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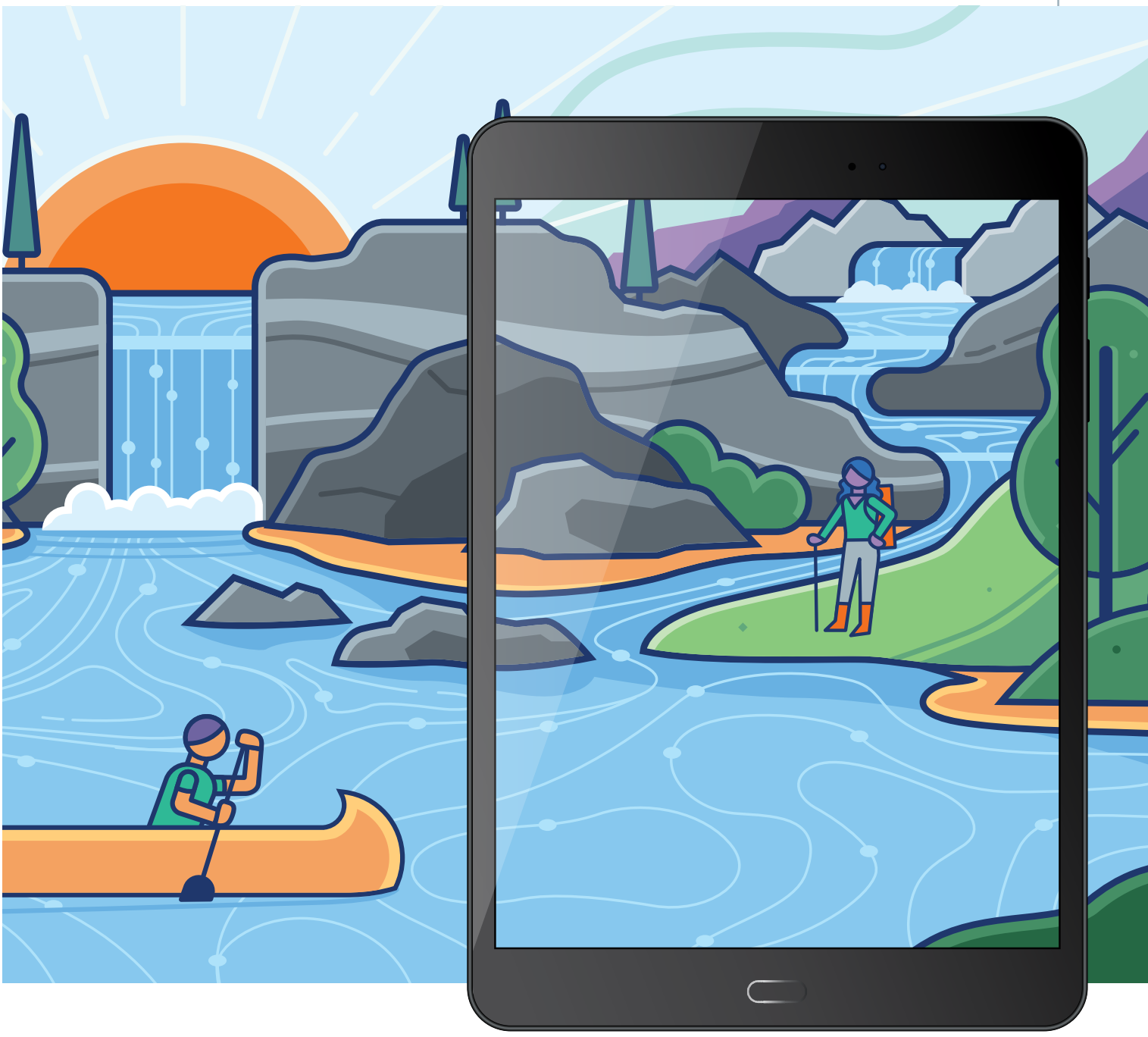
Confident Decisions, Faster

Approach Your Risk-Based Monitoring Strategy With Confidence

Tools and Technologies for Easy Implementation

October 2019 | White Paper



Introduction

As an industry, we have seen the benefits of successful risk-based monitoring (RBM) strategies over the last decade. In fact, since the FDA first released guidance in August 2013, adoption has grown rapidly. One survey concluded that as recently as 2016, just 18% of new trial starts employed some form of RBM oversight. Yet, in 2018, more than 60% of new trial starts were using RBM.

But as the size, number, and complexity of clinical trials continue to grow, the standard approach to monitoring — a resource-intensive approach involving regular site visits and source document verification (SDV) — has become costly and is no longer realistic. However, the fundamental principles — protection of participants and assurance of data quality — remain paramount.

In fact, when the U.S. FDA updated its guidance in March 2019, it gave suggestions to encourage the industry to adopt new RBM strategies to continue to support safer, more efficient, and higher quality clinical research. With many sponsors holding back from fully embracing a risk-based strategy, the FDA has begun to encourage and facilitate conversations like its recent public workshop held in conjunction with the Duke University's Margolis Center for Health Policy.

Former FDA Commissioner Scott Gottlieb has been a longtime supporter of RBM: "The FDA isn't alone. The advent of precision medicine is challenging the entire medical research ecosystem to develop more efficient approaches to testing and developing diagnostics and therapeutics…including frameworks that are more carefully suited to the kinds of precision technologies that underpin new treatments."

Implementing an RBM strategy at your organization does not need to be complicated. This paper outlines several key strategies that will allow you to confidently develop an effective RBM approach in your clinical research program, including what is needed for an effective RBM strategy and how you can confidently support your objectives with the right tools and technologies.

Constructing a Sturdy RBM Strategy

The goal of any RBM approach is to implement an oversight strategy that supports a study's data integrity and protects the safety, rights, and well-being of trial participants. Working together, your team should develop an approach that drives team alignment and efficiencies for all the monitoring activities in your study.

The following RBM considerations take a deeper look at the framework, technologies, and partners that support effective and efficient RBM. With the ever-changing clinical trial landscape, it is important that the solutions you choose:

- Prioritize patient safety and data quality
- Enable source data review (SDR) that focuses on the areas of greatest need
- Support centralized monitoring and off-site review

Establish a Framework

The first step to implementing an RBM strategy within your organization is to adopt an RBM model that can be both easily deployed and scaled. One such model is the Risk-Assessment Categorization Tool (RACT) from TransCelerate, which uses specific questions and considerations to determine the categories of risk that could affect your subject safety, data quality, and regulatory compliance. In the RACT, both program and protocol-level risk categories are outlined. The risks — flagged as high, medium, or low — help you understand your study and the areas that pose the greatest risk to your program's safety and efficacy.

RACT Categories of Risk Outlined at the Program and Protocol Level

Program Level RACT	Protocol Level RACT
Categories	
• Safety • Endpoints • IP • Technology • Operational experience	• Study phase • Subject population • Endpoints • Technology • Data collection & CRF source • Study medication/IP • Blinding • Clinical supply chain • Protocol complexity • Operational complexity • Geography

Additionally, your framework should outline your data collection processes and system — for example, how you lay out your forms and how you program your edit checks. These requirements, which ensure the effective and efficient implementation of risk mitigation, are typically defined at the program level, reassessed at the protocol level, and are monitored throughout your trial.

Some of today's technologies build in logic that help enforce and ensure compliance to your overall RBM approach. Clinical Ink's eSource ecosystem, Lumenis™, for example, gives organizations the ability to identify key fields and key forms within their study that are absolutely required to be reviewed, conditionally required to be reviewed based upon the data entered, or not required to be reviewed.

Choose the Right Technologies

Another important aspect of a successful risk-based management strategy is real-time data review and reporting. Organizations with integrated, adaptable technologies — where study stakeholders receive real-time data access — have the ability to reenter data or make decisions based on the information in front of them. Reports and dashboards like patient profiles, key risk indicator reports, and risk/signal indicators help study monitors focus on enabling the risk-based management strategy that they have outlined for their organization.

Direct data capture (DDC) tools, like Lumenis and its ePRO and eCOA modules, facilitate the capture of patient data at its source and according to the RACT. Additionally, DDC gives study stakeholders a more comprehensive picture of patient and study risk by pooling together data from all sources, and gives study monitors the ability to run queries and notify sites about data that might be missing to help minimize risk.

From a risk perspective, for example, it could be vitally important that subjects complete a daily symptom diary. Real-time data technology allows the patient or care provider to enter that information with edit checks and logic based on the RACT and questionnaire programming.

Employ Helpful Partners

Clearly, organizations cannot always do these things alone. A major key to success is finding the right partner to complement your strengths. Partnerships can help ease some of the burden from your organization by facilitating study setup, reducing redundant and unnecessary data review, and enabling more focused site visits.

Although there are many kinds of partnerships, here are three examples of the most common:

- Statistical partners: assist in determining risk tolerance levels, developing needed statistical reports and statistical views of data to enable your RBM team to focus its site visits

- Clinical partners: provide insight into the clinical risks associated with the program or protocol, incorporating on-site observations to make needed changes according to the RBM plan/approach

- Vendors: enable your RBM approach and support your specific requirements for how you collect data with both transactional and reporting tools

While on the search for vendors to facilitate your RBM strategy, you must first clearly define your requirements and then ensure your prospective partners can deliver what you need.

Deconstructing the Industry's Hesitancy

Before we can discuss the tools and technologies that can help you confidently implement your RBM strategy, we must first understand what is holding the industry back. In an informal survey conducted by Clinical Ink, we asked senior members in clinical data management from top three pharmaceutical organizations, midsized pharma companies, and a small, specialty clinical research organization (CRO) these questions:

- Are your organizations using a risk-based approach to data and clinical review on a regular basis?
- Why have your organizations been slow to adopt?

Top Three Pharma

Responses from top three pharma indicated that these organizations are just starting down the path. Although they haven't fully embraced RBM across their entire organization, these organizations seem to be exploring both transactional and reporting tools. Some have been diving into more analytics-driven, risk-based data review, with review plans driven by statistical analysis. Overall, these organizations are taking a cautious approach and hold the belief that traditional oversight methods are lower risk and that 100% SDV is the only way to ensure data quality and less scrutiny from regulatory bodies.

Medium-sized Pharma

In many cases, these organizations indicated that they have fully adopted RBM on certain protocols, but not necessarily across an entire program. Many have rolled out targeted source document verification and have begun to reduce site monitoring frequency. Additionally, they're using their RACT guidance to build out other areas of advanced analytics for their data management that align with their broader RBM practices, which feeds into their data and clinical management plans.

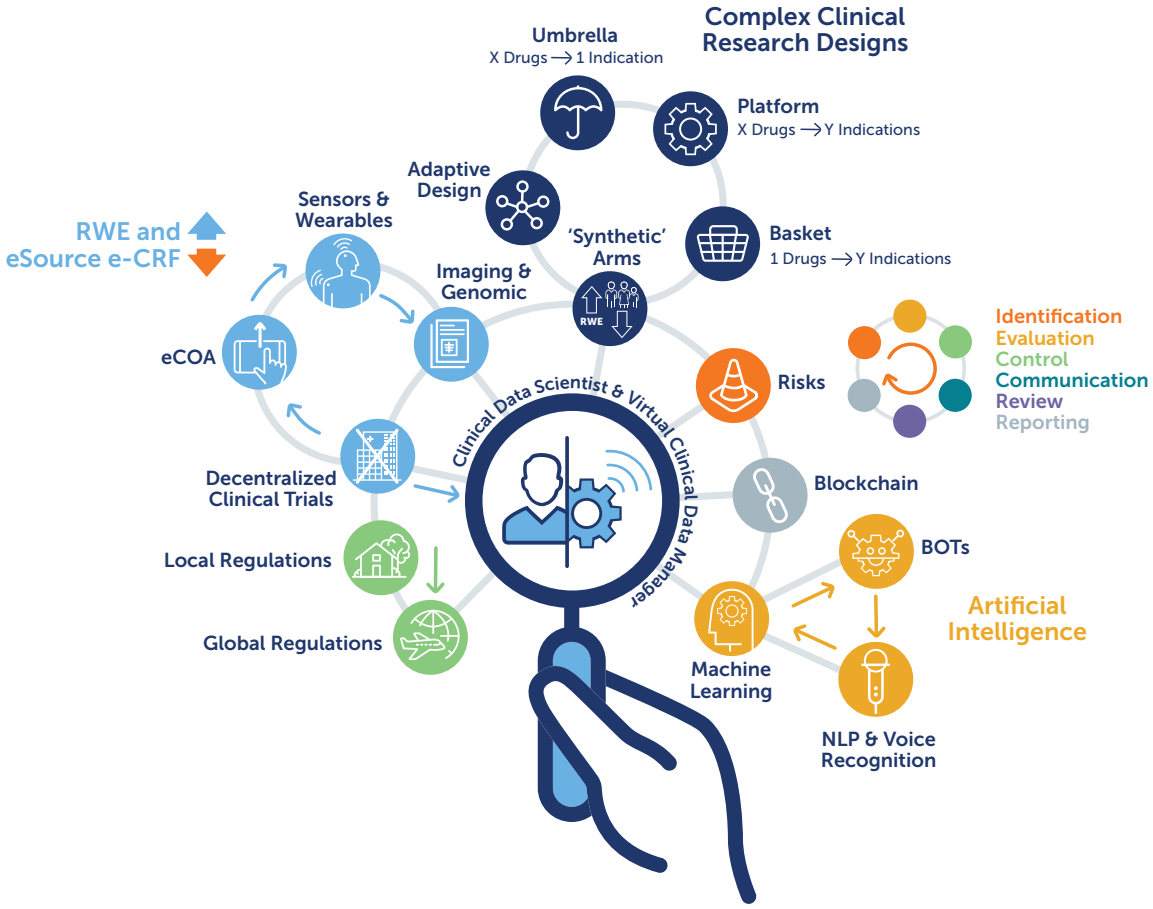
Small, specialty CROs

Smaller organizations are looking at ways to be more effective in the way that they carry out clinical site monitoring visits. For example, they're using the RACT to proactively identify areas of risk and then intervene if one of the risks approaches a threshold that would indicate intervention. In these organizations, project teams review and react to indicators that, given time, could have become a larger issue. Their adoption isn't about elimination of tasks, it's about doing things more effectively and efficiently and with risk in mind. They emphasize that they are trying to use data to help drive their research forward.

The overall sentiment on either end of the spectrum, which was echoed at the Duke-Margolis public meeting, seems to be that the questions about FDA guidance are coming primarily from larger pharmaceutical companies, and that CRO organization adoption appears to be high. But, we shouldn't be fearful. The FDA is not only encouraging the adoption of RBM, it's requesting we embrace it at a much faster pace to reduce the cost and time of bringing new therapeutics to patients.

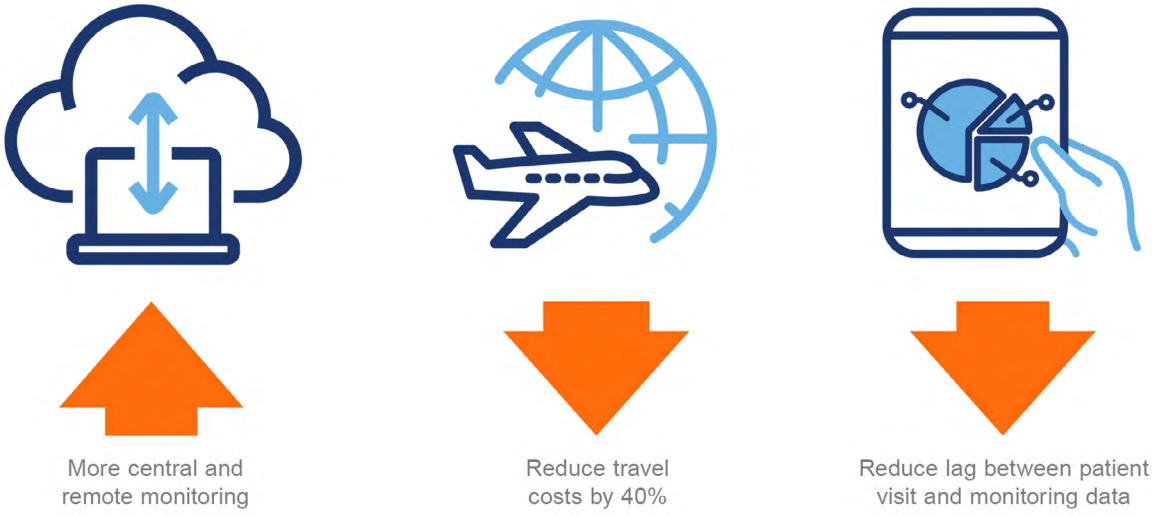
Building Confidence With New Tools and Technologies

The rapid advances in technology over the last decade have allowed us to reimagine what risk-based monitoring can achieve — from fewer monitoring visits to virtual and hybrid trials. Recently, the Society for Clinical Data Management (SCDM) published a white paper that helps us understand the evolution of where risk-based management is going. In it, the authors talk about embracing different tools and technologies to improve monitoring and data review approaches.



There are many configurable tools and technologies that can drive effective, efficient, and quality-oriented data review activities within your study. Here are a few:

Direct Data Capture



DDC technologies allow organizations to collect data directly from study participants with little to no transcription. Organizations that adopt this technology are able to reduce or even eliminate the need for SDV. With no lag between the patient visit and the ability to monitor data, study sponsors can enable central and remote monitoring for their studies and decrease travel costs by up to 40%.

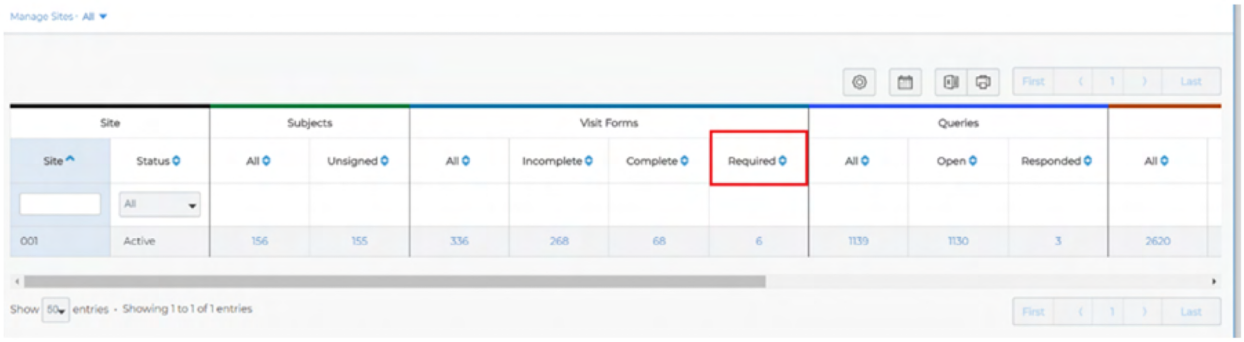
Source Data Review

When DDC tools are used, SDR can be utilized. The combination of DDC with SDR yields tremendous efficiency, increases quality, and reduces tedious tasks on the part of the monitor. In addition, by being able to carry out remote SDR, the monitor is able to focus on tasks at the site that have more clinical significance.

Multimedia Data Input

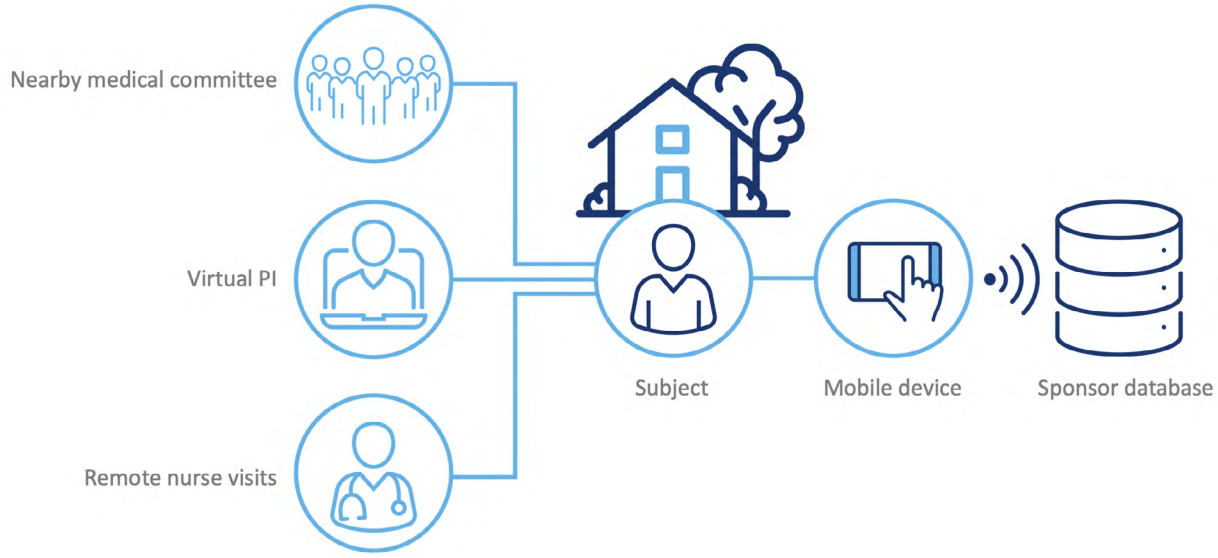
The ability to capture data in the form of audio, video, or still images can be imperative to some therapeutic areas and indications; for example, embedding audio and video from an ADAS-Cog assessment documenting a patient's symptoms of Alzheimer's disease. From a risk perspective, multimedia data input can provide remote reviewers with more information about how a study is being run.

Targeted Form Review



Targeted form reviews identify situations where important data from your study is out of range, or instances where data from assessments like the ADAS-Cog mentioned above need to be reviewed the first time they are administered. Lumenis allows you to program triggers into the system using logic from your RACT, which directly drives what does and doesn't need to be reviewed and indicates the specificity of review necessary.

Virtual and Hybrid Trials



Virtual and hybrid trials allow patients to participate in a research study from home. In the case of a virtual study, participants may never enter a care facility. Hybrid studies, on the other hand, allow patients to both participate from home and from the clinical research site. This is beneficial in therapeutic areas where patients are hard to recruit or in indications where patients may not be well enough to travel.

Conclusion

Despite slow adoption by the industry, costing the pharmaceutical industry huge amounts of both time and money, the benefits of monitoring trial conduct using a risk-based approach have become clear: safer, more efficient, and higher quality clinical research. With the help of the newest RBM tools and technologies, and through the power of on-demand data and ongoing management, streamlining your approach has never been easier.

If you have questions about supporting your RBM strategy with today's newest data collection and management technologies, get in touch with our team.

https://www.acrohealth.org/wp-content/uploads/2019/05/ACRO-2019-FDA-RBM-Implementation.pdf

https://www.fda.gov/media/121479/download

https://healthpolicy.duke.edu/events/improving-implementation-risk-based-monitoring-approaches-clinical-investigations

https://transceleratebiopharmainc.com/rbminteractiveguide/how-does-clinical-trial-site-monitoring-work-under-a-risk-based-monitoring-approach/the-transcelerate-model/

https://www.transceleratebiopharmainc.com/wp-content/uploads/2017/06/RACT_FINAL.xlsx

https://www.acrohealth.org/2019/05/16/acro-offers-unique-insights-on-risk-based-monitoring-of-clinical-trials-calls-for-adoption-of-rbm-as-a-best-practice/

https://www.raps.org/news-and-articles/news-articles/2019/5/risk-based-monitoring-pfizer-and-bms-seek-clarity

https://www.acrohealth.org/2019/08/16/advancing-the-adoption-of-risk-based-monitoring-strategies-in-clinical-trials/

https://www.scdm.org/wp-content/uploads/2019/06/SCDM-Reflection-Paper-Evolution-to-Clinical-to-Data-Science.pdf

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Direct Data Capture | eCOA | ePRO | eConsent

Clinical Ink, a global clinical technology company, offers data certainty from source to submission. Our eSource clinical technology and configurable ePRO and eCOA modules — a suite of solutions for capturing and integrating electronic data from sites, clinicians, and patients at its source — naturally enhance your clinical trial workflow by reducing manual labor, providing anytime, anywhere data access, and saving resources as your trials progress. Accelerate the completion of key clinical development milestones in your study and confidently manage your trial's critical decisions with our flexible menu of collaborative services, remote monitoring support, and a complete, real-time view of your trial.

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