

8 Best Practices for Adaptive Monitoring:

Techniques to Cut Monitoring Costs and Increase Efficiency

WHITE PAPER

Table of Contents

Introduction	3
What is Adaptive Monitoring?	3
8 Best Practices for Adaptive Monitoring	4
1. Replace manual processes with technology	4
2. Collect and analyze real-time performance metrics	4
3. Transform monitors from “box checkers” into site managers	4
4. Provide role-specific, customized reports	5
5. Remote monitoring enables a team approach	5
6. Dynamically allocate need-based site visits	6
7. Emphasize query prevention, not resolution	6
8. Ensure data is submitted, cleaned and made available as quickly as possible	7

Introduction

Monitoring and site management account for as much as two-thirds of the cost of a phase III clinical trial¹. These high costs stem from traditional, inefficient monitoring practices that allocate the same number of visits to all sites, at the same interval, regardless of individual site performance or the quality of data collected. This traditional approach is a key contributor to the inefficiencies the drug and medical device development industries can no longer afford. Adaptive Operational techniques, including Adaptive Monitoring, are the answer to efficient drug and medical device development.

When sponsors think of the term “adaptive” most immediately think of Adaptive Design. However, Adaptive Operations, which do not require FDA approval, take adaptive research a step further to address day-to-day operational strains like enrollment, monitoring, query management and database lock. Monitoring, a component of trial operations, not only bears a heavy financial burden on trials today, but also wastes time through unnecessary travel to sites. Ultimately, Adaptive Monitoring minimizes wasted time and effort by scaling monitoring activities and visits based on the actual data collected during the study.

What is Adaptive Monitoring?

Adaptive Monitoring uses real-time performance metrics to track sites on a daily basis, focusing attention on the areas that need it the most. By taking advantage of an advanced technology platform, monitors have easy access to a range of reports that enable them to focus their work based on continuously tracked site performance metrics. Now, problem sites receive earlier and more frequent visits, while exemplary sites receive fewer visits at greater intervals, as long as they continue to maintain a timely flow of high-quality data and show satisfactory performance on study activities.

Combined with remote monitoring, this intelligent allocation of resources helps sponsors dramatically boost efficiency, cut costs, increase quality and reduce risk, without collecting less data. Ultimately, Adaptive Monitoring reduces site visits by up to 75%, without sacrificing data quality or safety.

¹ Malakoff D. Spiraling costs threaten gridlock. *Science* 2008;322:210-3.

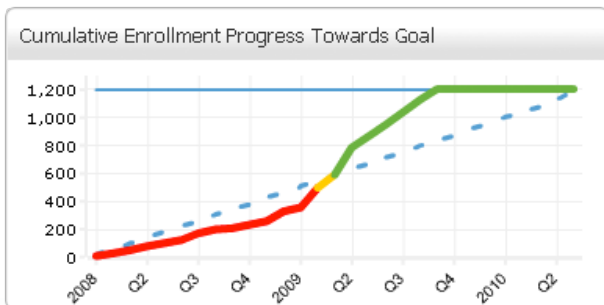
8 Best Practices for Adaptive Monitoring

1. Replace manual processes with technology

A fully integrated Clinical Trial and Clinical Data Management System (CDMS and CTMS) will reduce the manual effort required for monitors to resolve queries, track subject visits and transfer information between disparate systems and databases. This ensures all parties involved have complete visibility and control of the day-to-day functions of the trial. In addition, technology should automate manual, lower-level monitoring tasks such as pattern recognition and source document verification (SDV). For example, advanced electronic data capture (EDC) solutions, like the digital pen, can greatly reduce the amount of time CRAs need to spend on SDV.

2. Collect and analyze real-time performance metrics

A continuous flow of site performance metrics is key to implementing Adaptive Monitoring techniques, and essential for remote monitoring. Remote monitoring uses metrics to keep track of site performance across the entire study from one location, pinpointing issues needing immediate attention that can often be resolved without a site visit. Performance metrics that provide a basis for remote monitoring and allocating monitoring resources include:



- Current enrollment vs. study goal
- Mean time from patient visit to data submission
- Query Metrics: response time, queries by site, etc.
- Number of protocol violations
- Number of adverse events (AEs) and serious adverse events (SAEs)

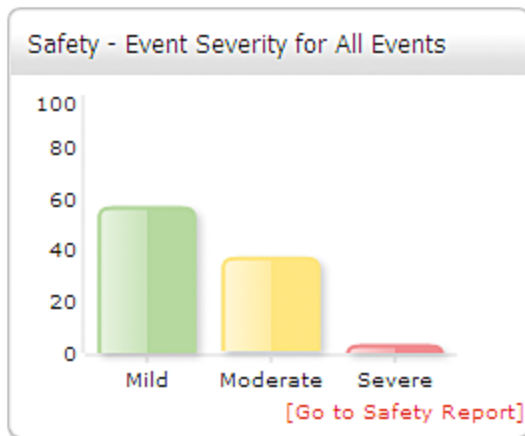
3. Transform monitors from “box checkers” into site managers

Historically, two activities have overwhelmingly consumed a monitor’s time: travel and meticulous, manual checking of details during monitoring visits. Automating repetitive tasks traditionally performed by CRAs frees them to leverage their expert knowledge of the study to guide an enrollment strategy, increase speed and accuracy of data collection and improve overall performance from site initiation to database lock. The results are higher quality data, more rapid transition to the next phase of development and studies that finish on time or ahead of schedule.

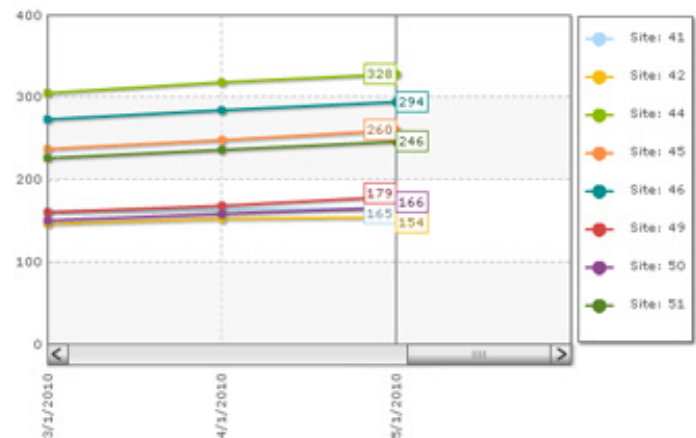
4. Provide role-specific, customized reports

Not all study data is relevant or required for each team member’s role. Site coordinators, monitors, project managers and executives all need different information to do their jobs effectively. In order to efficiently implement Adaptive Monitoring practices it is imperative to provide all team members and site personnel with role-specific reports from a centralized, integrated technology platform. The end goal is to provide a clear picture of the health of the study, available online in a format that can be interpreted by each team member at a glance.

Examples of Customized Reports:



Sites track their day-to-day enrollment, patient visit, safety, protocol and query metrics, compared to goals and the study average.



Monitors track performance across all sites to focus their visits on problem areas, eliminating unnecessary site visits.

5. Remote monitoring enables a team approach

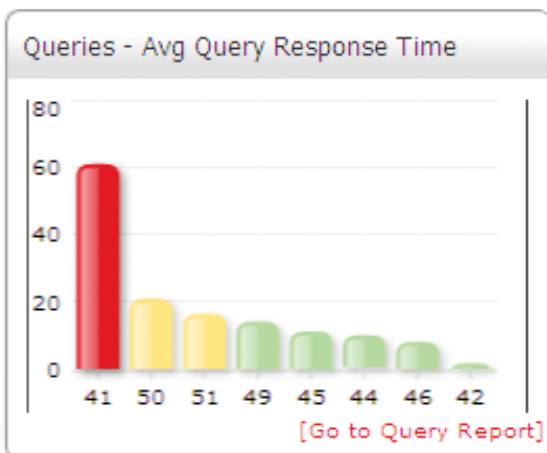
Remote monitoring helps individual monitors stay current on the status of their assigned sites, and, more importantly, establishes a team approach that reduces dependency on the performance of individual monitors. Remote monitoring includes greater involvement by senior monitors, whose experience and expertise enable them to recognize site issues that could be overlooked by less experienced monitors. At a glance, senior monitors know immediately if a problem is serious enough to require escalation to the project manager.

6. Dynamically allocate need-based site visits

Through real-time patient data and site performance metrics, monitors in an adaptive study dynamically allocate resources and attention based on actual site performance. This Adaptive Monitoring technique replaces the fixed schedules and rigid adherence to preordained plans used in traditional studies with a data-driven, needs-based approach to site visits. The focus can be moved to bringing underperforming sites up to standard, or allowing study managers to replace unsatisfactory sites when necessary. Dynamic resource allocation can be applied to all monitoring activities, including site closeout. Devoting more attention to closing out sites with the greatest number of unmonitored fields ensures that study closeout occurs early or on schedule. The worst-performing site will no longer delay closeout for the entire study.

7. Emphasize query prevention, not resolution

Resolving a single query in a large phase III clinical trial can cost as much as \$350^{2,3}. This means that merely resolving queries will not control costs. It is important to prevent recurrences by identifying and eliminating root causes on the first instance of each type of query. Technology should be used to automate query resolution whenever possible, and query-prone CRF questions should be examined to identify changes in wording or layout that will eliminate future mistakes. Reports should provide metrics illustrating:



- Average query response time, including trends over month-long periods
- Query metrics by site
- Most queries by fields, forms and range checks
- Outstanding queries
- SAE queries
- Additional query metrics specific to a particular study

2 Eisenstein et al, Reducing the costs of phase III cardiovascular clinical trials, *Am Heart J*, March 2005, 149(3), 482-8

3 Eisenstein et al, Sensible approaches for reducing clinical trial costs, *Clin Trials*, 2008, 5, 75-84

8. Ensure data is submitted, cleaned and made available as quickly as possible

Technology and reporting are only as good as the data that is available. Effective Adaptive Monitoring requires sites to submit data quickly after collection, so it is important to enforce this best practice through contractual requirements and potential incentives for timely submission. The earlier data is submitted, the sooner study team members can detect and correct problems that could compromise quality.

Health Decisions' HD360° Clinical Management System

Health Decisions' Agile Clinical Development approach cuts clinical trial timelines by 30% by combining Adaptive Design and Adaptive Operations, enabled by our proprietary HD360° Clinical Management System. HD360° combines flexible data capture and powerful data management with advanced reporting, collaboration and sophisticated business intelligence, enabling every member of a study team to work faster and more efficiently to meet development goals.

HD360° offers sponsors a range of features including:

- Full range of data capture options, including webEDC, SmartPen and OMR
- 360° view of study metrics with drill-down capability for critical details
- Automated subject and query management tools
- Advanced capabilities for tracking budgets and payments, resources and audits
- Auditable, version-controlled document management

About Health Decisions

Health Decisions is the leading contract research organization (CRO) in Adaptive Clinical Trials committed to shortening development timelines and maximizing pipeline value for pharmaceutical, biotech and medical device companies. Through Agile Clinical Development—a strategic three-pronged approach that combines adaptive design, adaptive operations and proprietary technology—Health Decisions delivers real-time performance metrics that enable sponsors to make the most of competitive market opportunities. Health Decisions is headquartered in Durham, NC, with over twenty years of experience helping sponsors exceed development goals in Phase I-IV clinical trials across all major therapeutic areas.

For more information, please visit the company's website at www.HealthDec.com

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