well on the way to selecting the system that is right for you.

A final tip: Don't forget your sponsor obligation of ensuring compliance of system related aspects, even if you source and buy hosted solutions. You don't need to repeat the work, but you must ensure things are in order. Do it (and document it) once -at decision and selection – and this will save you from bad surprises, retrofit or repeating at each trial (or scrambling for an inspection or due diligence).

Next Article

In the next article we will continue our journey through the system landscape and look at ePRO/ eCOA systems and services. Although EDC and eCOA have many commonalities and from some aspects are equivalent, they also have some very fundamental differences.

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