

# Mindful Clinical Trials

## What does risk-based monitoring have to do with it?

Apparently a lot. Risk-Based Monitoring, or RBM, became a permanent fixture at the turn of 2016 thanks to the ICH GCP E6 R2 Addendum.

While many Sponsors and CROs began laying the groundwork for integrating RBM into their processes early on, some have lagged behind, uncertain as to whether or not RBM is necessary. To allay any doubts, the FDA issued ICH GCP Step 5 mandating RBM for all clinical trials. The document is in grace period and goes into effect in June 2017.

## What is risk-based monitoring?

RBM is an adaptive approach to clinical trial monitoring that directs monitoring focus away from being indiscriminate (let's collect a lot of data and monitor everything equally zealously) towards being focused (let's figure out which data is critical to patient safety and study endpoints and make sure it receives our ample attention).

Thus, RBM shouldn't be a point of concern, but rather a point of validation of what matters. It is, above all, an opportunity to practice mindfulness in collecting clinical trial data within the site- and patient-centric environment.

It is important to note that RBM does not equal reduced Source Data Verification (SDV). It may involve reduced SDV, if the risk analysis favors it, but it may not just as well.

**“Quality in clinical trials may be defined by the absence of errors that matter.”**

Meeker-O'Connell A., Ball L., Current Trends in FDA Inspections March/  
April 2011



For sponsors, RBM implementation represents a shift. Instead of collecting data by mere volume, the FDA invites sponsors to think critically and understand what data is really important to the patient safety and study endpoints, and act accordingly.

In the past, pharma and biotech companies have tried to err on the side of caution when it comes to the amounts of clinical data, with patients' interests falling by the wayside. As a result, this led to protocols continuing to grow, study flow charts overflowing, and the collection (and monitoring) of extraneous data "just in case."

The new GCP protocol invites sponsors to think more critically of the data, moving away from a "more is more" mentality. With a lean protocol, created to answer specific questions based on most relevant data, reduced SDV may not even be necessary.

Yet, as a risk-averse industry when it comes to our own work, we continue to copy and paste the "old" protocols, for the sake of ease.

Risk-based monitoring invites us to practice a bit of courage and experiment, grounded in expertise and knowledge, to make the right choices by defining risky areas and thresholds and describing our tolerance levels towards them from the start.

If anything, it's a like a prescription for mindfulness now mandated by the new GCP, a catalyst for change.

*"The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials. The flexibility in the extent and nature of monitoring described in this section is intended to permit varied approaches that improve the effectiveness and efficiency of monitoring. The sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring. The sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan)."*

-- ICH GCP E6 R2 Addendum

## Next steps for sponsors and CROs

Implementation of RBM means improved data quality while ensuring subjects' rights protection and regulatory compliance. It means focusing on what matters by understanding where the greatest risks lie.

"Quality by Design," another catch phrase firmly associated with RBM, needs to become a leading principle in the work for every company department, from clinical to stats, from drug supplies to quality management.

We are seeing companies rearrange, upgrade and reformulate working principles across their entire functional areas, so that at every level what is important is brought to the forefront of focus, the risks are described, the actions planned according to what current data tells us, and not what "we have always done".

Risk-based thinking is a new paradigm for companies to adopt cross-functionally. It's a lot of work and it's not easy, but it's worthwhile, as it teaches everyone to think critically about what they do and why they do it. When companies are forced to think about these things, they come out stronger and more focused.

## What does RBM mean for sites?

Mindful planning and technology allows us to monitor sites on an as needed basis and check much of what needs to be checked off-line. Off-site monitoring is a gift that, if used correctly, allows for on-site monitoring to focus on people rather than data.

Mindful planning of an on-site visit allows the CRA to spend time with the sites staff, understanding what gets in the way of patient enrollment, on-time CRF completion or correct screening procedures.

Instead of keeping head down in paperwork, the CRA can now act as a true ambassador at the trial site, working with the site team to uncover the root-cause of problems, helping, consulting, and inspiring.



Needless to say, CRAs these days need to be helped to develop a whole new set of communication skills that they hardly had the opportunity to practice at large in the old days.

Sites are key when it comes to executing clinical trials. And the gap between the perceived importance and performance levels of CRAs is confirmed by CenterWatch survey from 2015 that shows that "... 71% of sites believe professional, knowledgeable CRAs are critical to study success, but only 48% of sites gave the average CRO an excellent rating for this attribute."

RBM enables site monitors, aka CRAs, to focus more on things that matter – building excellent helpful relationships with site teams.

When skillfully designed, RBM studies have great potential to allow us to focus more on patient enrollment influencers, data trends across regions, as well as common problems that are difficult to spot other than in hind sight. With central monitoring actively at play for every study, we can be much more hands-on, acting based on facts and current reality rather than tradition.



## Conclusions

RBM invites us to be mindful about clinical trial set-up, planning and execution, to think before we act, to be flexible and adjustable as unexpected outcomes show up along the way. It invites us to plan and work mindfully. It redefines clinical trials monitoring. A new era for clinical research is here, and we all need to learn to live and thrive in it.

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CenterWatch Survey, 2015

