

***An Industry-wide Effort of Pharmaceutical,
Biotechnology and Service Providers to
Develop and Implement Standardized
Clinical Performance Metrics to Drive
Process Improvement and Enhance
Partnership Performance***

Linda Sullivan, MCC VP Operations

December 3, 2009



Agenda

- Metrics Champion Consortium Overview
- MCC Clinical Trial Performance Metrics
- ECG Case Study
- Q&A



Industry Under Pressure to Improve R&D Productivity

Today's drug development industry is under increased pressure to improve R&D development performance/ strategies by reducing drug development times and costs, while at the same time increasing productivity and maintaining quality.



Building Partnerships Around Standardized Performance Metrics

A group of biotechnology, pharmaceutical and service provider organizations helped form a not-for-profit organization, the Metrics Champion Consortium (MCC).



MCC Mission

The mission of MCC is to develop, through a collaborative process, performance metrics within the Biotechnology and Pharmaceutical industry with the intent to **jointly** encourage performance improvement, effectiveness, efficiency, and appropriate levels of controls for both Sponsors and Service Providers in support of the drug development process.



MCC Board of Directors

- Brian Schrock, Eli Lilly (Chair)
- Karolyn Jackson, AstraZeneca
- Jeffrey Litwin, MD, ERT
- Guy Mascaro, MCC President
- Nick Astley, Pfizer
- Sean Larkin, PharmaNet (ACRO rep)
- Paul Colvin, PPD (ACRO rep)
- Julia Amo, formerly Valeant Pharmaceuticals (consultant)



Participating Organizations

<ul style="list-style-type: none">• Abbott• AstraZeneca• Biogen Idec• Bio-Imaging Technology• Biomedical Systems• Cardialysis• Cardinal Health• Cardioanalytics• Cardiocore• Cerexa• CHDI Foundations• ClearTrial• Covance• CRL Medinet• Duke Clinical Research Institute	<ul style="list-style-type: none">• Eli Lilly• ERT• Esoterix• Eurofins Medinet• Genzyme• Genentech• i3• ICON• Inc Research• Incyte• M2S• Macrogenics• MDS Pharma• Medarex• Merck• NERI	<ul style="list-style-type: none">• Novartis• Paragon Biomedical• Perceptive Informatics• Pfizer• PharmaNet• PPD• Quest Diagnostics• Rad-MD• RadPharm• Regeneron• Social & Scientific Systems, Inc.• Spacelabs• Synarc• TranSenda• Virtual Scopics• WorldCareClinical
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Collaboration with Other Industry Groups

- ACRO representation to the MCC Board of Directors
- CDISC
- FDA
- PhRMA
- Research Initiatives Foundation for the NIH
- eClinical Forum
- SCDM



MCC Value Proposition

- MCC organizations work collaboratively to develop standardized performance metrics which aim to improve the efficiency and effectiveness of clinical trial operations *for each* sponsor/supplier relationship.
- Organizations use the standardized performance metrics to identify opportunities to improve performance within their own sponsor / supplier relationship where results do not meet expectations within a study or across a group of studies.

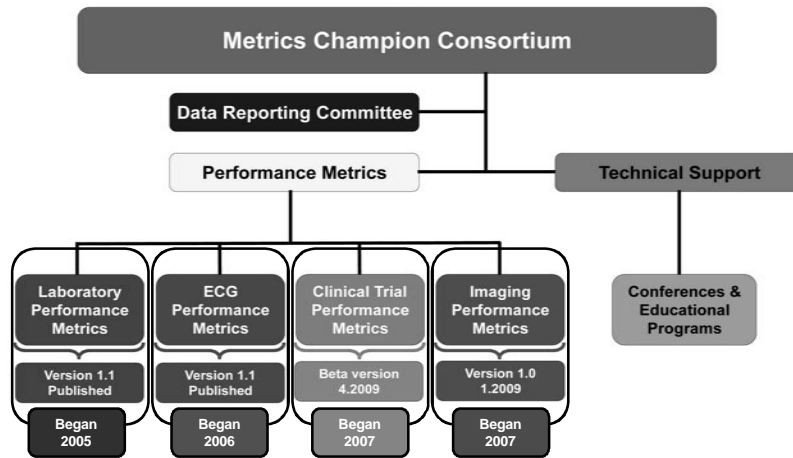


MCC Value Proposition

- After identifying opportunities for improvement, sponsor/service provider partners work together to determine how best to enhance the process in order to ***improve performance and strengthen their partnership.***
- The MCC provides an environment 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.



Overview of MCC Activities



MCC Clinical Trial Performance Metrics Initiative



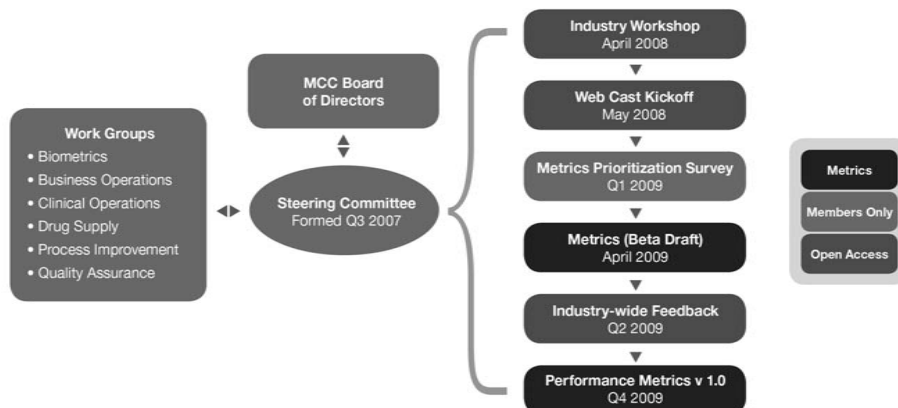
Clinical Trial Performance Metrics (Beta version)

Purpose of MCC Clinical Trial Performance Metrics:

- Create a set of performance metrics that are **key indicators** of performance that are utilized by sponsor/service provider partnerships to manage clinical trial performance
- Constructive conversations are generated between all parties because of metrics
- Sponsors and service providers grow more productive as a direct result of utilizing MCC metrics



Clinical Trial Performance Metrics Development Timeline





MCC Clinical Trial Metrics Development Oversight

Clinical Trial Metrics Steering Committee

- Cory Gutterman / Abbott
- Ed Cannon / AstraZeneca
- Jennifer Holmes / Eli Lilly
- Colleen McCoy / Genentech
- Keith Dorricot / i3
- Pam Howard / ICON Clinical Research
- Kathe Balinski / Medarex
- Magaly Woolard / Merck
- April Davis / Perceptive Informatics
- Lorraine Waring / Pfizer
- Julie Szabo / PharmaNet



MCC Clinical Trial Metrics Development Work Groups

Clinical Trial Metrics Work Groups

Biometrics WG	Biostatistics & Data Management
Business Operations WG	Business Operations & Finance
Clinical Operations WG	Clinical Operations, Medical Writing & Project Management
Drug Supply WG	Drug Supply
Quality Assurance WG	Quality Assurance



Work Group Participants

Abie Ekangaki	David Rodin	Joan Farrington	Lee Davis	Ned Connell
Allison Houghteling	Dawn East	Joanne Bailey	Li Ding	Nicolle Keally
Andrew Marvuglio	Dawn Porthouse	Joanne Machalaba	Linda Donahoe	Nobuhide Shimizu
Andy Bakker	Deidre Bevard	John Griffin	Linda Dunford	Olga Crowther
April Davis	Diane Mizerak	John Humphreys	Linda Gala	Pam Howard
Beth Cabage	Dianne Laumann	Joseph Giuliano	Linda Stevens	Patric Donaghue
Bonnie Beaver	Elise Kayson	Judith Chiostrri	Lisa Chen	Patty Godfrey
Brenda Muldrow	Dorothy Hartley	Judith Goud	Lorene Bottom	Piper Laird
Brett Bishop	Ed Cannon	Julia Amo	Lori Carman	Randy Krauss
Brian Schrock	Eileen Ryan	Julie Engel	Lorraine Waring	Renee Lafaive
Carol Zhao	Eileen Ryan	Julie Szabo	Louis Grue	Richard Brotherton
Cassandra Kelley	Elizabeth Shewell	Julie Tscharland	Louise Rochon	Richard Musselman
Catherine Elliott	Elizabeth Stankevich	Kate Haratnik	Lynn Watson	Robert Holman
Charles Chesson	Eric Hildebeutel	Kathe Balinski	Magaly G. Woolard	Ronald Knickerbocker
Chili Li	Eric Strait	Karl Kieburz	Marc Hamm	Rose Braxton
Christine Fitzpatrick	Eva Kantanas	Karl Meyer	Mary Baldovsky	Ryan Shortreed
Christopher Oligny	Gary Urban	Karolyn Jackson	Mathew Bryant	Scott Sawicki
Cindy Casaceli	Gene Trimble	Kathy M Haag	Matthew Stephens	Stacy Gletzakos
Colleen McCoy	Gina Petrizio	Kati Gutierrez	Michael Malicsi	Stephanie Chan
Connie Seckel	Goran Kecman	Keith Dorricott	Michael Neidl	Stephen Kay
Connor Blakeney	Gordana Vucinic	Kelly Mizer	Michael Sobczyk	Sunshine Watkins
Cornelia Kamp	Greg Pendell	Kelly Ong	Melika Davis	Tara Coughlan
Cory Gutterman	Guy Mascaro	Kelly Vaillant	Michael Bruns	Teleen Norman
Courtney Bryant	Hannah Legesse	Krista Peters	Michael Friedman	Tess Pangan
Cynthia Hooper	Hartmann Ammann	Kristen Tomita	Michelle Stevens-Brogan	Thomas Purcell
Danie Montinard	Heidi Shea	Kristin Lucas	Mike Lange	Tiffany Crowell
Daniel Christen	Holly Hankins	Kristy Morgan	Mike Soenen	Tracy Mayer
Daniela Popa	Jean Pan	Kristyn Karas	Monica Reddy	Vickie Crocker
Darren Hart	Jeff Marquis	Lakshmi Mahadevan	Monika Frey	Yvonne Baran
David Chambers	Jennifer Sugarman	Larry Blankstein	Morgan Shethah	Yvonne Ulrich
David Polakovs	Jeremy Hemiup	Lauren Freese	Nancy Yeates	



MCC Clinical Trial Metrics Development Process

Each working group was asked to:

- Develop a list of key metrics
- Create metrics that can be **key indicators** of performance
- Clearly define measurement criteria



MCC Clinical Trial Metrics Development Process

Proposed Metric - Qualities

- | | |
|---|---|
| <ul style="list-style-type: none">• Well defined• Be measurable• Be High Level – but allow for further analysis | <ul style="list-style-type: none">• Provide a benefit to Sponsor and Service Provider• Add Value |
|---|---|



UNDER CONSTRUCTION



MCC Clinical Trial Metrics Development Process

Proposed Metric - Qualities

- | | |
|--|---|
| <ul style="list-style-type: none">• Timeliness (T)• Cycle Time (CT)• Efficiency / Cost (E)• Quality (Q) | <ul style="list-style-type: none">• Leading Indicator• Lagging Indicator• Business Driver / Benefit Statement |
|--|---|

Relationship metrics will be added in future version

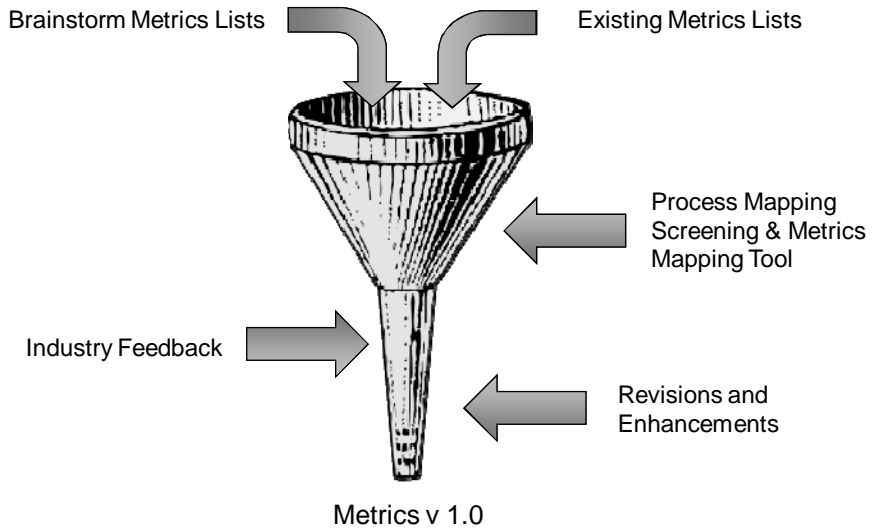


UNDER CONSTRUCTION

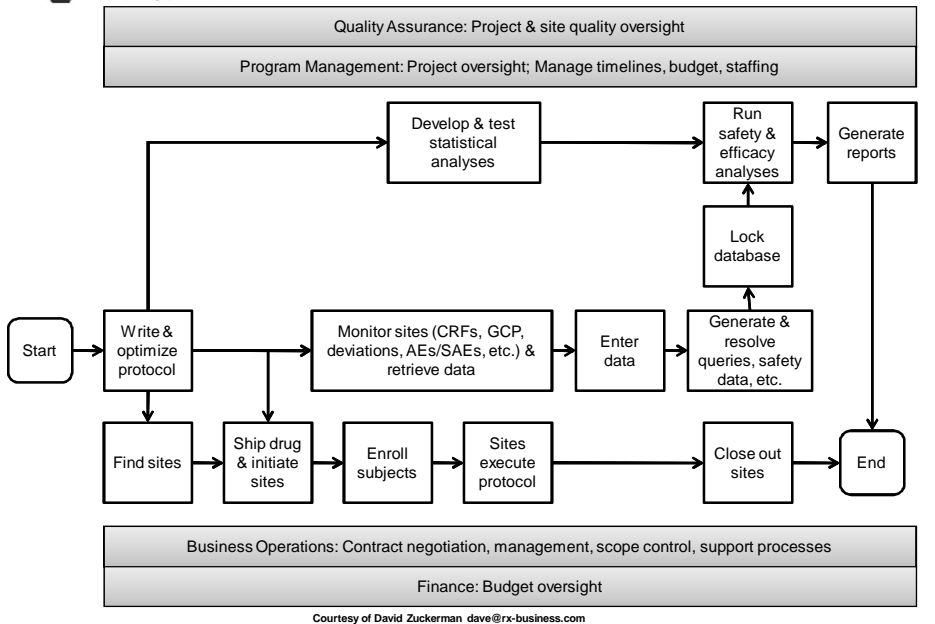




MCC Clinical Trial Metrics Development Process



Typical Trial-Level Process





Metrics Mapping Tool Process/Task Definition Form

Process/Task Name: CRF Data Completed and Entered Group 4a		REVIEWED	
Process/Task Objective: Ensure that CRF Data is entered into the correctly and within an acceptable cycle time.			
Pharma Inputs - Final Protocol - CRF Design or required fields - CRFs	Suppliers DM Bios MW CRF Designer PM	Subtasks in this Process/task Beginning Boundary: Paper: CRF Received by Data Management Site. EDC: Patient Visit completed and/or source docs completed	Products CRFs Discrepancies Listings
Supplier Issues - Poor CRF design - Volume of CRFs to enter - Complexity of CRFs		Subtasks Paper: - Receipt and logging - Scanning/imaging/indexing - Pre-entry processing - 1 st pass entry - 2 nd pass entry - Verification EDC: Viewing Patient Visit Complete Source documents/worksheets collected Entry of data into EDC system Screen/page submitted to EDC system	Customers Data Coordinators Sponsors
CRO Inputs - CRF Design - CRFs - Retrieval Plan - Training - Data entry guidelines - Obvious corrections / self-evident corrections	Suppliers Sponsor Bios MW CRF Designer PM	Ending Boundary: Paper: 2 nd pass entry complete EDC: eCRF submitted to	Metrics (T, CT, Q, E) <ul style="list-style-type: none"> % of paper pages completing 2nd pass entry within target (T, E) Sub-processes: Time from receipt to scanning (CT) Time from scanning to ready for entry (CT) Time from ready for entry to 1 st pass entry (CT) Time from ready for entry to 2 nd pass entry (CT)
Supplier Issues Poor CRF design		Factors that drive cost/cycle time Lack of standardization of CRFs Training and experience of data entry personnel Systems, WAN, and response time CRF design	<ul style="list-style-type: none"> % of eCRFs entered into within target after patient visit (CT) # of discrepancies generated per CRF (Q) Query Rate (Q) to be expanded on Pages double entered/hour/FTE (E) not sure this is universal...is this a single company standard only?

Courtesy of David Zuckerman dave@rx-business.com



Clinical Trial Performance Metrics (Beta version)

Each MCC Clinical Trial Performance Metric has the following components:

Metric Type	Metric Title	Category	Definition	Formula/ Example	Additional analysis on a "for cause" basis:	Metric Indicator	Reporting Detail	Unit of Measure	Reporting Frequency	Target	Business Driver(s)/ Benefit Statement	Comments
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Metrics Type = Cycle Time(CT), Timeliness(T), Quality(Q), Efficiency(E)

Metrics Indicator

- Leading Indicator = End user will use metric to identify opportunities to affect change in the current trial.
- Lagging Indicator = End user will use metric to identify opportunities to affect change in future study trials.

Reporting Detail = Examples of how the data might be reported (i.e. by country, by site, etc.)

Target = Threshold level to prompt further review & discussion



Clinical Trial Performance Metrics (Beta version)

Metric	Metric Title	Metric Indicator	Metric	Metric Title	Metric Indicator
1	Contract finalization and execution timeliness	LAGGING Indicator	9	Cycle time from Site Activation to First Patient First Visit	LAGGING Indicator
2	Final Approved Protocol to Final Approved CRF	LAGGING Indicator	10	Site Productivity	LEADING Indicator
3	Cycle Time protocol approval to first site activated	LEADING Indicator	11	Screen Failure Rate	LEADING Indicator
4	Investigator Site Reg pack approval rate	LEADING Indicator	12	Correct Drug Inventory & Resupply	LEADING Indicator
5	Cycle time from final Protocol Approval to First Patient-First Visit (all sites)	LEADING Indicator	13	% Patients randomized	LEADING Indicator
6	% Planned Sites Activated	LEADING Indicator	14	Patent Retention rate	LEADING Indicator
7	Drug Onsite at Initiation	LEADING Indicator	15	% Sites Prematurely Terminated	LAGGING Indicator
8	Drug Supply Planning	LEADING Indicator	16	Audit Findings	LAGGING Indicator

LAGGING INDICATOR = End user will use metric to identify opportunities to affect change in the future study trials.
LEADING INDICATOR = End user will use metric to identify opportunities to affect change in the current trial.

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Clinical Trial Performance Metrics (Beta version)

Metric	Metric Title	Metric Indicator	Metric	Metric Title	Metric Indicator
17	Final CRF/eCFR to Database "Go Live"	LAGGING Indicator	24	SAP Finalization to Final Pre-lock Blinded TLGs	LAGGING Indicator
18	CRFs Received to Data Entry Complete - Paper	LEADING Indicator	25	TLGs delivered within target date	LAGGING Indicator
19	Patient Visit Complete to eCRF data entered - EDC	LEADING Indicator	26	Determination of project progress versus planned	LEADING Indicator
20	Data discrepancies generated by automated edit checks	LAGGING Indicator * *Could be LEADING Indicator if reported on a monthly basis	27	Invoice and payment timeliness	LEADING Indicator
21	Receipt of Query Response to Database Update Time	LEADING Indicator	28	Issue identification, management and criticality	LAGGING Indicator
22	QC Rounds Required to Meet Target Error Rate	LAGGING Indicator	29	Measure of true change orders and timeliness of execution	LAGGING Indicator
23	LPLV (last patient, last visit) to Database Lock	LAGGING Indicator	30	Budget and pricing accuracy	LAGGING Indicator

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Clinical Trial Performance Metrics (Beta version)

Type of Metrics

- Cycle Time (CT) 13
- Timeliness (T) 6
- Quality (Q) 11
- Efficiency (E) 2

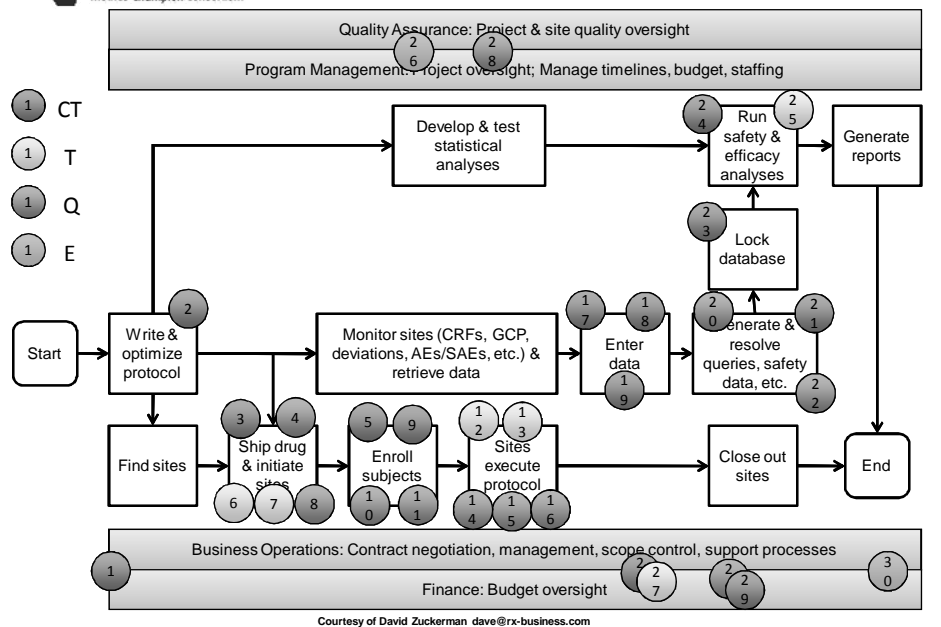
Total 30*

* Note: Metrics 27 & 29 each have 2 metrics

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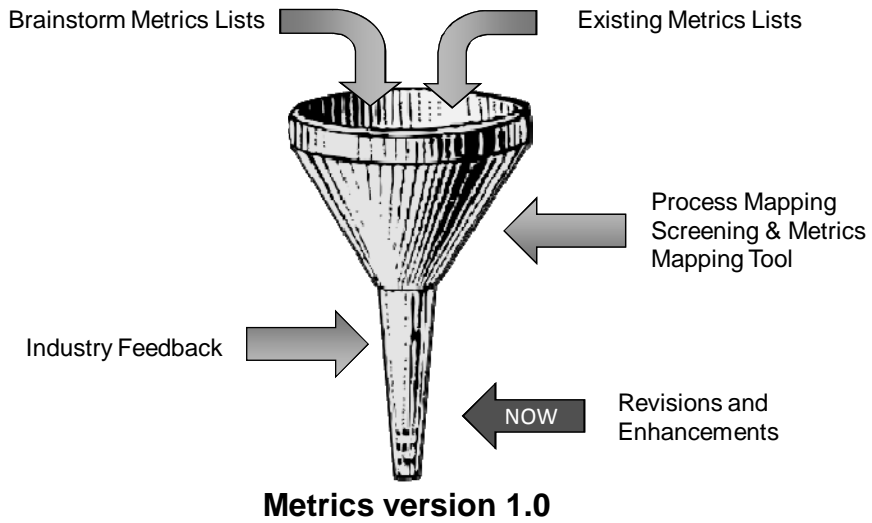


Metrics Distribution





MCC Clinical Trial Metrics Development Process



MCC Clinical Trial Metrics Development Process

Clinical Trial Metrics Work Groups

Process Improvement WG Launched October 2009	Biometrics WG	Biostatistics & Data Management
	Business Operations WG	Business Operations & Finance
	Clinical Operations WG	Clinical Operations, Medical Writing & Project Management
	Drug Supply WG	Drug Supply
	Quality Assurance WG	Quality Assurance



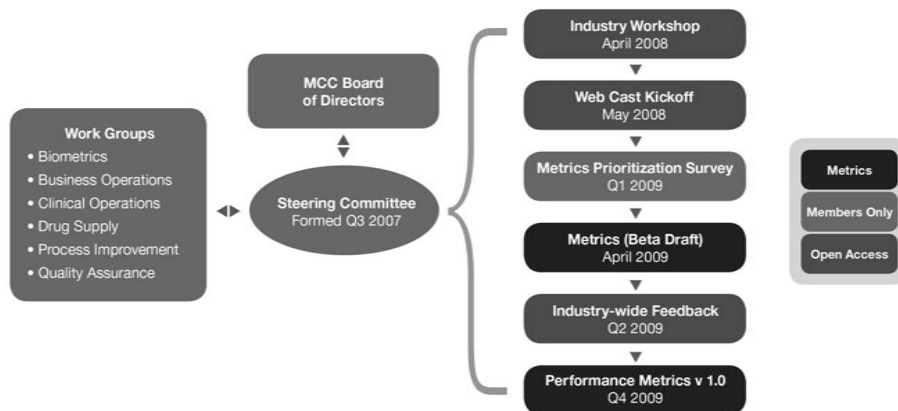
Process Improvement WG Purpose

1. Review the Clinical Trial Performance Metrics (Beta Version) holistically to determine if there are significant gaps in coverage of the clinical trial process where the aim is to improve the overall process
2. Consider the potential pitfalls of use of the metrics and generate guidance on how to use them for greatest impact
3. Assess each of the proposed metrics and determine how it could be used for process improvement. Aim to ensure that data gathering is focused on high-value improvement opportunities

This will feed in to the deliberations of the other Working Groups and the Steering Committee



Clinical Trial Performance Metrics Development Timeline



Expect to release MCC Clinical Trial Performance Metrics version 1.0 Q1 2010



Using MCC ECG Performance Metrics to Improve Sponsor, Site, and Core Lab Clinical Trial Operations



Sponsor / ECG Core Lab Case Study

Why organizations decide to collaborate in utilizing MCC performance Metrics?

- Identify Sponsor's and Core lab's business requirements
- Enhanced understanding of processes
- Improved monitoring of critical deliverables
- Greater focus on achieving meaningful process improvement
- Enhanced communication



Sponsor / ECG Core Lab Case Study

Example 1: Percentage of ECGs reported within agreed turnaround time Target
>95%



Review Steps – Examined the “below target” studies to determine underlying cause(s) of reporting delays

- Many studies missed turnaround time target by less than 1 hour.
- Coordination between Core Lab Operations and Clinical departments not completed efficiently.
- Sponsor protocol requiring only 1 of the 3 ECG copies be reported to Investigative Sites; ECG Core Lab using a manual faxing process to accommodate Sponsor protocol.



Sponsor / ECG Core Lab Case Study

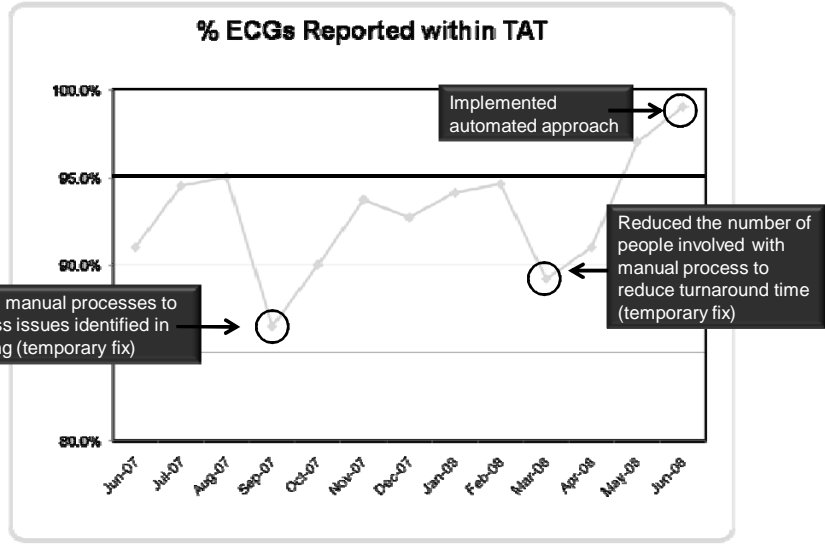
Example 1: Percentage of ECGs reported within agreed turnaround time Target
>95%

Action Steps

1. ECG core lab automated the coordination between internal departments to enable the ECG processing to flow more efficiently
2. ECG core lab updated the “autofax” system to accommodate Sponsor’s protocols

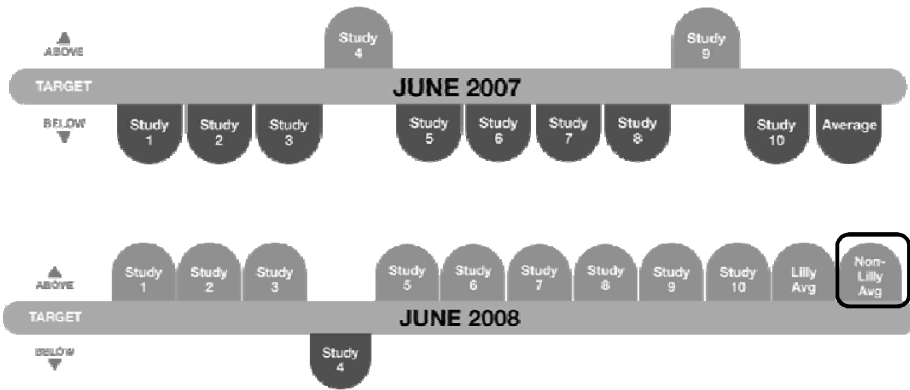


Sponsor / ECG Core Lab Case Study



Sponsor / ECG Core Lab Case Study

Example 1: Percentage of ECGs reported within agreed turnaround time Target >95%





Sponsor / ECG Core Lab Case Study

Example 2: Target
>95%
Percentage of on-time ECG equipment shipments to sites



Review Steps

- **Studies 1 & 6:** These studies had their own equipment so no equipment was being shipped to sites (demonstrating the need to fully understand the studies that are being reported and understanding what the metrics are telling you)
- **Studies 7 & 8:** Found a problem related to how the “on-time” date was established
 - Sponsor set optimistic start dates (which were revised prior to the launching the study)
 - ECG Core lab was using the original start date



Sponsor / ECG Core Lab Case Study

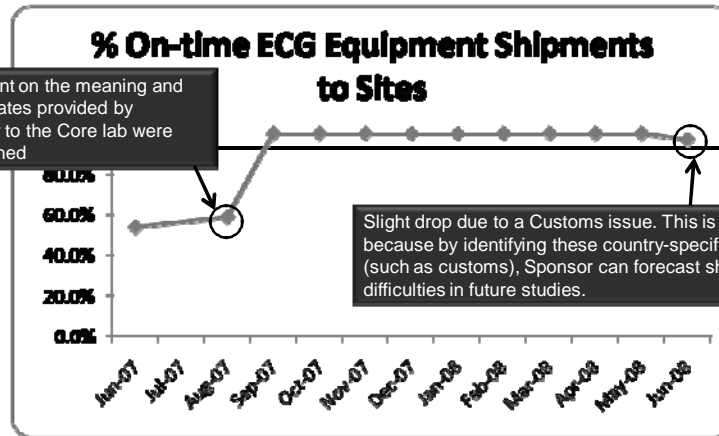
Example 2: Target
>95%
Percentage of on-time ECG equipment shipments to sites

Action Plan

1. ECG Core lab will indicate “*not applicable*” for studies where site-owned equipment is used
2. Sponsor will establish realistic start dates and communicate them to core lab

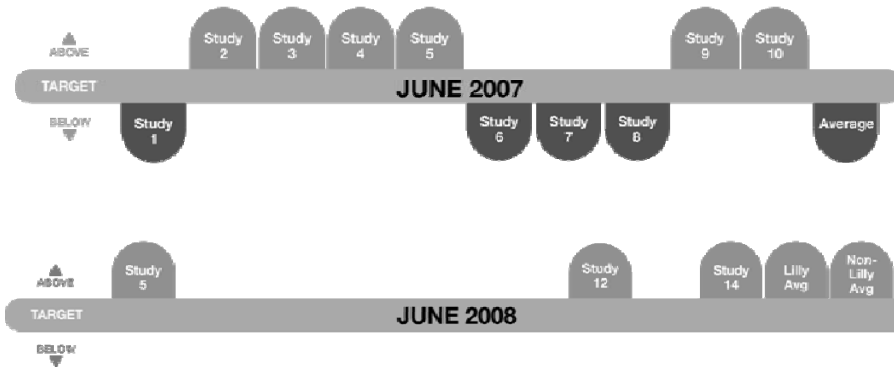


Sponsor / ECG Core Lab Case Study



Sponsor / ECG Core Lab Case Study

Example 2: Target >95%
Percentage of on-time ECG equipment shipments to sites





Risks of Using Performance Metrics

- Failing to identify what the key performance areas really are and wasting time
- Only accepting the metrics on Initial “Face Value” and not looking at underlying reasons
- Sharing metrics without providing explanations
- Failing to understand the processes which lead to the metrics



Rewards of Using Performance Metrics

- Improved Performance
- Improved Communication
- Improved Processes
- Improved Delivery
- Improved Relationship



Key Requirements

- Open, honest communication
- A structured approach (i.e. The MCC)
- Recognition that both vendor and sponsor have areas for improvement
- Understanding of both partners positions
- Willingness to seek *mutual process improvement*
- Acceptance that process improvement can apply to everyone



Conclusions

In 2010, the MCC plans to:

- Release Clinical Trial Performance Metrics (version 1.0)
- Review/revise Central Lab and ECG performance metrics
- Develop additional case studies
- Support metrics implementation among sponsor/service provider partnerships
- Explore developing data reporting templates and industry-blinded database

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Questions?



Please contact Guy Mascaro or Linda Sullivan at 317.848.2908 for additional information about participating in MCC activities.

www.metricschampion.org