



Lab, ECG and Imaging Metrics Adoption, Implementation and Updates

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IIR Central Labs East - Boston, MA

September 22, 2010





Agenda

- MCC Overview
- Metric Initiative Updates
- Central Lab Case Study (Julie DeBus-Levy)
- ECG Case Study (Debbie Walton)
- Panel Discussion



Mission Statement

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 Member Organizations

Abbott Laboratories

AstraZeneca

BARC Global Central Lab

BioClinica

Biogen Idec

Biomedical Systems

CardiaBase

Cardio Analytics

Cardiocare

Carefusion

Cerexa

CHDI

Clinical Reference Laboratory

Clinsys Clinical Research

CoreLab Partners

Covance

Duke Clinical Research Institute

Eli Lilly

ERT

Esoterix Clinical Trial Services

Eurofins Medinet

ExecuPharm

Genentech

Genzyme

i3

iCardiac Technologies

ICON

Imaging Endpoints

INC Research

Incyte

Intrinsic Imaging

Ixico

M2S

MacroGenics

Medidata Solutions

Medtronic

Merck

New England Research Institute

Novartis

Paragon Biomedical

Parexel / Perceptive Informatics

Pfizer

PharmaNet

PPD

Quest Diagnostics

RadMD

Regeneron

Research Point

Roche

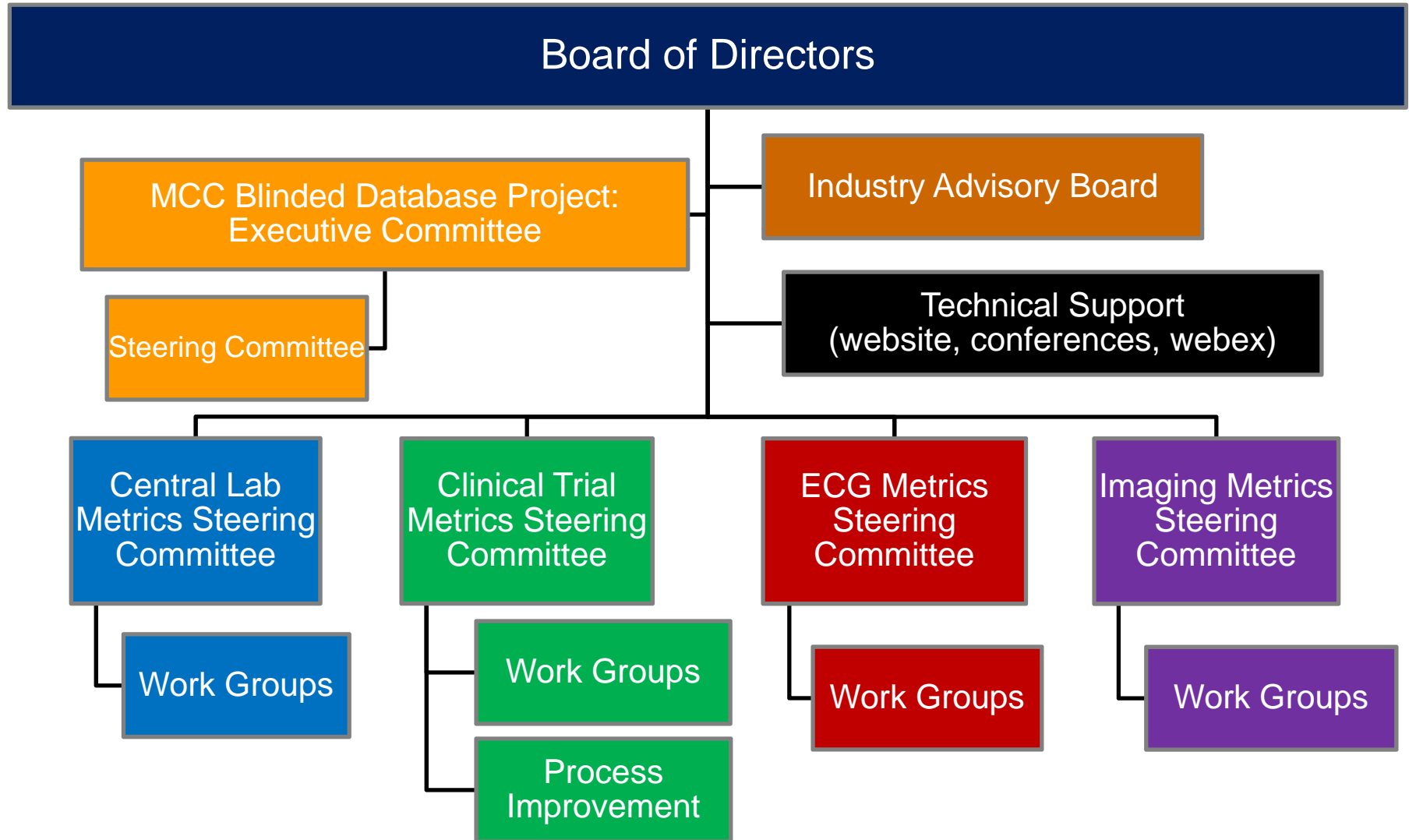
Synarc

Virtual Scopics

WorldCare Clinical

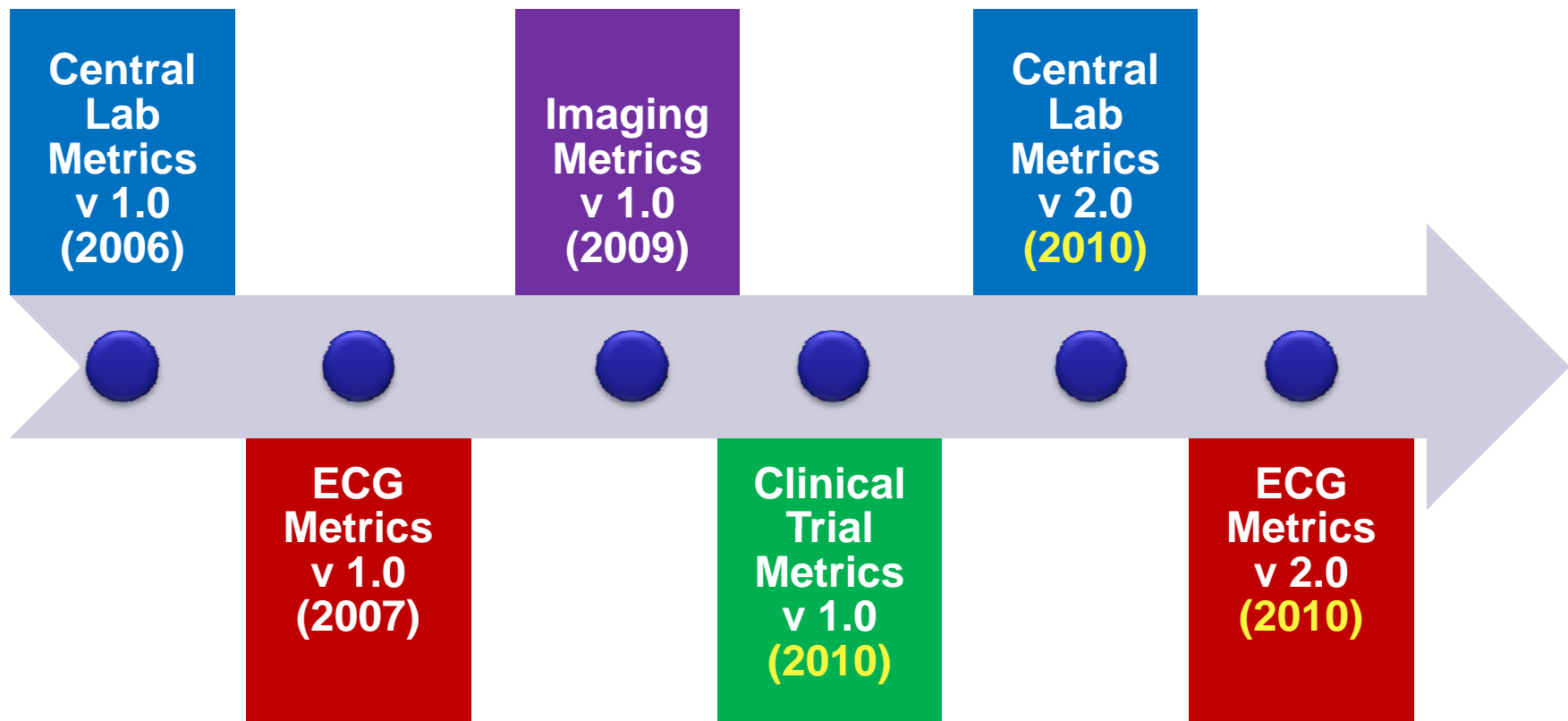


Organizational Structure





Metrics Development Timeline





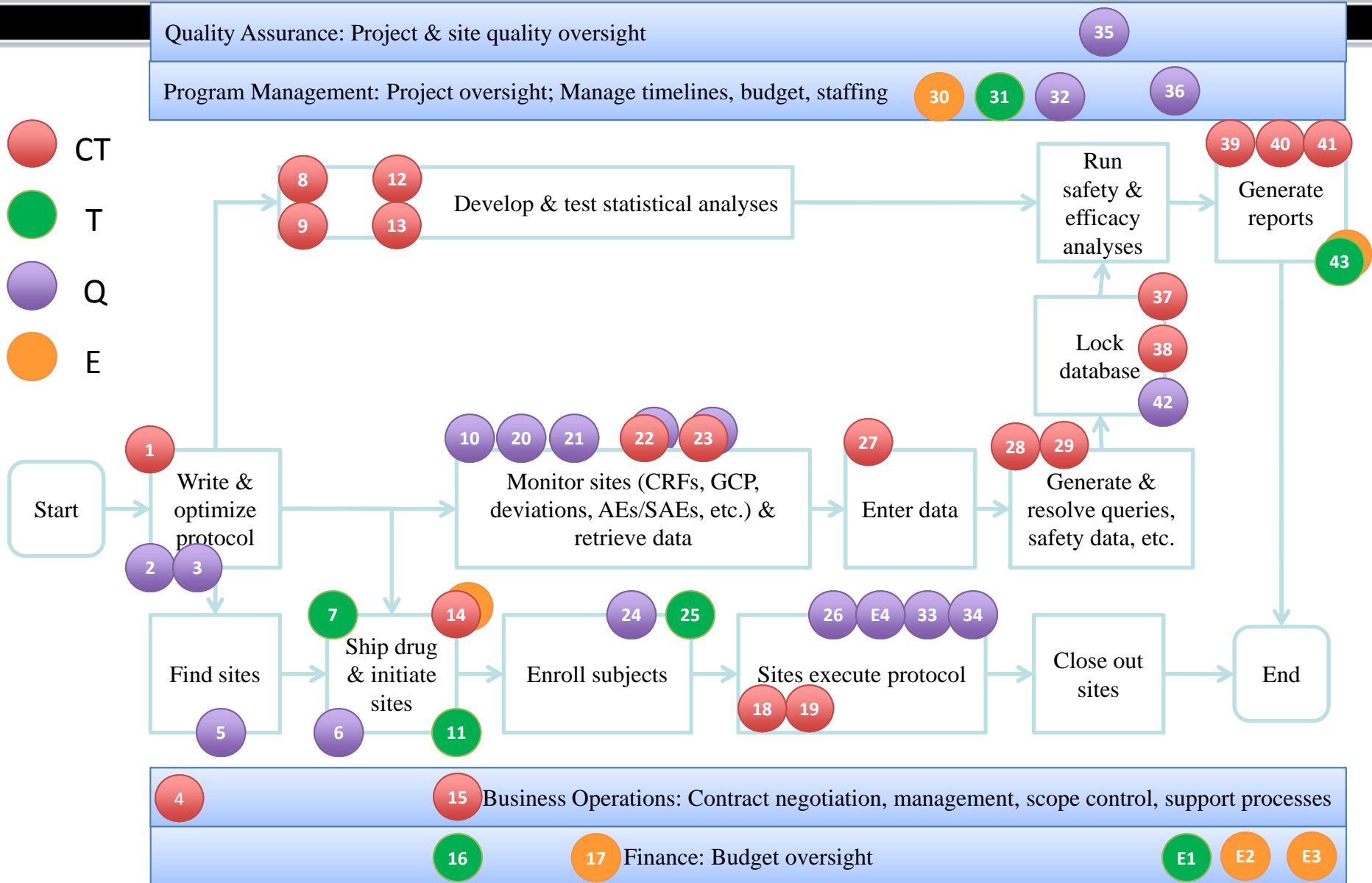
MCC Metric Initiative Updates



**MCC Clinical Trial Performance
Metrics Version 1.0 released
September 16, 2010 ...**

**Lessons Learned Are Already
Being Shared with Lab, ECG
and Imaging Initiatives**

MCC Clinical Trial Performance Metrics v 1.0



Process Improvement WG (launched Fall 2009)

Provides opportunity for MCC Members to work together to develop metrics and tools to drive process improvement

Area of Concern:

Time / Cost / Quality balance needed to avoid sub-optimization

New Approach:

- Created new quality metrics, including protocol writing, site assessment and site quality scoring tools
- Developed MCC companion metrics
- Created *How to use the metrics for process improvement* guidance paper

MCC Lab
Initiative

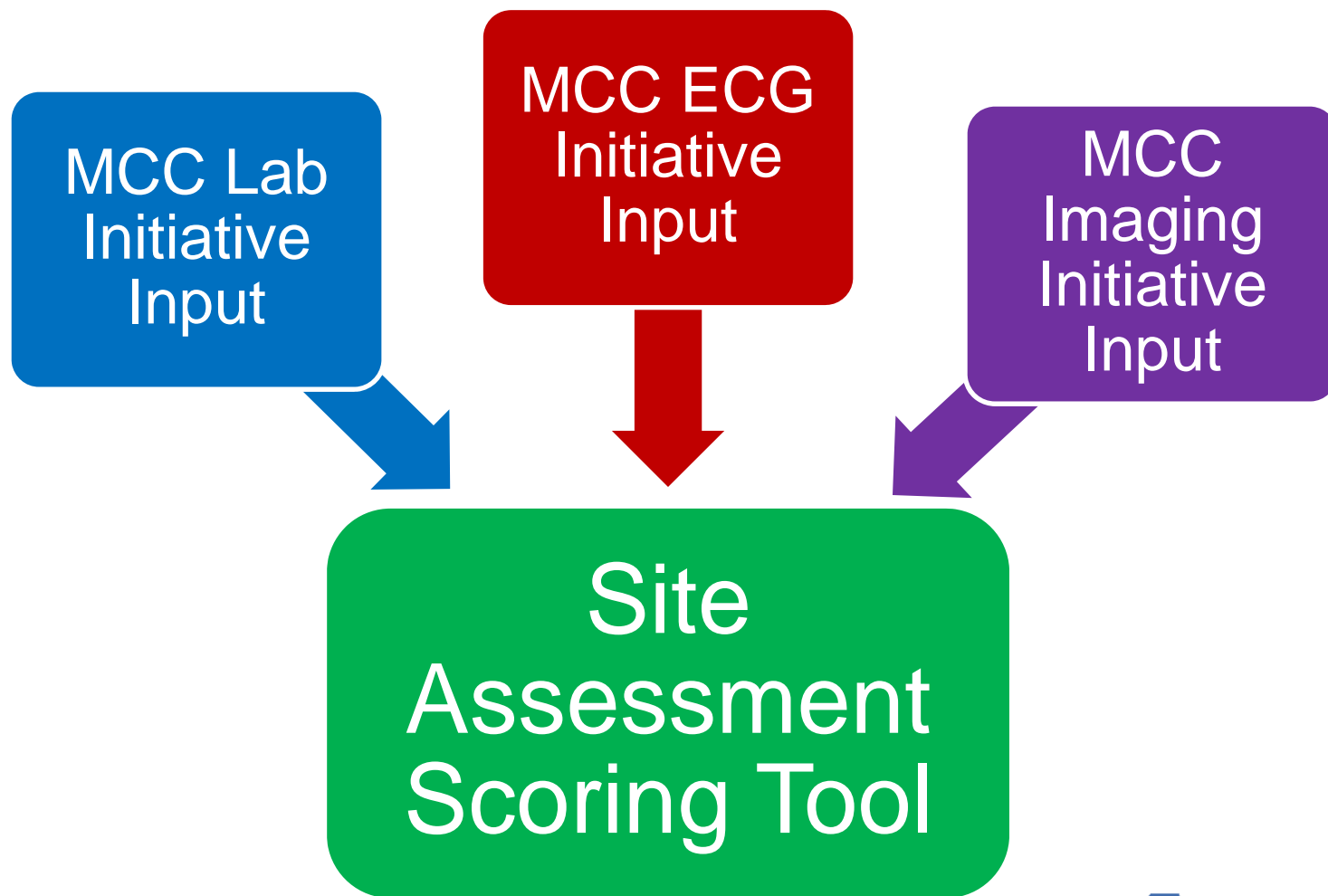
MCC ECG
Initiative

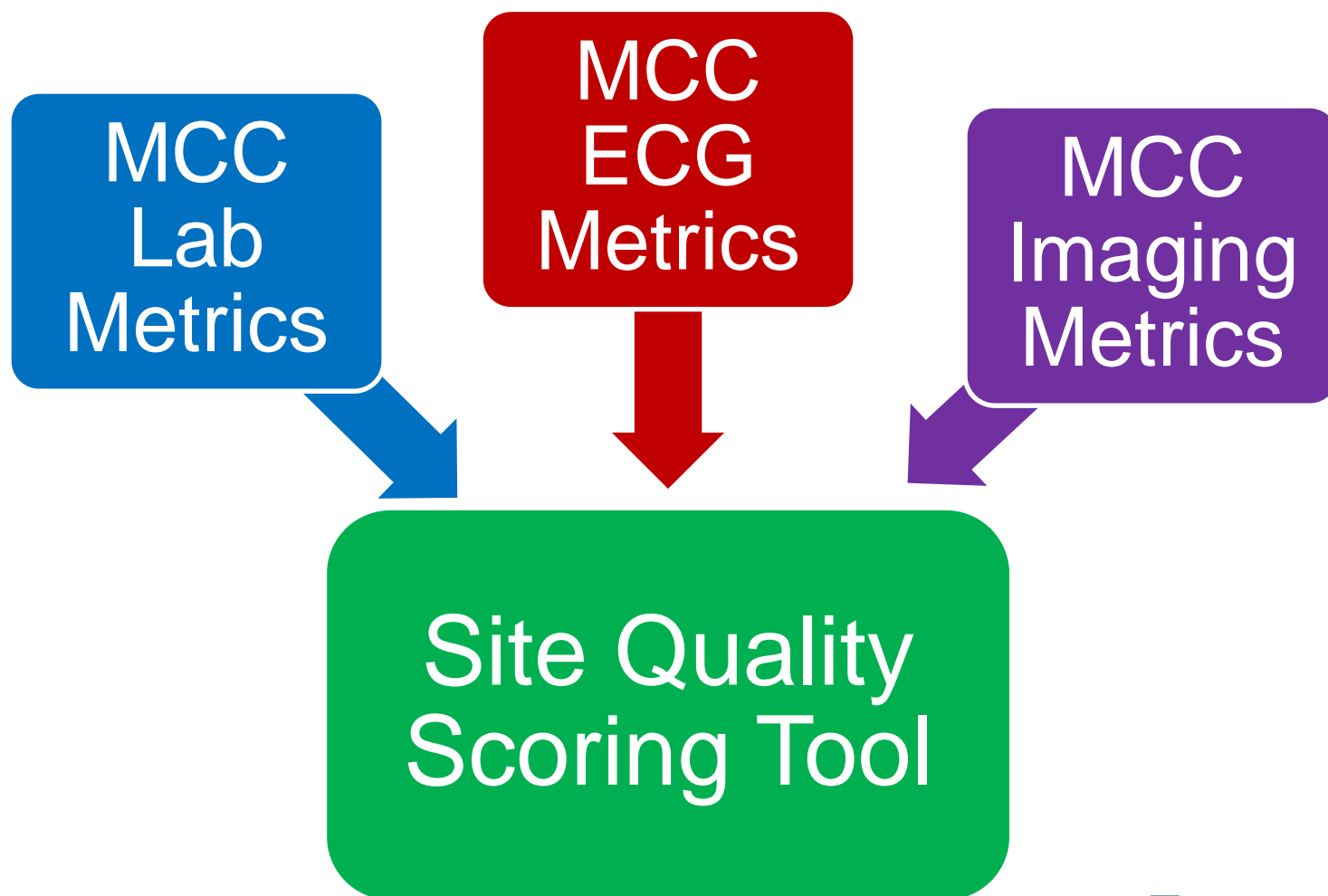
MCC
Imaging
Initiative

**Version 2.0 Updates
will include:**

- Quality metrics
- Site metrics
- MCC Companion metrics

MCC CTPM
Process
Improvement
WG Shared
Learning





- MCC Lab & ECG Metric review processes include:
 - Metric Utilization Survey: how metrics are being used and reported
 - Monthly Metric Review meetings:
 - removal & addition of metrics – including quality metrics
 - level of reporting
 - Site level metrics for Clinical Trial Performance Metrics Quality Scoring Tools (e.g. escalated queries, etc.)
- Supported roll out of metrics across industry
 - Industry conferences (USA and Europe)

- Complete review & release updated versions of MCC Central Lab & ECG Metrics (version 2.0)
 - ECG Initiative considering adding *ECG quality* metrics & expanding metrics into related areas (Ambulatory BPM, Spirometry, etc.)
- Provide **“Lab Initiative”** & **“ECG Initiative”** input to MCC Clinical Trial Performance Metric – Quality Scoring tools
- Develop additional Case Studies
- Promote use of MCC Performance Metrics throughout the Industry

Imaging Metrics Version 1.0 launched in 2009 – efforts shifted to Implementation Phase ...

- Focused on supporting implementation of Imaging Metrics version 1.0
 - Created Imaging Clinical Trial Process Map with Metrics
- Conducted Implementation WG meetings
 - *Metric Utilization Survey*: how metrics are being used and reported
 - Reviewed metrics to determine how vendors are defining and reporting metrics

- Implementation WG – continue to support implementation and foster shared learning
 - Share case studies
 - Discuss areas of concern
- Provide *“Imaging Initiative”* input to MCC Clinical Trial Performance Metric – Quality Scoring tools
- Clinical WG – may reconvene work group to revisit reader variability and/or adjudication metrics



Upcoming MCC Activities

MCC Lab Metrics

- Release Version 2.0
- Input to Quality Tools

MCC ECG Metrics

- Release Version 2.0
- Input to Quality Tools

MCC Imaging Metrics

- Support Version 1.0 Implementation
- Input to Quality Tools

MCC Clinical Trial Metrics

- Support Version 1.0 Implementation
- Pilot Quality Tools
- Continue Process Improvement WG

MCC Member Blinded Database Project

- Develop database structure
- Pilot database



MCC Lab Metrics Case Study

Julie DeBus-Levy

Manager, Outsourcing and Contracts

ABBOTT LABORATORIES



Metric	Category	Metric Title
1	General Operations	Project management turnover
2	Protocol Initiation	Percentage first supplies shipped on time to the first site for first patient
3	Site Initiation	Percentage first supplies shipped on time for all sites (all regions)
4	Data Cleaning	Percentage of queries from central laboratory to site based upon requisitions received
5	Data Cleaning	Average turnaround for resolution of queries from central laboratory to site
6	Site Support Services	Percentage of queries from site to central laboratory based upon requisitions received
7	Site Support Services	Average turnaround time on queries from site to central laboratory

Metric	Category	Metric Title
8	Safety	Percentage of panics that had both 1st attempt made and were successfully communicated to the sites within the defined turn around times
9	Laboratory Operations	Percentage specific test(s) reported within expected turnaround time
10	Laboratory Operations	Percentage tests not reportable
11	Data Management	Percentage on time accepted file transfers
12	Financial Management	Plan, Forecast and Actual Financial Report
13	Financial Management	Comparison of budgeted and actual transportation costs by region and/or country
14	Quality Assurance	Percentage of audit findings closed within sponsor and central laboratory agreed upon timeframe

Financial Management Metric

Comparison of budgeted and actual transportation costs by region and/or country

Minimum: The transportation costs will be added by region and/or country to each of the segments.

Additional analysis on a “for cause” basis:

The transportation costs could be further defined by type (e.g. ambient, frozen and combination).

- % Sites Outside of US/Canada
- Location of Sites
 - Gateway City vs. Outlying City
- Length of Enrollment
- Plan for Shipment of Outbound supplies
 - Use of a central receiving site Ex-US

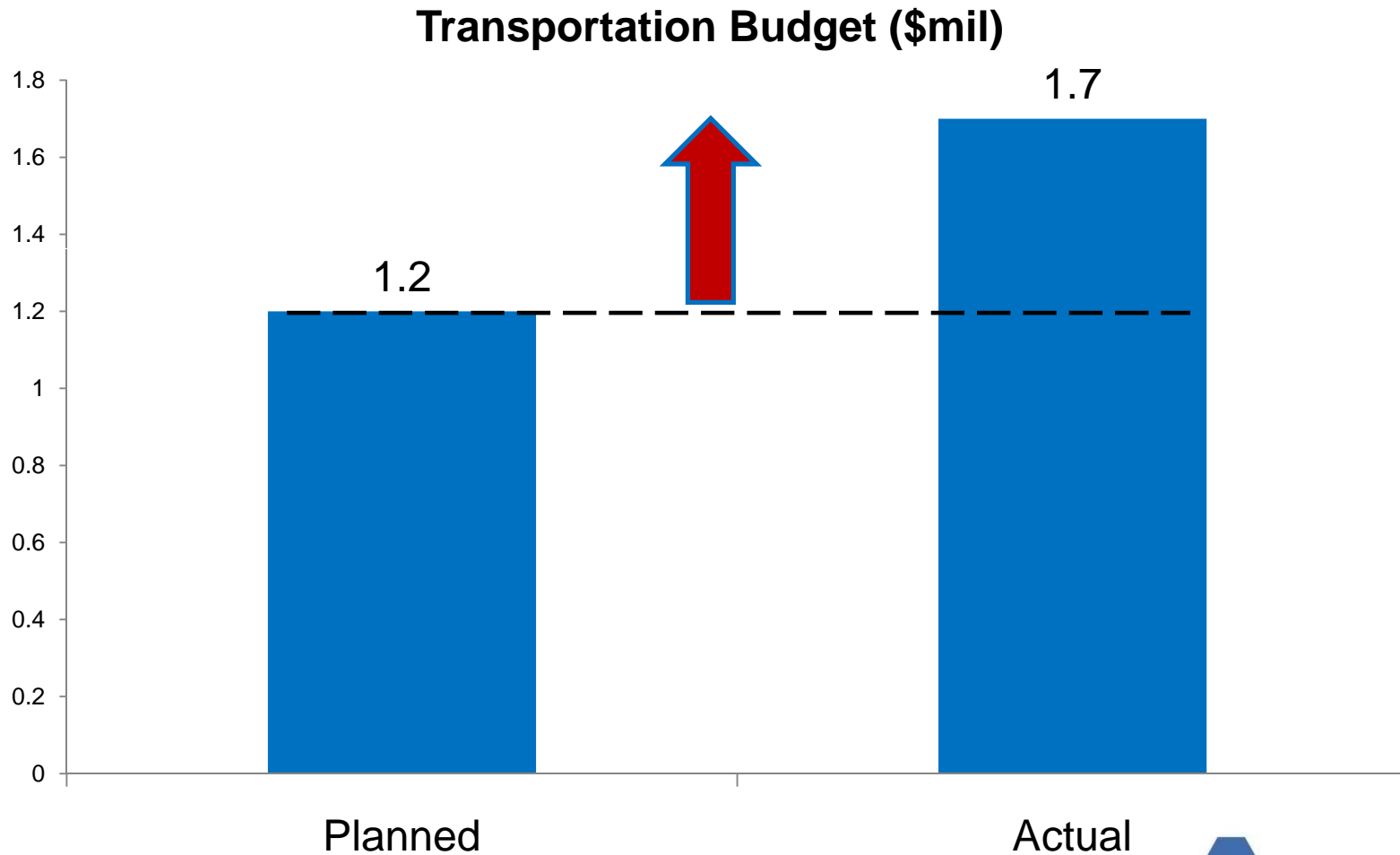
- Plan for shipping inbound supplies
 - # subjects in each package
- Type of Packaging needed
 - Ambient Shipper
 - Frozen (Dry Ice) Shipper
 - Combo Shippers

- In a large Global Study, the transportation budget is often >25% of the Central Laboratory Budget.
- The Initial CL transportation proposal can be done in many ways.
- At the time of Budget estimation, study site locations are often not known.
- How do we manage these Pass Through expenses?

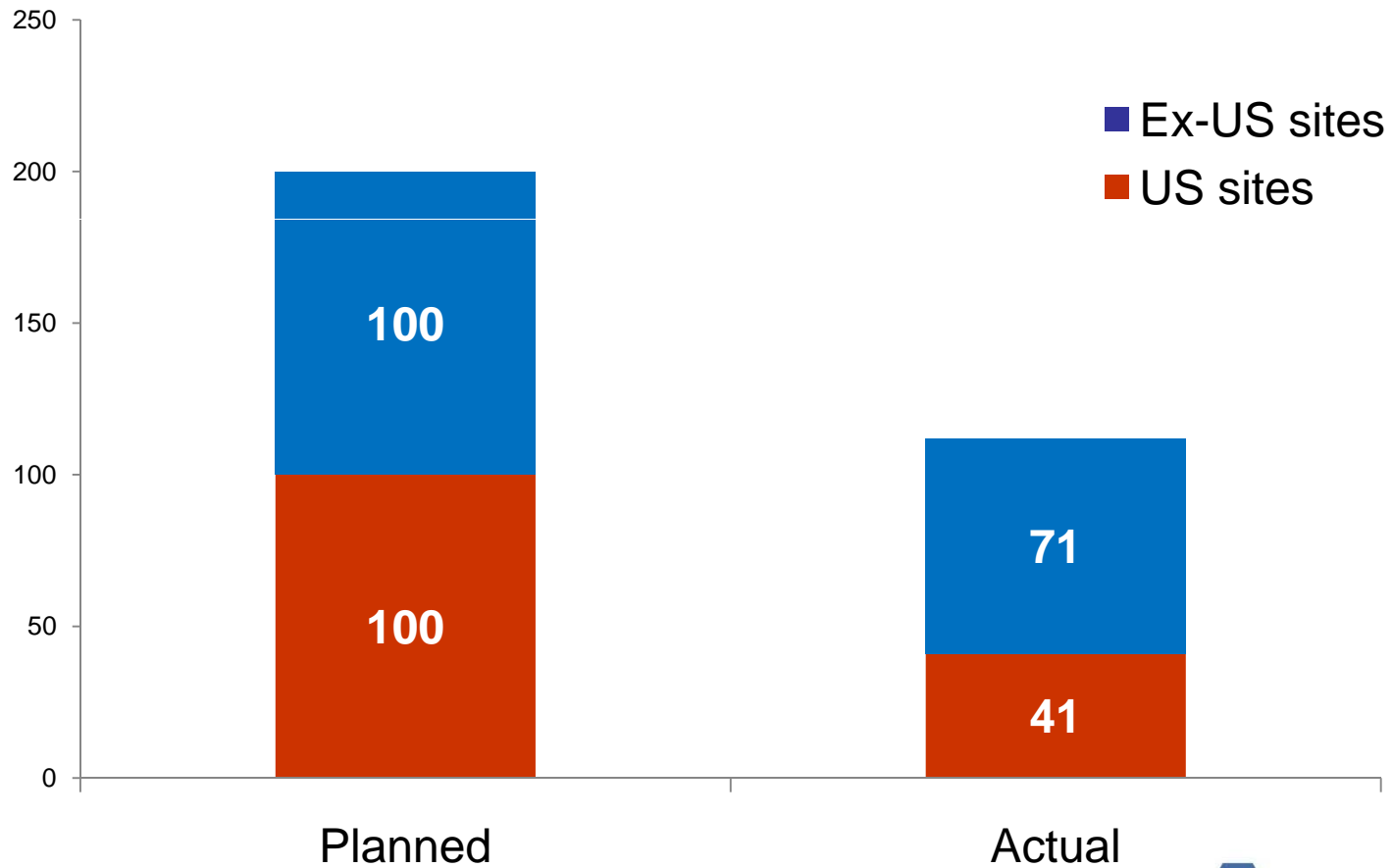
- Estimate inbound costs conservatively – 1 subject per package for inbound shipments
- Use a gateway city to estimate site costs if the exact location is unknown
- Estimate outbound costs with no built in excess
- Use packaging as recommended by CL

- Phase III Study
- 100 US Sites
- 100 Ex-US sites across 23 countries
- 600 subjects (780 to be screened)
- 10 month enrollment period
- Both Frozen and Ambient shipments needed
- CL Budget \$5.3mil (\$1.2mil transportation)

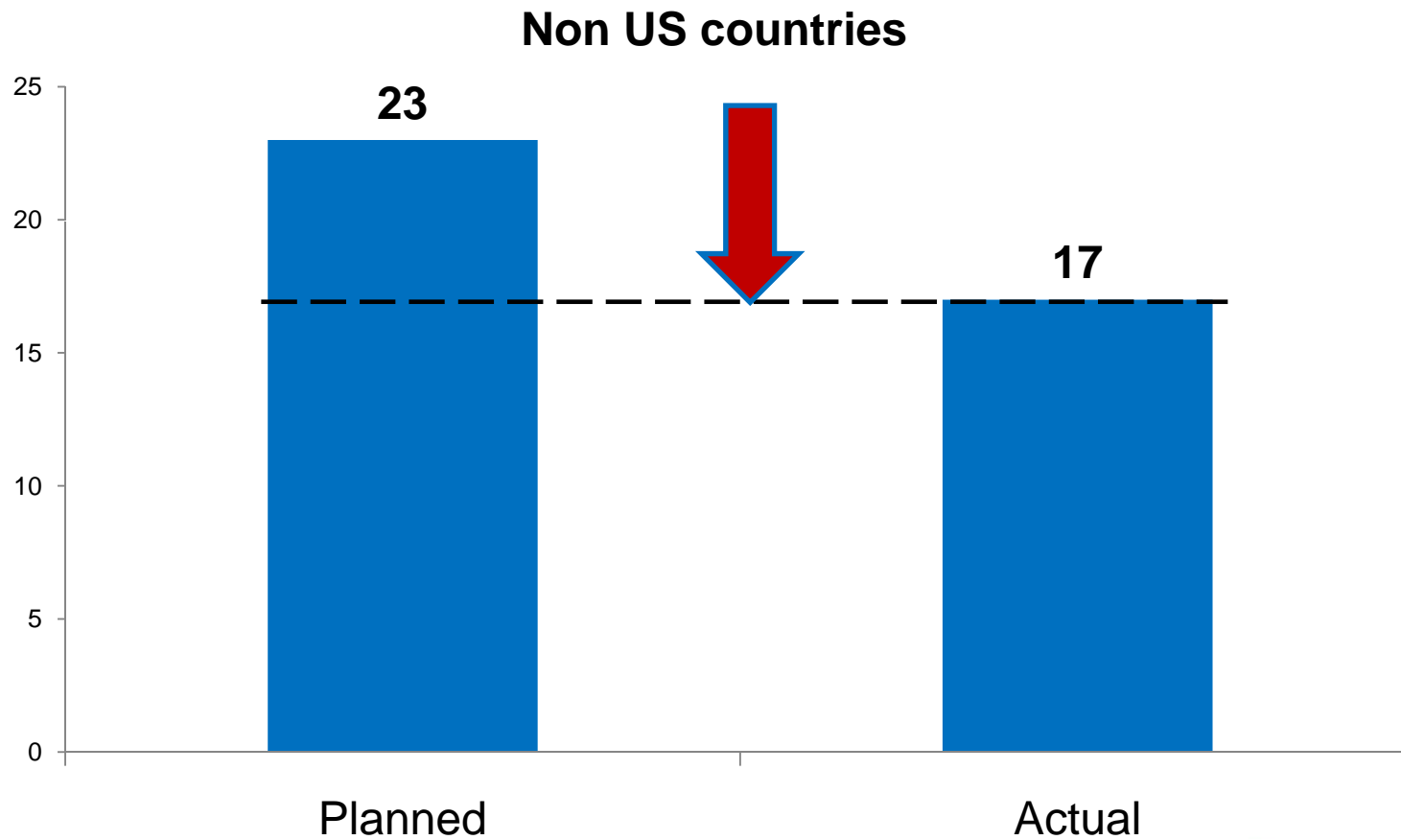
Transportation Costs Increased



Number of Sites Decreased



Number of Countries Decreased

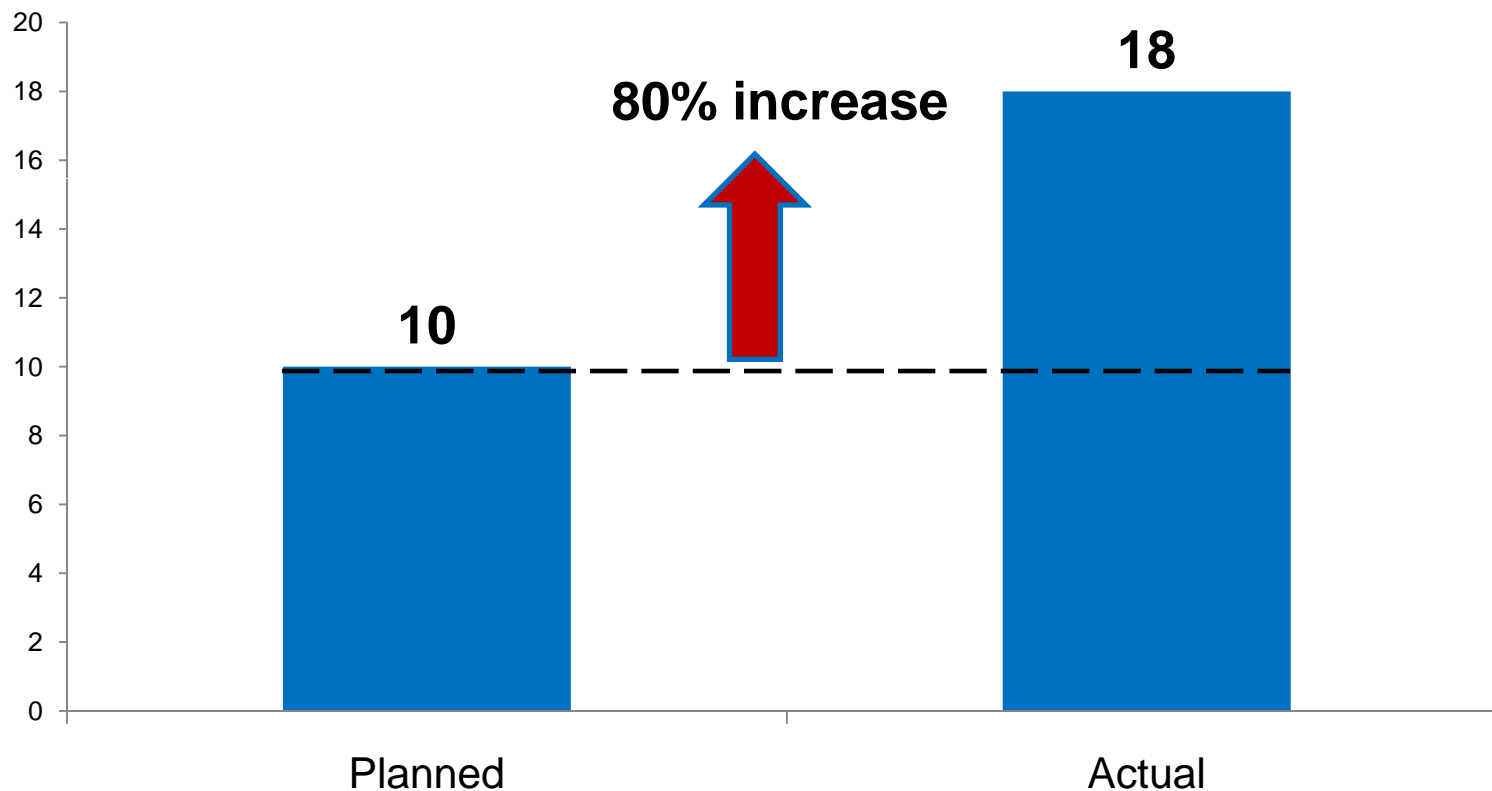


Challenges with Implementation

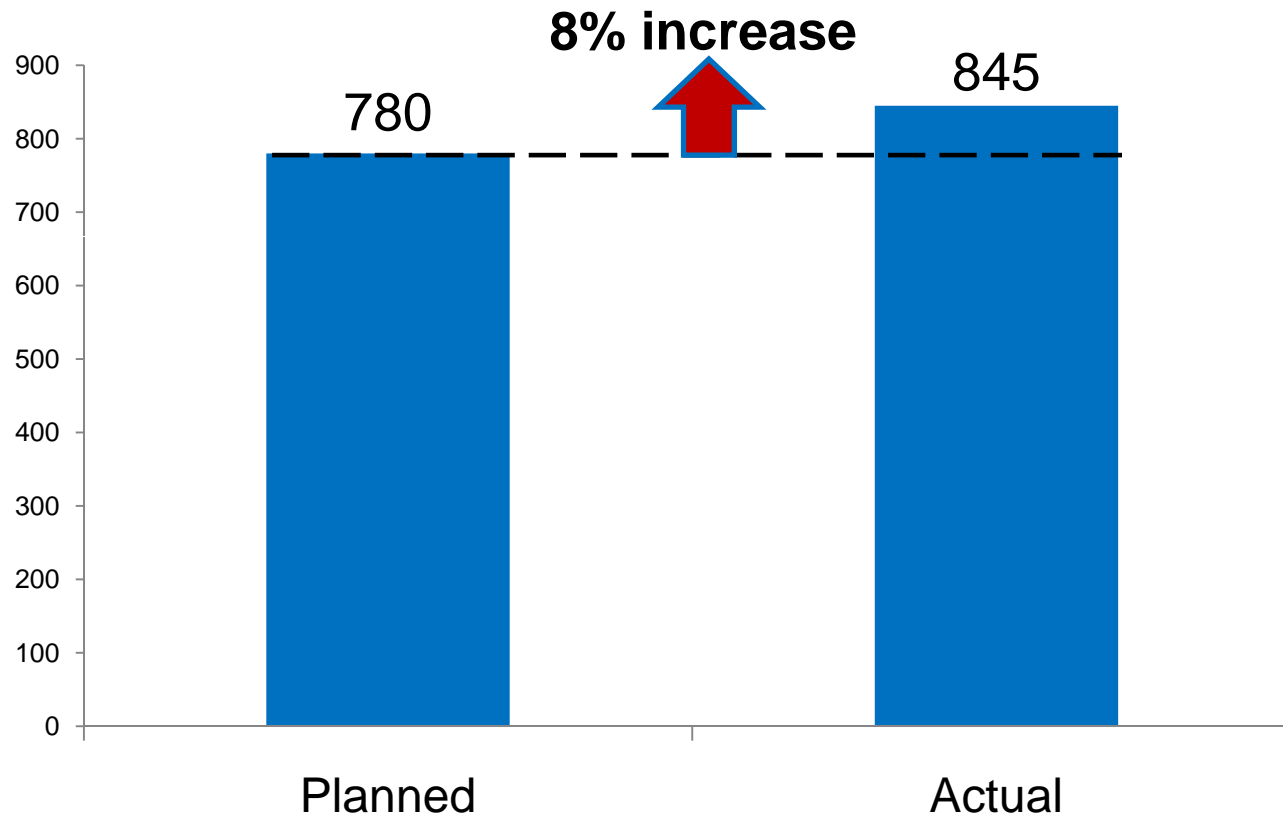
- Study sites were in more remote locations than originally proposed causing an increase in the transportation costs.
 - The further a site is from the Gateway City location used to estimate the costs, the more expensive transportation becomes.
 - For example, a gateway city estimated at \$470 turned into a remote city with actual costs of \$1125 per package.

Enrollment Period Increased

Enrollment period (months)



Screened Subjects Increased










Challenges with Implementation

- Outbound shipments increased due to lengthened enrollment time and increase in screening numbers. (as did the direct costs)
 - Kits now expired and replacement kits needed to be sent to sites
 - More kits needed to be sent to some sites due to the distribution of subjects across the sites.

Challenges with Implementation

- Subject screening was not as predicted.
 - Screening had to be extended due to a higher amount of screen failures than estimated.
 - From 10 months to 18 months
 - More subjects had to be screened to meet the enrollment goal

Challenges with Implementation

Plan	Change	Actual
100 US Sites		41 US Sites
100 Ex-US sites across		71 Ex-US sites
23 countries (50%)		17 countries (63%)
600 subjects	=	600 subjects
780 to be screened	8% increase 	845 screened
10 month enrollment period	80% increase 	18 month enrollment period
CL Budget \$5.3 mil		CL Budget \$5.0 mil
\$1.2 mil transportation		\$1.7 mil transportation

- Review the transportation budget regularly using MCC Metric 13
- Amend the Agreement once all sites have been identified
- Amend the Agreement once all subjects have been enrolled.
- Partner with your CL provider to come up with alternate transportation solutions.

Resolution of a Data Management “Headache”

Use of Metrics to Optimize Merck-Quintiles ECG Partnership

Debbie Walton, MS, MBA, CPM

Relationship Manager, Central Labs and Diagnostics

MERCK



- Setting up for “The Perfect Storm”
- Key Challenges
- Summary of Analysis Plan
- Results
- Lessons Learned with Metrics
- Wrapping Up

- Multiple Protocols of Phase II/III Migraine programs requiring Cardiac Safety Services with overlapping enrollment initiated 2Q2008 - 3Q2008
 - Rapid Enrollment (< 6 months)
 - Large Patient N
 - ECGs required at multiple visits, with final ECG visit just prior to DBL

- Misaligned Data Management Processes and Expectations;
 - Many CRF queries (demographic, missed visit) outstanding >1 -2wk, some > 2 wks;
 - Sites/CRAs receiving numerous queries, some duplicate from Merck and Quintiles;
- Multiple Work Streams impacted to meet Database Lock (DBL);
 - Data Management
 - Clinical Research Specialists
 - Clinical Research Associates/Global Trial Specialists

- Issues Escalated through Management;
 - Merck ramped up internal oversight of query resolution process to ensure multiple DBL timelines were met;
 - Merck set up routine meetings with Quintiles to monitor progress of outstanding queries and assist in resolution.

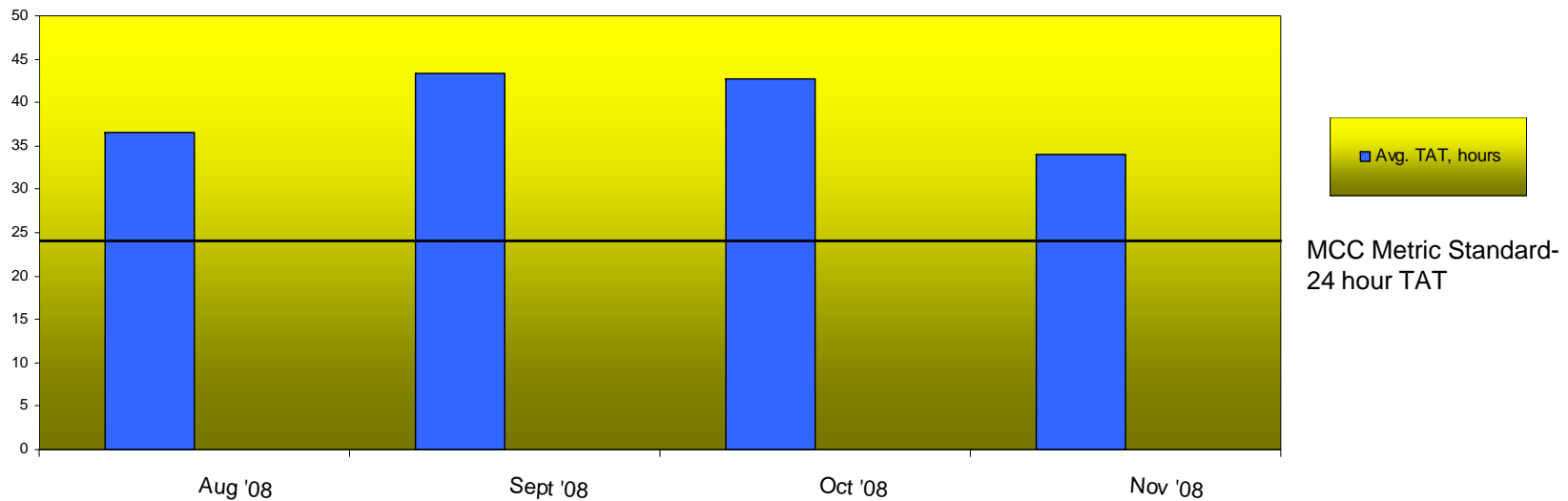
- Evaluate Subjective Feedback
 - Discussion with Team, Sites, CRAs
 - Satisfaction Surveys
- Evaluate Objective Feedback
 - Review MCC Metric “Data Query Resolution, Turnaround Time”
- Identify Root Cause— “Deeper Dive”
 - # Queries by Sites;
 - # Queries by Type; Missing ECG tracing, Missing ECG demographic information, etc.
 - # Queries broken out by length of time outstanding;
 - ex. # queries >1 wk, >2 wks, etc.

Summary of Analysis Plan, cont'd.

- Metrics collected:
 - Length of time between contract award and final execution of agreement
 - Number of Change Orders/Amendments per contract;
 - % On-Time equipment shipments to sites;
 - List of sites with equipment delays by study with reason/code;
 - *Turnaround Time (TAT) on resolution of site queries;*
 - % ECGs reported within agreed TAT;
 - Number of days from study close out to final equipment return
 - Key personnel turnover;
 - Number of calls into Help Desk during study period

Summary of Analysis Plan, cont'd.

Data Query Resolution, in Hours



2008 Average Turnaround Time (TAT) on Data Queries: 36.4 hours
Maximum TAT observed: 528 hours (22 days)

Summary of Analysis Plan, cont'd.

- Merck-Quintiles Collaborate and Implement Solutions-post 2008.
 - Routine Teleconferences scheduled between Merck/Quintiles
 - Open queries,
 - Process pain points, etc.
 - Strategy for Tracking Queries
 - Reporting of all queries every 2 weeks
 - Web Portal access
 - Strategy for Tracking “Missing ECGs” (After First Visit)
 - Missed Visit Reminder
 - Web Portal access
 - Training/Educating for Sites, CRAs, and Monitors to check Transmission Status

Summary of Analysis Plan, cont'd.

- Merck-Quintiles Collaborate and Implement Solutions-post 2008 (cont'd).
 - Strategy to reduce automatically generated Demographic Queries
 - First ECG will be baseline for all future ECGs if demographic information is missing.
 - Strategy for Sites supporting more than one Study with one machine.
 - Discrete programming to reduce manual entry errors.

Data Query Resolution, in hours	2008	2009
Average TAT	36.4	9.85
Maximum TAT	528	42.8

Lessons Learned with Metrics

- Collect Meaningful Metrics
- Ensure both Sponsor and Vendor have common definitions, and agreed upon reporting units/measures.
- Review Metrics regularly to identify potential 'drifts' in performance. Don't wait until there is a problem before reviewing.
- Consider 'drill down' metrics for critical performance functions- ex. Query resolution TAT could be impacted by
 - Site (training required?)
 - Vendor (process improvements needed?)

Identifying root cause allows targeted remediation.

Questions, Comments?

-Thank You



Group Discussion

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ABBOTT LABORATORIES

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MERCK





Thank you

Please visit the

MCC website (www.metricschampion.org) or
contact Linda Sullivan at lsullivan@metricschampion.org
for additional information about MCC membership.

