

AstraZeneca and ERT Case Study:
Utilizing a Multi-Phased Approach to MCC ECG Performance Metrics Implementation

Metrics Champion Consortium - Overview

Today's drug development industry is under increased pressure to improve its research and development performance/strategies by reducing drug development times and costs, while at the same time dramatically increasing productivity and maintaining quality.¹ Biotechnology and pharmaceutical organizations that are currently achieving efficient clinical trial cycle times attribute their success to the following "best practices"¹:

- Maintaining focus on core competencies
- Prioritizing the utilization of resources
- Outsourcing services

The utilization of standardized performance metrics by the drug development industry to reduce clinical development times and to improve clinical trial deliverables is essential to its success. Sponsors and service providers need to effectively manage and track their resources, including people, time, and money, as each has an impact on productivity and efficiency over the course of a clinical trial.

Building Partnerships Around Standardized Performance Metrics

Biotechnology, pharmaceutical, and service provider organizations have joined together to form a not-for-profit organization, the Metrics Champion Consortium (MCC), where member organizations work collaboratively to develop and implement a set of standardized performance metrics which aim to improve the efficiency and effectiveness of clinical trials. Implementing standardized performance metrics benefits sponsor and service provider organizations by enabling them to compare clinical trial performance across all of a sponsor's studies, even if they utilize multiple service providers. Together, sponsors and service providers can review performance with the aim to identify both best practice scenarios and opportunities for improvement. Once opportunities for improvement are identified, sponsor/service provider partners can review the specific procedures that determine the process in question and determine appropriate action steps to improve performance.

Throughout the metrics development and implementation process, the MCC provides a safe harbor for biotechnology, pharmaceutical, and service provider organizations to share "best practices" and learn from each other through participation in MCC learning forums and collaborative work groups.

MCC ECG Performance Metrics – Mission Statement

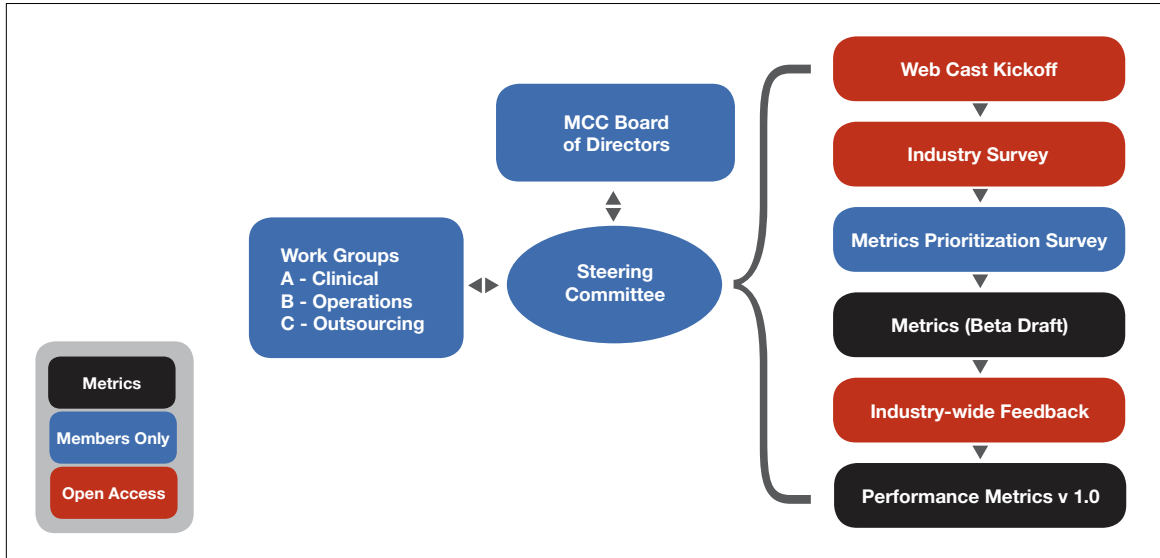
To develop and support a baseline set of ECG performance metrics provided by service providers within the biotechnology and pharmaceutical industry with the intent to jointly encourage the sponsors, service providers, investigative sites, and equipment manufacturers in gaining performance improvement, effectiveness, efficiency, and appropriate levels of controls in support of the drug development process.

MCC ECG Performance Metrics Development Process

In 2006, a group of sponsors, ECG Core Labs, and other ECG-related service providers began developing a set of standardized MCC ECG Performance Metrics. The group worked together on a Steering Committee and in three Working Groups to develop a draft set of standardized ECG performance metrics [Figure 1].

1. Kaitin KI. "Pushing the Innovation Envelope: Drug Development Metrics and the Changing Dynamics of Pharmaceutical R&D." Presented at the 6th Annual Pharmaceutical Metrics Event: Driving Quality, Cost, & Time; October 16-18, 2007; Cambridge, MA.

Figure 1. MCC Metrics Development Process Model



In January 2007, the MCC ECG Performance Metrics Steering Committee shared the MCC ECG Performance Metrics (beta version) with the industry at a national conference and invited organizations to provide comments regarding the proposed set of metrics. In October 2007, after reviewing industry feedback, the MCC released the ECG Performance Metrics version 1.0 [Figure 2].

Figure 2. MCC ECG Performance Metrics (v 1.0)

Metric	Metric Title	Metric	Metric Title
1	Average number of days from ECG study award to contract signature	9	% of ECGs received from one study that were interpretable by the core lab
2	Average number of days from signed ECG TSD signature to vendor ready to receive ECGs	10	% of manual adjustments of automated QT annotations from one study
3	% of on-time ECG equipment shipments to sites	11	% of ECG equipment failure
4	% of sites who conduct a successful test ECG transmission prior to 1st subject visit	12	Average turnaround time on replacing faulty ECG equipment
5	% of ECGs reported to Investigator Sites within agreed turnaround time	13	% of on-time, accepted ECG file transfers
6	% of ECG data queries from vendor to site	14	Key ECG core lab personnel turnover during protocol
7	Turnaround time on resolution of ECG site queries from central vendor	15	% of ECG core lab audit/assessment findings closed within agreed timelines
8	% of ECG alerts successfully communicated to sites within defined turnaround time	16	Average percent of variance maintained in the ECG budget

Why Did AstraZeneca and ERT Decide to Collaborate in Utilizing the MCC ECG Performance Metrics?

AstraZeneca and ERT agreed to collaborate in utilizing MCC ECG performance metrics with the expectation that metrics would enhance their already existing long term collaboration. Both organizations strongly believed that metric utilization would:

- Facilitates constructive conversations among all parties
- Enables each organization to become more productive by supporting continuous improvement programs
- Builds a collaborative culture between AZ and ERT that strengthens the sponsor/service provider partnership

From the sponsor perspective, implementing MCC metrics leads to

- Better insight into services provided by the core lab
- Enhanced understanding of a core lab's internal processes
- Improved monitoring of the core lab's ability to meet critical timelines
- Transparency to operational procedures needed to compare and analyze results across all types of studies
- Visibility to areas of interest that allow both sponsor and core lab to proactively identify and apply process improvements
- Enhanced partnership relationships through improved and open communication among all parties

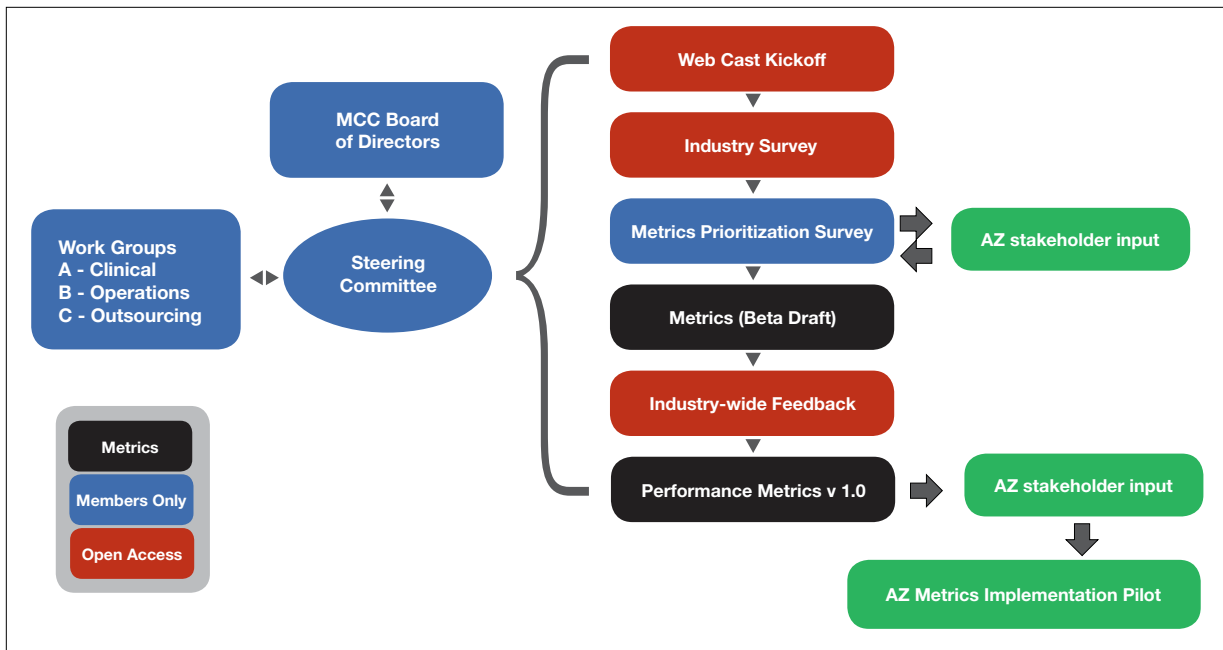
From the service provider perspective, implementing MCC metrics leads to

- Identification of a client's business requirements
- Visibility of sponsor to areas for internal process improvements and/or training opportunities
- Improved transparency and appreciation of how services are delivered not just that they are delivered
- Greater focus on achieving meaningful process improvement
- Higher customer satisfaction

MCC ECG Performance Metrics Development

AstraZeneca and ERT participated in the development of the MCC ECG Performance Metrics (beta and version 1.0) through their representatives on the MCC ECG Metrics Steering Committee, as well as the three work groups (Clinical, Operations and Outsourcing WGs). To ensure that various AstraZeneca stakeholders' views were represented in the metrics development process, the AstraZeneca Global Account Manager for the ECG Relationship gathered input from a diverse network of key experts and stakeholders within their organization, including the following: global and operational study delivery teams, data management staff, QT vendor taskforce representatives and the QT strategy group of scientists [Figure 3].

Figure 3. MCC ECG Metrics Development Process



The feedback solicited was provided to the MCC ECG Steering Committee and later used during the implementation phase with AstraZeneca’s partner ERT.

The AstraZeneca / ERT Performance Metrics Pilot Project: Metrics Selection and Implementation

Following the release of the MCC ECG Performance Metrics (v 1.0) in early 2007, AstraZeneca and ERT decided to implement the ECG metrics in a 2-step approach, beginning with pilot program of five metrics. This pilot approach gave AstraZeneca time to ensure that preliminary discussions provided a solid foundation for the successful launch of the metrics within the organization. The following critical areas were addressed at the beginning of the pilot to ensure successful implementation of the metrics:

- Senior management sponsorship of a consistent and collaborative approach to utilizing Performance Metrics across Clinical Trial services
- Resource allocation to manage ECG performance metric results, including accountability for stakeholder input, metric analysis and internal reporting
- Strategy for managing internal stakeholder expectations for metrics utilization and reporting
- Early involvement of a broad array of key stakeholders to create “buy-in” during the metrics development process

The two organizations worked together to determine which MCC ECG metrics to include in the pilot program. Both organizations agreed that initially the selected metrics would be used by the AstraZeneca Global Account Manager and ERT to retrospectively establish baseline values from which to identify any immediate trends. The longer-term goal was to use the performance metrics to identify areas for AstraZeneca and ERT to improve their joint processes, ensure a high degree of quality, and enhance the operational working relationship at the study team level. The AstraZeneca / ERT team limited the number of metrics included in the pilot study, in order to ensure that both parties had sufficient time and resources needed to review data, evaluate outliers, and develop action plans to address issues.

AstraZeneca, in close collaboration with ERT, carefully reviewed each MCC ECG Performance Metric in the context of how and if the data collected would be used and distributed. This assessment and dialogue was the most critical and valuable component of the metric implementation and pilot project. The areas considered included the following:

- **“Action-ability” Factor.** Would improvement or lack thereof impact speed, quality & cost?
- **Key Stakeholders Value.** What is the potential value of monitoring the metric
- **Utilization Strategy & Resources Allocation.**
 - Tactical: Does the metric solve for issues in real time?
 - Strategic: Does the metric identify Sponsor/Supplier trends, provide data for opportunity of root cause analyses, action plans, etc.?
- **Metric Availability and Implementation Complexity.** Identification of “retrospective” and “prospective” metric data collection plans based on electronic vs manual attainability and complexity to implement:
 - How much immediate manual manipulation was required?
 - Is the metric “turnkey” in terms of collection of data?
 - Is the metric of immediate value to both organizations in terms of prioritization?

After reviewing the input, AZ in collaboration with ERT decided to include the five MCC ECG Performance Metrics highlighted in purple in Figure 4.

Figure 4. MCC ECG Performance Metrics (v 1.0) Selected for AstraZeneca / ERT Pilot

Metric	Metric Title	Metric	Metric Title
1	Average number of days from ECG study award to contract signature	9	% of ECGs received from one study that were interpretable by the core lab
	Average number of days from signed ECG TSD signature to vendor ready to receive ECGs	10	% of manual adjustments of automated QT annotations from one study
	% of on-time ECG equipment shipments to sites	11	% of ECG equipment failure
	% of sites who conduct a successful test ECG transmission prior to 1st subject visit	12	Average turnaround time on replacing faulty ECG equipment
5	% of ECGs reported to Investigator Sites within agreed turnaround time	13	% of on-time, accepted ECG file transfers
6	% of ECG data queries from vendor to site	14	Key ECG core lab personnel turnover during protocol
7	Turnaround time on resolution of ECG site queries from central vendor	15	% of ECG core lab audit/assessment findings closed within agreed timelines
8	% of ECG alerts successfully communicated to sites within defined turnaround time	16	Average percent of variance maintained in the ECG budget

The AstraZeneca / ERT team reviewed the results of the selected metrics and determined that all of the selected metrics were reported to be at or better than the agreed upon targets [Figure 5]. The team utilized a green/yellow/red color coding system to make it easy to identify areas of concern. According to the color coding system, a yellow or red flag indicated that the team needed to investigate the underlying cause(s) for suboptimal results and develop an action plan to address the issues. Depending on the metric, service delivery problems could be related to any or all of the following areas:

- Core lab
- Site
- Sponsor
- Protocol
- Communication

In 2007, all five performance metrics received a green code signifying the results were within the target range.

Figure 5. Summary Results of AZ / ERT ECG Performance Metrics

Metric	Metric Title	Target	2007
1	Average Number of Days from ECG Study Award to Contract Signature	Per Contract	Green
2	Average Number of Days from signed ECG technical specifications document (TSD) Signature to Vendor Ready to Receive ECGs	Per Contract	Green
5	Percentage of ECGs Reported to Investigator Sites within Agreed Turnaround Time	>95%	Green
9	Percentage of ECGs from one study that were interpretable by the core lab	>99.5%	Green
13	Percentage of On-Time, Accepted ECG File Transfers	>95%	Green

Green = At or better than target **Yellow** = Close to achieving target **Red** = Did not achieve target

The AstraZeneca / ERT pilot team concluded that this was a valuable experience for both organizations. In analysis of the results, the collective team learned that it was important to work together to comprehend the true meaning of the metric formula and the results. Both organizations found that it was important to build in time for a joint analysis of the results at the study level to determine if data were consistent across all studies or being skewed by a particular study. Overall, the MCC ECG metrics pilot provided a positive platform for dialogue and an invaluable tool for monitoring and measuring performance.

AstraZeneca / ERT ECG Performance Metrics Phase 2: Additional Metrics Selection and Implementation

After implementing the pilot metrics, AstraZeneca and ERT worked together to determine which of the remaining MCC ECG Performance Metrics should be added to the 2008 MCC ECG Performance Metrics report. AstraZeneca asked ERT to provide feedback on the following questions:

- Which metrics were easy to report?
- Which metrics required some additional work to report?
- Which metrics were challenging to produce?

After a review of ERT’s response, AstraZeneca requested that ERT add MCC ECG Performance Metrics # 6, 8,14 and 15 to the performance metrics report to enable the organizations to view a more complete picture of the process. [Figure 6].

Figure 6. MCC ECG Performance Metrics (v 1.0) Selected for 2008 AZ / ERT Program

Metric	Metric Title	Metric	Metric Title
1	Average number of days from ECG study award to contract signature	9	% of ECGs received from one study that were interpretable by the core lab
	Average number of days from signed ECG TSD signature to vendor ready to receive ECGs	10	% of manual adjustments of automated QT annotations from one study
	% of on-time ECG equipment shipments to sites	11	% of ECG equipment failure
	% of sites who conduct a successful test ECG transmission prior to 1st subject visit	12	Average turnaround time on replacing faulty ECG equipment
5	% of ECGs reported to Investigator Sites within agreed turnaround time	13	% of on-time, accepted ECG file transfers
6	% of ECG data queries from vendor to site	14	Key ECG core lab personnel turnover during protocol
7	Turnaround time on resolution of ECG site queries from central vendor	15	% of ECG core lab audit/assessment findings closed within agreed timelines
8	% of ECG alerts successfully communicated to sites within defined turnaround time	16	Average percent of variance maintained in the ECG budget

The organizations agreed on an implementation schedule that provided a realistic workload for both parties – to ensure that ERT could provide appropriate, accurate metrics, and that AstraZeneca had the appropriate resources to examine and act on them. AstraZeneca did not alter the metrics to make them AstraZeneca / ERT specific but utilized the data that was available.

The AstraZeneca / ERT ECG Performance Metrics: Phase 2 Results

In 2008, ERT collected and reported to AstraZeneca nine of the sixteen MCC ECG Performance Metrics [Figure 7]. They continued to utilize the color coded reporting system developed in the pilot phase: yellow or red flags indicated that the team needed to investigate the underlying cause(s) for suboptimal results and develop an action plan to address the issues. All nine performance metrics received a green code signifying the results were within the target range. ERT was able to retrospectively report 2007 results for most of the nine metrics, although 2007 data was not available for metric 14.

Figure 7. Summary of AZ / ERT ECG Performance Metrics

Metric	Metric Title	Target	2007	2008
1	Average Number of Days from ECG Study Award to Contract Signature	Per Contract	Green	Green
2	Average Number of Days from signed ECG technical specifications document (TSD) Signature to Vendor Ready to Receive ECGs	Per Contract	Green	Green
5	Percentage of ECGs Reported to Investigator Sites within Agreed Turnaround Time	>95%	Green	Green
6	Percentage of ECG Data Queries from Vendor to Site	<20%	Yellow	Green
8	Percentage of ECG Alerts Successfully Communicated to Sites within defined TAT	>95%	Green	Green
9	Percentage of ECGs from one study that were interpretable by the core lab	>99.5%	Green	Green
13	Percentage of On-Time, Accepted ECG File Transfers	>95%	Green	Green
14	Key ECG Core Lab Personnel (Project Management and Over Readers) Turnover during Protocol	Minimal	Data Not Available	Green
15	Percentage of ECG Core Lab Audit Findings Closed within Agreed Timelines	Minimum: >95%	Green	Green
<p>Green = At or better than target Yellow = Close to achieving target Red = Did not achieve target</p>				

Metric 6 (Percentage of ECG Data Queries from Vendor to Site).

The AstraZeneca / ERT team discussed the results of Metric 6 (Percentage of ECG Data Queries from Vendor to Site). Although Metric 6 was a new metric added to the AstraZeneca data report in 2008, ERT was able to go back and report results based on 2007 data. As noted in Figure 7, ERT reported a percentage rate above the <20% of ECG Data Queries from Vendor Site target rate (yellow designation). However, by 2008 the query rate had improved enough that the results fell within the <20% target range (green designation). What happened to improve the results?

- Fewer number of start-up studies
- Increased efforts to call sites and train site staff

The team agreed to monitor the query rates to ensure the percentage rate remains less than the 20% target point **while producing high quality ECG data.**

Executive Summary

AstraZeneca and ERT agreed to collaborate in utilizing MCC ECG performance metrics within their partnership with the expectation that metrics would enhance their already existing long term collaboration. Both organizations strongly believed that metric utilization would:

- Facilitate constructive conversations among all parties
- Enable each organization to become more productive by supporting continuous improvement programs
- Build a collaborative culture between AstraZeneca and ERT that strengthens the sponsor/ service provider partnership

The full list of fifteen MCC ECG Performance Metrics seemed daunting at first, so the two organizations decided to utilize a phased approach to ensure that the implementation process was easy and the outcomes would be beneficial to both parties. During the pilot phase, the organizations worked together to identify five MCC ECG metrics to implement. After setting outcome parameters, the metrics were measured and a red/yellow/green color coding reporting system was created to track performance. The pilot program was successful – all five performance metrics received a green code, signifying that the results were within the target range.

Based on the success of the pilot, AstraZeneca and ERT decided to proceed with the second phase, and an additional four MCC ECG metrics were added to the performance metrics report. The phase two program was successful – all nine MCC ECG performance metrics were measured and received a green code, signifying that the results were within the target range.

The phased pilot process worked well for both organizations; it allowed for meaningful discussions on how the metric data would be collected, in what way the metric formula would be used, and how both organizations planned to use the data. From a practicality perspective, it would have been difficult to collect and review the entire set of fifteen MCC ECG metrics at the beginning. It was better for these organizations implement a pilot phase and build the program from the solid foundation. Overall, both parties agreed that this process has strengthened the partnership between the organizations.

Metric	Metric Title
1	Average number of days from ECG study award to contract signature Note: For stand-alone ECG projects
2	Average number of days from signed ECG technical specifications document (TSD) signature to vendor ready to receive ECGs
3	Percentage of on-time ECG equipment shipments to sites
4	Percentage of sites who conduct a successful test ECG transmission prior to 1st subject visit
5	Percentage of ECGs reported to Investigator Sites within agreed turnaround time
6	Percentage of ECG data queries from vendor to site
7	Turnaround time on resolution of ECG site queries from central vendor
8	Percentage of ECG alerts successfully communicated to sites within defined turnaround time
9	Percentage of ECGs received from one study that were interpretable by the core lab
10	Percentage of manual adjustments of automated QT annotations from one study (semi-automatic “computer assisted” method with visual inspection and manual adjustment whenever necessary)
11	Percentage of ECG equipment failure
12	Average turnaround time on replacing faulty ECG equipment
13	Percentage of on-time, accepted ECG file transfers
14	Key ECG core lab personnel turnover during protocol
15	Percentage of ECG core lab audit/assessment findings closed within agreed timelines
16	Average Percentage of variance maintained in the ECG budget

© 2008 Metrics Champion Consortium, Inc. All rights reserved

Metrics Champion Consortium
 706 Pro-Med Lane, Suite 100
 Carmel, IN 46032
 [office] 317.848.2908
 [fax] 317.848.8861
www.metricschampion.org