

Review Article

Benefits of integrated clinical trials systems in risk based monitoring

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ABSTRACT

In the global world of integrated system, most industry recognized system integration is critical for optimal use to generate globally acceptable data, even clinical research industry is going through a paradigm shift from use of traditional system to integrated system to enhance the data availability on real time and supplements faster review and reporting of critical data points. But altogether to achieve 100% system integration, we need to create all compatible system with each other which require less mapping of different databases with reduced low data migration time.

Keywords: Data integration, Risk based monitoring, Clinical trials, Data integration, Clinical trial systems, CTMS, Leaner integration, Cross functional integration, Data quality, Data coding, Issue management, Risk management, Trends, Patterns, Clinical site, Adaptive design

INTRODUCTION

In the past, information technology served a mere support help for medical and pharma companies. Many pharma companies now acknowledge that well defined IT system approach is a critical phase of managing and gaining competitive advantage. The current economic crisis lead pharmaceutical companies to cut the R&D cost and increases the use of innovative IT system is the need of the hour in clinical development phase. Managing and planning of drug development through its life cycle employ huge use of information technology. How the different services providers integrate the system seamlessly to achieve efficiency is depends on the ability to use the best in class IT solution available in the industry like; middleware hub, cloud architect and wide range of mobile applications. Many clinical trial systems have greater up-front cost as compare to existing systems, particularly when migration and transition costs such as training. However many system have enormous possibilities to accelerate and streamline the clinical trial process with keeping cost in mind.^{1,2}

Today's systems are progressively focusing on new wellsprings of data from patients, perceiving the uniqueness of individual subjects and creating enormous amounts of information. As of right now, the clinical trials tool stash has developed so broadly that the examination group is no more restricted by the devices themselves — we are constrained rather by our capacity to join, convey and deal with these mind boggling apparatuses in ways that empower us to drive advancement.

Surely, the drive to advance has incited scientists and controllers to investigate novel and more confounded approaches to examine promising new items, yielding trial plans that are quicker, more adaptable and more focused on. In numerous regards, the fate of clinical exploration lies in the fruitful culmination of these complex clinical trials, a large number of which require the concurrent advancement of novel mixes, including drug/biologic, drug/analytic, drug/gadget, and so forth.³

Currently in clinical research industry data migration and integration of drug trail is happening in two methods.

Leaner integration

The traditional way of data migration, in which cross trial and program is difficult to achieve. It increases the IT dependency for mapping, cleaning and validating. In Leaner method, data from trial work is silos and do not interact with different studies in same program as well as other therapeutic area for same molecule.

Cross functional integration

It cross functional method, system are integrated in such way that data is available on real time basis from multiple system for better analysis and reporting across trials from same program.

Changing environment

Visualization and data integration goes hand in hand

Today's mind boggling clinical trials yield information sets that are unbelievably substantial and complex. Accordingly, the procedure of changing trial information into usable learning essentially can't be refined utilizing customary presentation techniques, for example, traditional diagrams and charts. Rather, inquire about associations are starting to shrewdly apply information combination and visual examination instruments in ways that empower analysts to both investigate and interface with total information. What results is another level of revelation with inside and out knowledge that would never have been accomplished through a conventional audit of the crude information.^{4,5}

Wielding these propelled devices and rendering information in this extended limit are difficulties requiring the organization of settled visual examination speculations, advanced programming and a capable pool of developers. Yet notwithstanding the difficulties, when legitimately connected, these information combination and visual examination instruments convey genuine potential to developing ideas that would somehow or another be consigned to "wish for" status:

- Adaptive trial design
- Immediate data transfer to safety monitoring committees
- Near real-time dose adjustments
- Risk-based monitoring

To show a portion of the particular routes in which information joining and representation are changing the clinical trials scene, we should pause a minute to unload one: hazard based observing.

Risk is an unavoidable part of living and working in a dynamic culture, yet hazard can be lessened by distinguishing and mediating at focuses with the best probability of disappointment. For instance, crossing an occupied city road can be dangerous, yet by executing

proper security measures — activity lights, person on foot lights, walkways — the dangers are moderated. The likelihood of being hit by an auto is lessened when systems are legitimately.⁶⁻⁸

Likewise, the challenge in clinical trials also lies in associating a risk factor to the most likely failure points, establishing procedures to reduce risk at those points and monitoring closely. This process is known as risk-based monitoring (RBM). RBM is the study of identifying and mitigating the points where a trial and its subjects are at greatest risk for harm through data negligence, lack of education or incorrect conclusions.

Enabled by advanced data integration and visualization techniques, RBM improves real-time (not just retrospective) visibility of a continuous flow of data by automating centralized data collection and connecting the personnel analyzing it, helping them make informed and impartial decisions.

RBM takes its underpinnings largely from signal detection theory, which describes the ability to discern between real information-bearing patterns (signal) and random patterns that distract from the information (noise). By employing concepts of signal detection, we can create monitoring protocols better designed to detect anomalies effectively and quickly.⁹

Risk can be reduced by monitoring sites for subject visit information and verifying the transcription process of source data being dutifully entered into an electronic data capture (EDC) system. However, is that where one should look for risk? Can the opportunity for uncovering data entry error or EDC entry field interpretation truly drive the reduction of risk for study results, or is it a review of the source data itself?

Studies have shown — and an experienced monitor will confirm — that the risk lies at the source of the information.

RBM allows earlier action to be taken for operational study conduct and provides awareness of the potential for in-study subject risk, enabling corrective action to be taken sooner. The opportunity for analysis of near real-time data analysis becomes a value-based objective.

As a result of focusing on areas of risk, areas of non-risk receive lower-level scrutiny in the study monitoring process, bringing efficiencies and cost reductions. Source document verification to the EDC entry system becomes less important as predictive analytics drive determination of risk.

Implementing RBM can be challenging, but many research sponsors have forged a path to success by following these steps;

- Design operational processes and data flow for monitoring, data collection and review services.
- Identify areas of greatest scientific risk based on historic error rates, and develop metrics to quantify the potential risks.
- Build predictive and adaptive statistical knowledge for running trials.
- Categorize and assign roles for staff, including written operational instructions.
- Assign appropriate response-time guidelines based on the potential damage that could result with failure at each risk point.
- Create decision trees for responses based on failure events.
- Map data relationships between operational and clinical data for a project.

With proper oversight, RBM offers numerous benefits. Electronic health records data can be mapped into EDC systems, thereby automatically populating integrated systems. RBM also offers the benefit of integrating new data streams into familiar reports, whereby the process of visualizing and understanding the information is much simpler. What's more, when RBM-created data is presented via visual analytics, decision makers have the ability to see data relationships in new and intuitive ways. Finally, RBM can usually be integrated into existing technologies; there is rarely a need to start from scratch.¹¹⁻¹³

Yet for all its promise, RBM is saddled with several misconceptions and challenges. The largest misconception is that RBM is a cost reduction process. While cost reduction is an expected secondary result of proper implementation of RBM, the primary benefit is quality. In addition, RBM is based on big data, and big data takes big brainpower; deploying the right technologies and techniques requires serious expertise and sustained effort. Finally, RBM presents a multitude of HIPAA challenges that can't be overlooked.

In the end, the promise of RBM will only be realized when it is appropriately customized. Indeed, all of the advancements supported by augmented data integration and visual analytics tools require effective customization. Since a one-size-fits-all approach isn't feasible, sponsors may benefit by partnering with an experienced CRO as they work to design a robust data integration and visualization strategy.^{14,15}

Benefits and challenges of integrated clinical trial system

Benefits

- **Time:** Early data migration from parent system to data ware house will reduced analysis timeline and make analytics work on near real time basis. It will also help in identifying trend and observation across

site, country and trials in similar program. Since data is cleaned and on a regular basis, it will boost faster regulatory submission and gaining competitive age for marketing.

- **Quality:** Early detection of issue in data related to conduct of clinical trial will help industry to work on robust quality frame work for ongoing as well as for future projects.
- **Real time risk and issue management:** Integrated system will resolve issue of identification of risk and its mitigation from retrospective to prospective basis. It will also move industry to take more preventive action rather working on corrective as well as preventive actions.
- **Clinical sites/ data analytics trending:** Quick data availability will help in getting real time trend & observation on site performance and it impact on patient safety and efficacy.
- **Single platform interface:** Since all the data will be pulled in single platform, it will be easy to access and manage data from multiple sources. It will reduced dependency on multiple user access to different system and comparative review and analysis will be easy.
- **Implementing of risk based monitoring:** Since RBM is the next paradigm Shift in industry, hence faster availability of data will make RBM more robust to implement on real time basis.

Challenges

- **Cost:** Frequent data migration will impact on the cost for companies, it will also increase resources requirement to keep pulse check on the smoother data load and cleaning for small data sets.
- **Incomplete data:** In complete data from vendor/site will hamper the real time data integration and analysis, which in result delay the risk identification and its mitigation.
- **Data quality:** Poor quality data will take more time in cleaning and standardizing activities and it will increases analysis as well as submission timeline.
- **Data coding:** Since all the system are not following uniform standard codes, it will be laborious and cost consuming task for different vendors to adapted common business rules.

It a high time for industry to device a process aligned with FDA RBM requirement guideline to successfully implement RBM on organizational level.¹⁰

CONCLUSION

The eventual fate of clinical trial advancements, Productive clinical information joining, accomplished through a middleware center point course of action will pick up in infiltration. Items which can promptly incorporate with trial supports systems will progressively be sought after. As information incorporation turns out to

be more practical, trial supports progressively look for "best in class" items, driving them to get a scope of suppliers. This will expand the requirement for profoundly interoperable answers for risk based checking. In parallel, patients, site staff and trial managers will get to trial programming utilizing an extensive variety of channels and gadgets for smooth behavior of clinical trials.

Risk based monitoring methodology will only be successful, if we utilize and analyze data on real time basis with efficient manner to report and take action on trends and observation. It will also provide holistic view on trial progress in compression with other trials within the organization to plant future course of action. Subsequently, the present day innovation stands regarded for delivering such an instrument which is helping the clinical trial and Pharmaceutical industry for proficient Clinical trials information administration, blunder free investigation of clinical trials, decrease of dullness and bulky work, in this way meeting the difficulties and prerequisites of quickly developing Clinical research and pharmaceutical industry.

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