MANA RBM
Delivering Risk-Based Monitoring Solutions

10 Things C Level Executives in Biotech, Devices, and CROs Need to Know about Risk-Based Monitoring (RBM).

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RBM has been a topic of conversation for the teams of Clinical Operations and Data Management for several years. We are often asked by C Level executives why the company needs to change the way trials are done. We hope these items will help you to understand the value of adopting RBM for your development programs. For more details on implementing RBM, please see our White Paper on RBM Implementation.

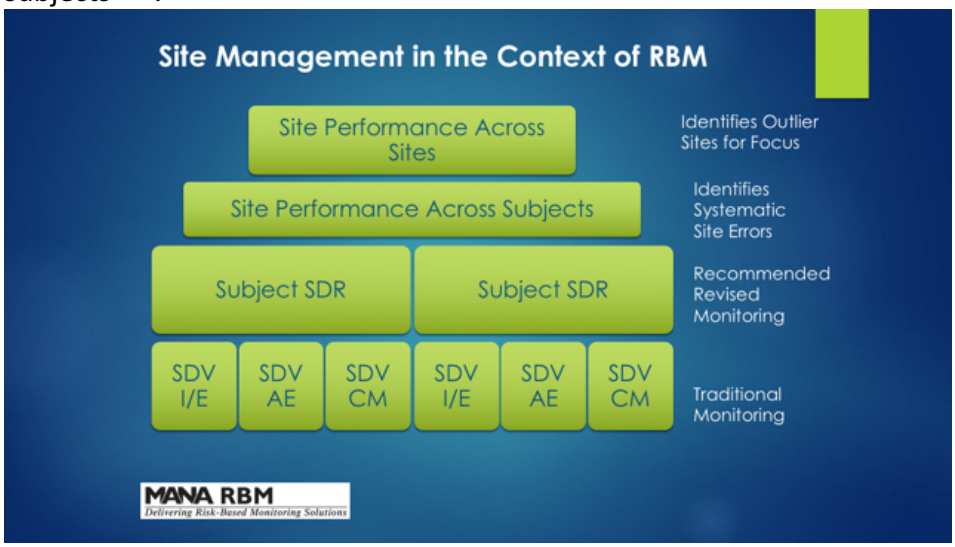
1. The standards for monitoring trial conduct have changed significantly since 2013. The current "Gold Standard" of frequent onsite visits and 100% Source Data Verifications (SDV) for quality oversight of clinical trials is no longer sufficient. The FDA and EMA (Regulators) have signaled that they expect a change in trial oversight to an approach called Quality by Design[1,2]; a methodology the auto industry and pharmaceutical manufacturing have used for many years. Regulators expect that clinical trial oversight will move to a more "Risk-based" approach, focusing on the most important areas of trial conduct: subject safety, protocol compliance, Investigational Product Oversight, and Good Clinical Practice (GCP). The industry has adopted a name for it - Risk-Based Monitoring (RBM).

   Numerous articles have been published showing the inadequacy of SDV as a method of trial quality oversight and it is not recommended as the preferred approach to trial quality by TransCelerate BioPharma (a consortium of major Pharma Companies).[3,4]

2. The term Risk-Based Monitoring is NOT about decreasing Source Data Verification (SDV) and monitoring visits—it is about using a comprehensive approach to focus oversight on the most important aspects of the trial and subject safety. This includes:
   a. Identifying and classifying potential trial risks across key areas: efficacy, safety, GCP, Investigational Product Management, and protocol compliance.
   b. Monitoring for identified risks starting as early as possible after a subject visit.
   c. Instituting an issue management approach to capture issues, evaluate its scope, determine root cause, institute remediation, and follow through to assure the issues are resolved.

3. Risk-Based monitoring should be instituted in all trials. In most cases when monitors use SDV, they look at each subject's forms in isolation (see figure below). They review the vital signs for one subject and one visit, then move to another form and repeat the process. It is almost impossible to identify trends using this approach or even see if the data make sense from one form and one visit to another.

With RBM, Monitors should conduct a comprehensive Source Data Review, which should include all data sources for the trial (e.g., the clinical data, patient reported outcomes, labs). RBM should also include a data review across subjects to identify consistent errors across all subjects in a trial and a review of all sites to identify outliers. 483's have been issued to major Pharmas for missing consistent errors across research subjects[5,6,7].



4. RBM **may** save you money. The Regulators have recommended more review be done faster and remotely—optimizing the use of technology. Fewer monitoring visits decreases travel costs, however, monitors will need additional time to conduct more comprehensive reviews. This additional review enhances the quality of the data, lowers risk to research subjects, and enhances the likelihood of the data being accepted by Regulators. RBM, however, may not save as much in monitoring time as originally anticipated when the RBM guidance was first released.

   MANA RBM has developed and implemented unique tools to comprehensively evaluate subject data in a fraction of the time compared to traditional subject review. This approach should significantly further decrease monitoring time while enhancing subject oversight.

5. Cross functional collaboration enhances the process. Instead of the silos that have become the norm in clinical development, RBM is optimized through the cross-functional (e.g., Clinical, Data Management, Medical Monitoring) interactions and discussions of findings. When adopting RBM, you should develop a cohesive approach that covers all aspects of trial conduct including Clinical Research, Clinical Operations, Data Management, Medical Monitoring, and Pharmacovigilance.

6. Anticipate changing your pricing model from paying CROs based on onsite monitoring visits to one that recognizes the amount of time remote oversight RBM requires.

7. There are a variety of technology tools available to meet your needs and budget for implementing RBM. You can usually incorporate all the technology tools needed and still stay within the existing trial budget.

8. RBM is not going away according to the consistent guidance from the FDA and EMA. The International Council on Harmonization (ICH) also released a draft guidance that encompassed new recommendations for trial oversight and Good Clinical Practice (GCP) that aligned with the FDA and EMA guidance[8]. The Regulators have shown great vision in helping the industry identify how to improve its quality oversight.

9. RBM involves changes in the skills monitors need to move beyond SDV. This new skill set includes knowledge of technology and new processes designed to focus efforts on the most important aspects of the trial as described above.

10. Adopting RBM requires incorporating a Change Management process. This ensures your organization will successfully adopt the changes that need to take place.

References:

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For more information, including a comprehensive White Paper on RBM Implementation, or questions on how to adopt Risk-Based Monitoring, please contact Penelope Manasco, M.D (pmanasco@manarbm.com, 919-556-9456)

