Clean Clinical Research

RBM as Competitive Advantage for Mid-sized CROs

Cyntegrity's White Paper

Applying RBM analytics to improve patient safety and preventive care

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Introduction

"Risk varies inversely with knowledge."
Irvin Fischer

Recent research shows, the size of sponsors correlates with the size of service providers. Big Pharma relies on the large, full-service CROs if they are running a large clinical trial [Janice Hutt, 2012]. As the outsourcing world has always moved in cycles, today, there is a chance to change the situation. Mid-sized CROs can demonstrate to sponsors their experience and provide an evidence-based proof of expertise, needed to win a bigger project, e.g., multinational phase III trial.

The life of mid-sized CROs is full of highs and lows. The marketplace is not the only area where there is competition. CROs are currently fighting for investigators, for high-quality sites, and for patients. No wonder many mid-sized CROs ask how they can survive in such a competitive environment?

Embracing RBM, a company's smaller size can become an advantage.

CRO companies have a chance to attract bigger projects, by means of implementation of Risk-based Monitoring (RBM) of a trial. Holistic integration of RBM, based on quality-by-design principles, demands changes on many stages of clinical research. Clinical Monitoring, data management, project management, etc. A big-CRO is not able to cope with such change efficiently. In contrast, mid-sized CRO can manage such change.

RBM, when implemented correctly, following the quality-by-design principles, can offer to a sponsor transparency in CRO decision-making, proactive trial controls and the ability to learn from previous trials' data. RBM drives trial management to new frontiers of efficiency while improving patient safety and patient care. RBM introduces management by design, not by default.

In order to implement RBM a change on almost each stage of clinical research is needed [Alsumidaie et al., 2015]. For a big CRO – a big challenge, for a mid-sized CRO – a chance to win market share, a chance to win a strategic partnership with a sponsor.

What is Data-driven RBM?

Risk-based Monitoring (RBM) is becoming an essential concept in pharmaceutical clinical research. It has the potential to improve data quality, patient safety and a medicine's time-to-market. In August 2013, the FDA underlined its wish to support risk-based monitoring [FDA, 2013].

The idea described in the guidance document was simple: not to monitor sites at a "flat" rate, but to do so adaptively. In practice, it means identifying key risk indicators (KRIs) to understand the pain points of a study and apply the RBM monitoring strategies:

- → Centralized Monitoring. An integrated approach based upon the perceived risk at each site.
- → Remote Monitoring. The application of technologies to access data remotely, saving the cost of on-site visits.
- → Reduced Monitoring, e.g., targeted Source Data Verification (SDV).
- → Triggered Monitoring. Certain KRIs trigger monitoring.

The FDA also stated that a "mix of centralized and on-site monitoring practices" would work best for human subject protection and trial integrity [FDA, 2013].

One of the first good definitions of RBM appeared in a position paper from TransCelerate: "RBM is an adaptive approach to clinical trial monitoring that directs monitoring focus and activities to the evolving areas of greatest need which have the most potential to impact subject safety and data quality." [TransCelerate, 2013]

EMA: "the reactive (fire-fighting approach) versus the preventive approach."

The EMA sets a wider scope than the FDA in its reflection paper, speaking about risk-based quality management (not only monitoring). It describes how the new risk-based approach facilitates existing quality practices, requirements and standards. It opposes two methods of trial management: the reactive (fire-fighting approach) versus the preventive approach.

Cyntegrity, following the EMA's advice, considers RBM to be not only a tool in the CRA's toolkit, but a deep change in the way of trial conduct. Change to be more preventive.

RBM as a Competitive Advantage

Why does RBM provide a valuable competitive advantage for mid-sized CROs? At the root of all strategic partnerships is the intention to create efficiencies in order to facilitate lower costs for the sponsor and greater profit for CRO. RBM can solve both tasks.

However, as a new concept, RBM demands flexible and agile decision-making and changes at each level of corporate processes. Mid-sized CROs have these advantages and now they can offer sponsors another level of transparency, data quality and predictable success. CROs can use the data to focus on safety and the improvement of patient care.

RBM is part of the risk management of a trial, part of quality by design, moving the emphasis from a reactive approach to a proactive approach.

The classic goal of clinical research monitoring is to be able to guarantee that the participants' rights are protected and the trial data are correct. Additionally, monitors look for protocol compliance, amendment compliance, GCP compliance and compliance with the law.

The data-driven RBM leverages these activities: it controls data integrity, patient safety and all types of compliance. This happens remotely, rapidly and constantly.

RBM systems will not make monitoring visits redundant, but optimize the time spent on site.

RBM allows the monitor to focus on what really matters, providing a specialized graph for each area: insufficient recruitment, safety issues, serious protocol deviations, poorly performing sites and worthless data.

By centralizing the location where all risk data are saved, managed, monitored and reported a CRO gains the following competitive advantages:

- → Clinical projects run safely and more predictably
- → The dangers of delays are easy to see on the dashboard, before an issue occurs
- → Data quality is increased through the elimination of systematic data noise sources
- → Clinical sites become more engaged as they receive earlier feedback

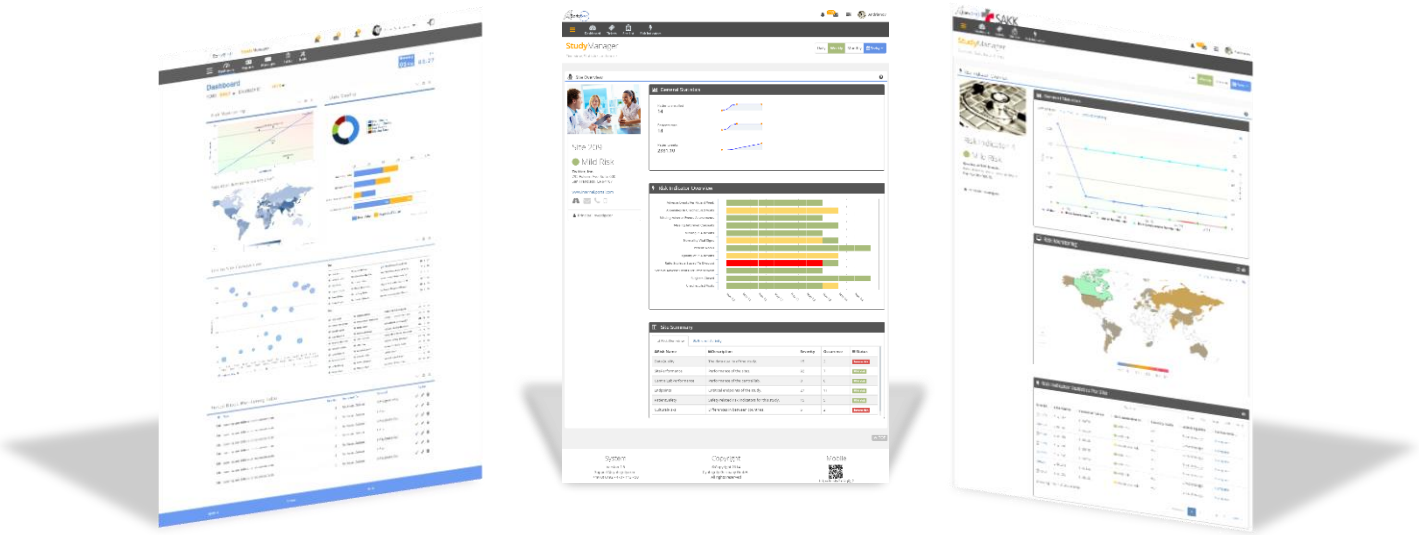

Figure 1. RBM Analytics from Cyntegrity

RBM, with its high-quality analytics capabilities has the ability to integrate knowledge from previous trials with contextual real-world data, improving patient-risk and patient care.

It is beneficial both for CROs and sponsors to take a step back and look at the current process in order to make them more efficient, to build sustainable, practical and efficient model. RBM offers a good opportunity for this change.

How to Get Started?

Our experience has shown that, rather than a big bang launch, the systematic introduction of an RBM approach is the best change management strategy [Alsumidaie et al., 2015]. A three-step approach has been proven to work best on many occasions:

Step 1. Proof of Concept (PoC):

- → Involve the most enthusiastic people
- → Generate essential learning for the next steps
- → Deliver success stories for other teams

Step 2. Pilot:

- → Apply tools and approaches to a larger number of trials
- → Involve teams, who tend to be more skeptical
- → Generate a road map to full implementation
- → Heavily involve the IT, Data Management and other Project teams

Step 3. Full Deployment:

- → Transfer experience gained from the PoC and the Pilot to the whole pipeline
- → All trials will now benefit from an RBM approach and from inter-trial knowledge sharing.
- → Continuously refine tools, processes and methodologies

Can RBM Negatively Influence Data Quality and Patient Safety?

The brief answer is - yes, it can. There are two main reasons for this:

- → RBM introduces its own risks
- → There is always a residual risk, which is not controlled & monitored.

How can we deal with that and what can be done?

A responsible team should be aware of the most common mistakes & pitfalls. Bringing in expertise from outside is the best approach during PoC and Pilot projects. Experts can identify situations where a certain hazard could occur and they will be aware of not considered so far. Cyntegrity is ready to offer its experience, and the expertise of its partners, to make RBM implementation comfortable and efficient for its customers.

Conclusions

In today's competitive environment, with the centralization of clinical research outsourcing, smaller CRO size can become an advantage. Mid-sized CROs have a chance to leverage their flexibility and agility to offer a structured, holistic RBM approach to clinical trials. Mid-sized CROs can improve their attractiveness to a sponsor by offering more transparency in decision-making, better data quality, and efficiency by using a new data-driven RBM concept.

To do things right, it is advisable to bring expertise from outside for the proof-of-concept and pilot projects. Align all processes, gain needed experience and lessons learned, leverage the processes with technology.

Technology plays a critical role in effective RBM. However, monitoring team is more important. An RBM pilot trial demands well-trained monitors.

However, RBM is not a "formula" to configure and forget. It demands a structured, holistic approach. Only then, it can be used as a powerful tool to gain business, win strategic partnership and grow further.

About Us

Cyntegrity is an innovative company, which offers a specialized service with proprietary software for the efficient Risk-based Monitoring (RBM) of a clinical trial. Cyntegrity's mission is to offer high quality analytics that are more predictive than retrospective, which have the ability to integrate the knowledge from previous trials with contextual, real-world data to reduce patient risk and to optimize preventive care.

Cyntegrity offers expertise, technology and experience to make the transition to data-driven RBM fast and comfortable. We are happy to work closely together with our customers through this transformation.

Cyntegrity's Research Partners

In our passion for achieving excellence and sustaining innovation, Cyntegrity cooperates with a number of top companies and institutions that deal with pharmaceutical development. Among them are Goethe University, Frankfurt Innovation Center (FIZ Biotech), PPH plus, WSQMS, SynapCon and the Institute of Biostatistics and Mathematical Modelling at Frankfurt am Main university.

Cyntegrity and our research partners are passionate about moving RBM to a new level of efficiency.

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