



# Identification and Implementation of Metrics that are Targeted to Assess Quality of Clinical Trials

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<http://www.metricschampion.org>



# Agenda

- Background - Mission, Goals & Organization
- MCC Clinical Trial Performance Metrics
- MCC Quality Scoring Tools
- Additional Programs to Support the Use of MCC Metrics & Quality Tools
  - MCC Member Blinded Database
  - MCC Institute
- Q & A



# MCC Mission

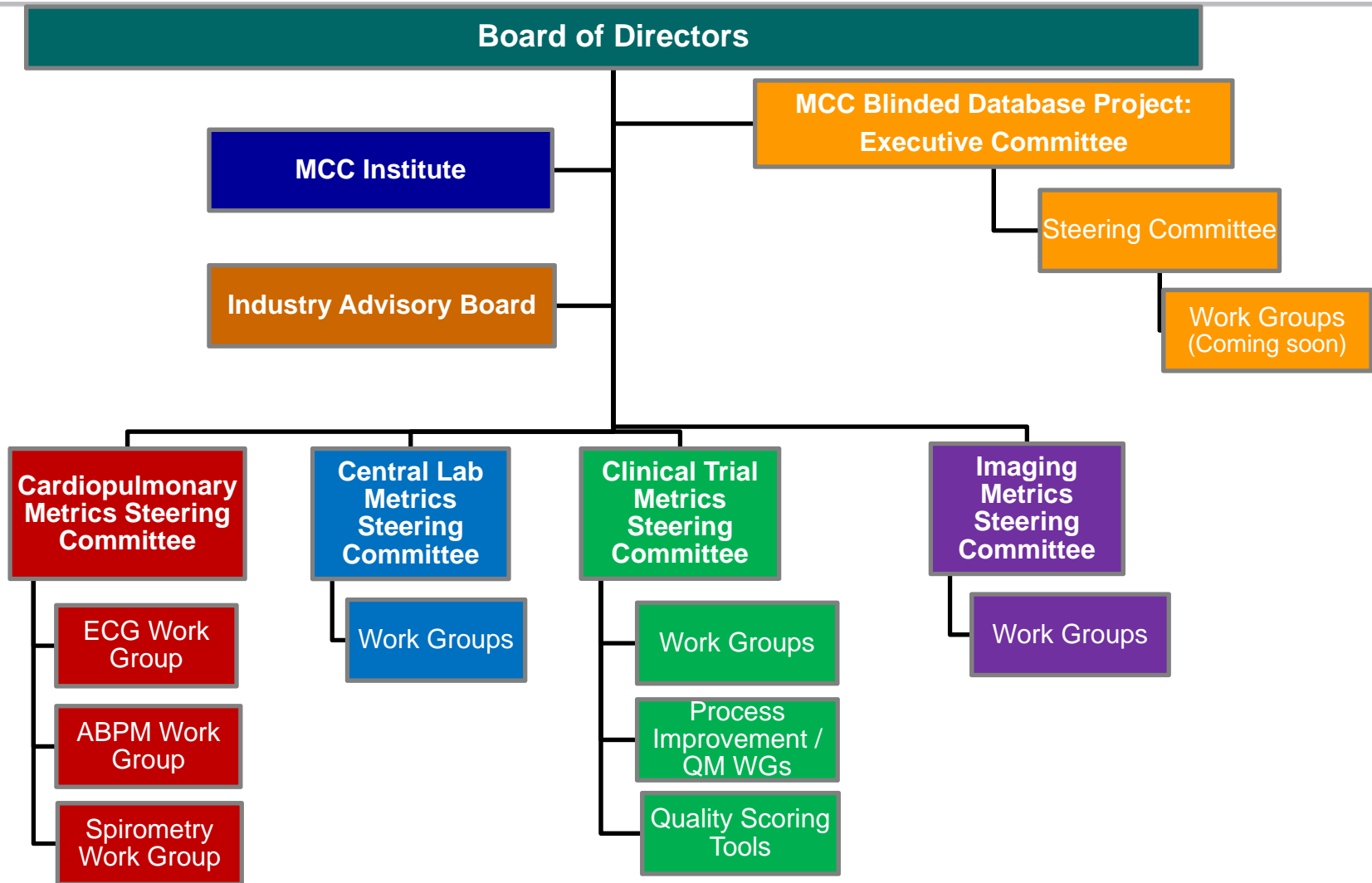
The Metrics Champion Consortium (MCC) is an open, multidisciplinary, non-profit organization comprised of biotechnology, pharmaceutical, medical device and service provider organizations.

**Our mission** is to help sponsor and service provider organizations involved in the pharmaceutical, biotechnology and medical device industries improve their overall clinical trial development processes through the utilization of MCC standardized clinical trial performance metrics (time, cost & quality) by:

- ❖ Supporting the ongoing collaborative development of standardized performance metrics and process improvement tools
- ❖ Encouraging the continuous implementation of the metrics and tools among MCC members
- ❖ Providing a collaborative learning environment for members to share best practices, discuss challenges and industry trends
- ❖ Offering live and online educational opportunities to support the use of performance metrics and tools in member organizations



# Organizational Structure





# MCC Members

Abbott Laboratories  
Actelion Pharma  
Acorda Therapeutics  
AG Mednet  
AstraZeneca\*  
BARC Global Central Lab  
Bayer Healthcare  
Beaufort CRO  
BioClinica  
Biogen Idec  
BioMarin Pharmaceuticals Inc  
Biomedical Systems  
CardiaBase  
Cardio Analytics  
Cardiocore  
Celgene  
Cerexa  
CHDI  
Clinical Reference Laboratory  
Clinical Systems Ltd.  
Clinsys Clinical Research

Cognizant  
Corelab Partners  
Covance  
Covidien  
CSL Limited  
Customized Improvement Strategies  
DecisionView  
Duke Clinical Research Institute  
ERT\*  
Esoterix Clinical Trial Services  
Eurofins Medinet  
ExecuPharm  
Forte Research Systems  
GE Healthcare  
Genentech  
Genzyme  
Halloran Consulting Group  
i3  
iCardiac Technologies  
ICON

Imaging Endpoints  
INC Research  
Incyte  
Intrinsic Imaging  
Ixico  
Lilly\*  
M2S  
MEDIDATA GmbH  
Medidata Solutions  
Medtronic  
Merck  
MLM Labs  
New England Research Institute  
Novartis  
Novella Clinical  
Paragon Biomedical  
Parexel / Perceptive Informatics  
Pfizer\*  
PharmaNet\*  
PPD\*  
PRA International

QD-Quality & Training Solutions  
Quest Diagnostics  
Quintiles\*  
RadMD  
Regeneron  
Roche\*  
Seattle Genetics  
Sunovion Pharmaceuticals  
Synarc  
Virtual Scopics  
WorldCare Clinical

\* MCC Board of Directors

**70+ members  
and growing!**



# MCC Standardized Performance Metrics

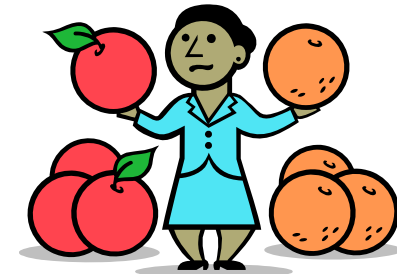
- Central Lab Performance Metrics (2006, *2011\**)
- Cardiopulmonary Performance Metrics
  - ECG Performance Metrics (2007, 2011)
  - Ambulatory Blood Pressure Monitoring Performance Metrics (*2011\**)
  - Spirometry Performance Metrics (*2011\**)
- Imaging Performance Metrics (2009, *new metric 2011*)
- Clinical Trial Performance Metrics (2010)

*\* In development*

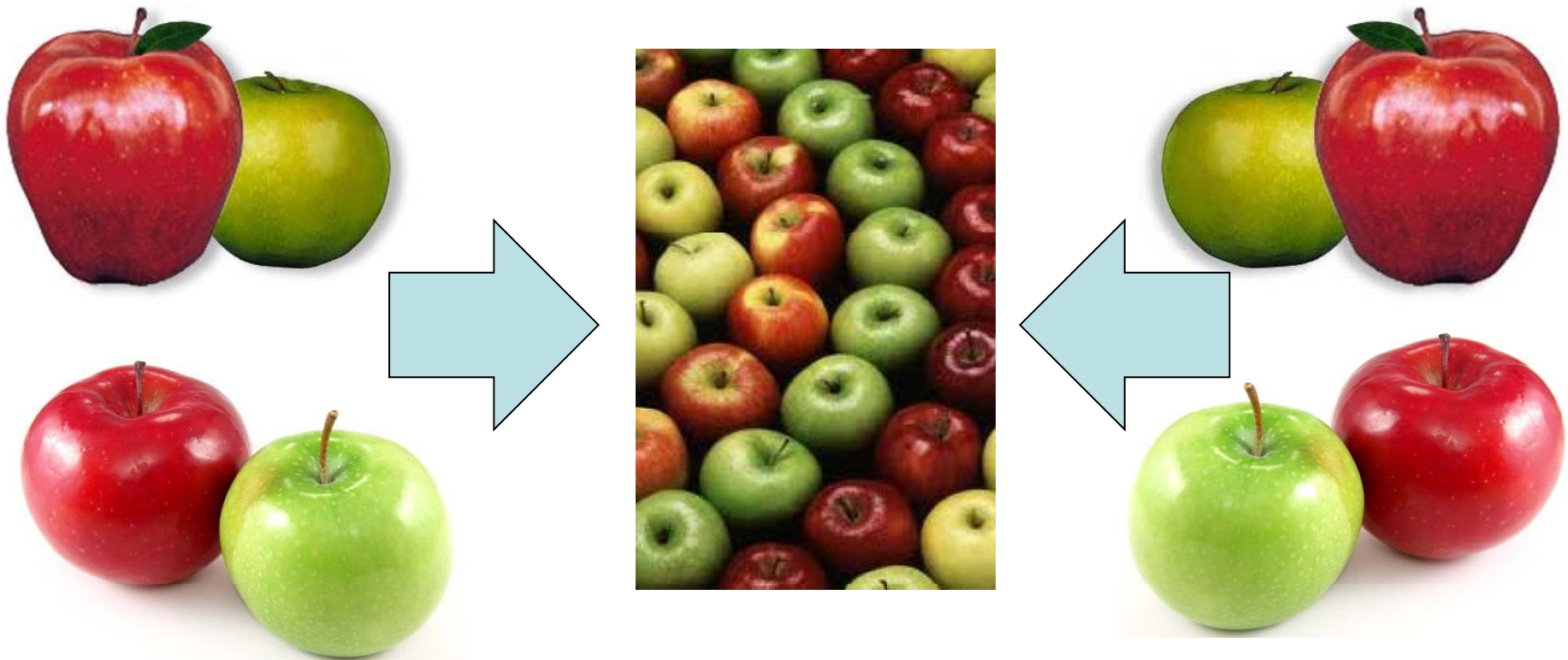


- Sponsors use different service providers
  - Managing metrics across portfolios across service providers is a challenge

- Service providers are faced with managing varying performance based metrics from Sponsors



Mutually beneficial standardized performance metrics can be achieved and fruitful for all parties



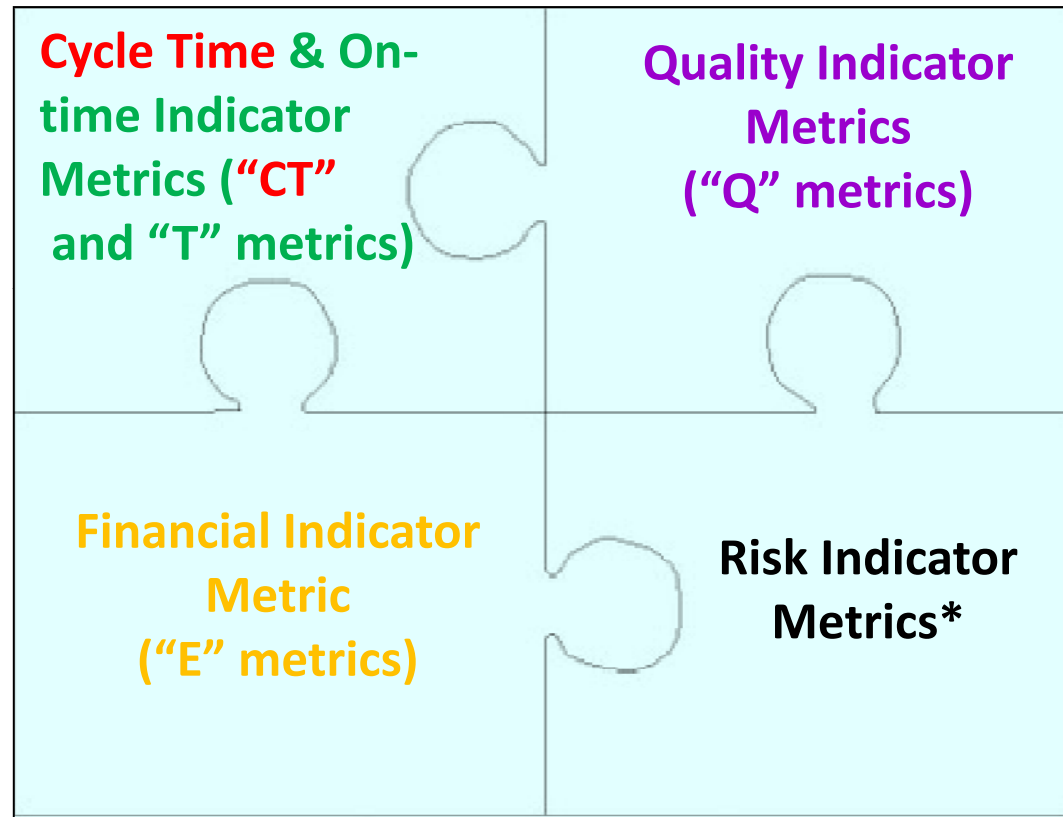


## MCC Metrics Include Sub-Metrics

Each set of MCC performance metrics provides a metrics hierarchy:

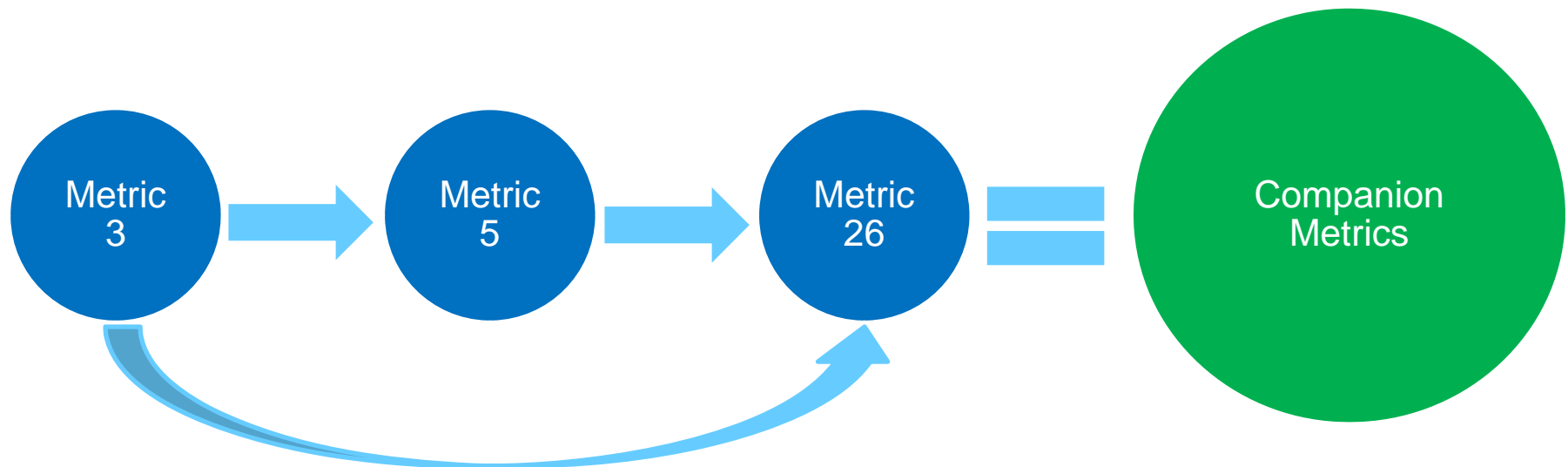
- MCC metrics are performance indicators
- Most metrics include sub-metrics that should be reviewed when performance does not meet target expectations

Thus reducing the number of metrics that need to be reviewed on a quarterly/monthly basis



\* Some MCC metrics can be used as Risk Indicator Metrics – this designation is determined by an organization.

Provide guidance on which MCC metrics should be reviewed together to understand the combined performance of related tasks.....





# New Programs to Support MCC Mission

## Quality

### MCC Quality Tools

- Protocol Quality Evaluation Tool
- Site Selection Quality Tool
- Site Study Conduct Evaluation Tool

## Benchmarking

### MCC Metrics Database

- MCC Members only
- Blinded Comparisons
- Hosted by IBM Clinical Cloud
- **COMING SOON**

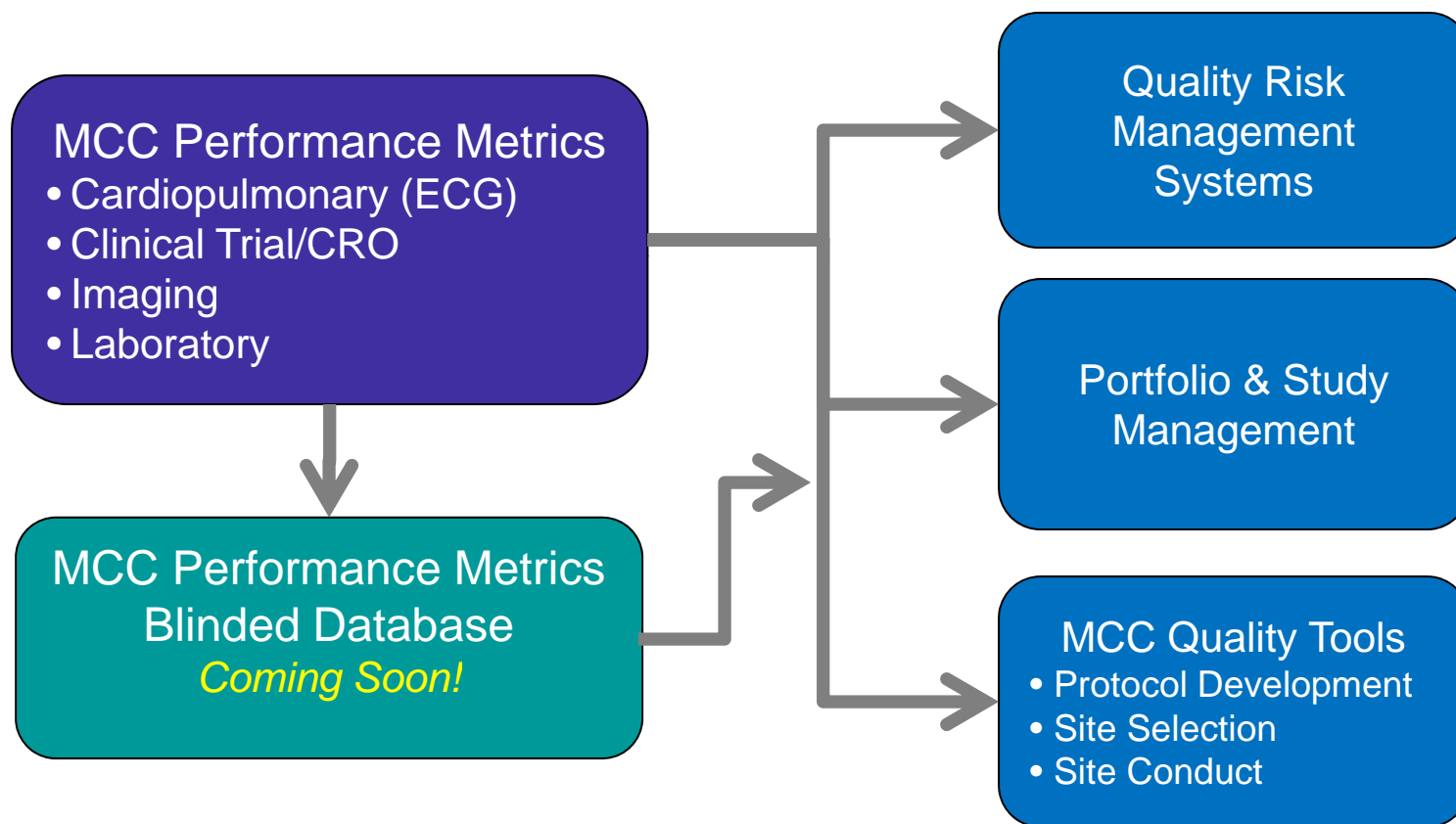
## Training

### MCC Institute

- Member Only Program
- Experienced Faculty
- Live Workshops
- Online Learning Modules
- 100-400 level courses
- **COMING SOON**



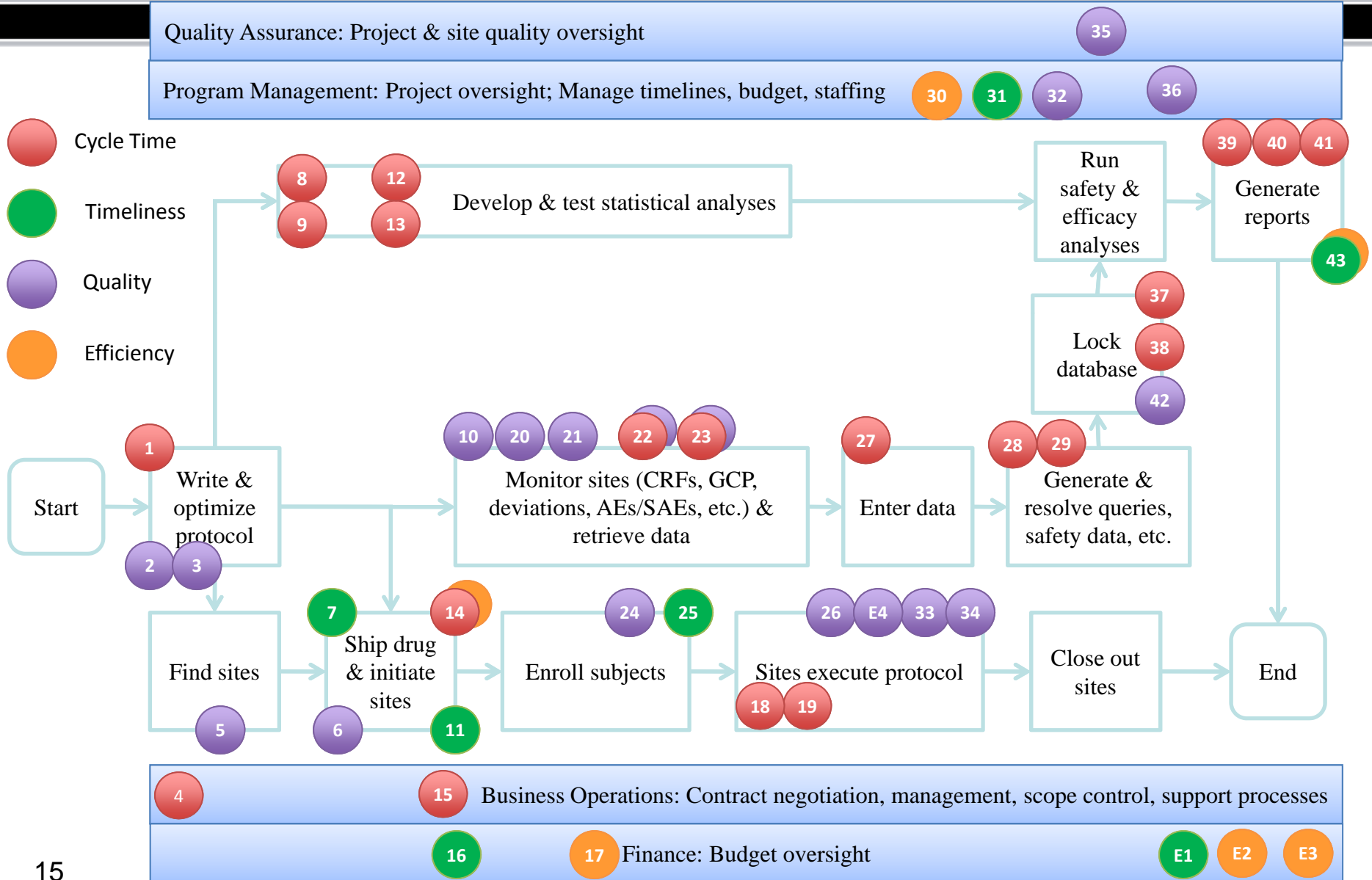
# Standardized Performance Metrics Provide Foundation for Management Approaches



MCC Institute – Training Modules *Coming Soon!*



*Clinical Trial Performance Metrics  
Initiative*



Metric #	Metric Type	Metric Title	Metric Indicator
1	CT	Protocol Feasibility	LEADING Indicator
2	Q	Protocol Versions	LEADING Indicator
3	Q	Protocol Quality Tool	LEADING Indicator
4	CT	Contract execution timeliness for non functional outsourcing models	LAGGING Indicator
5	Q	Site Selection Quality Tool	LEADING Indicator
6	Q	Regulatory Authority Package Approval Rate	LEADING Indicator
7	T	Protocol approval to first site activated	LEADING Indicator
8 - EDC	CT	Final Approved Protocol to Final Approved eCRF - EDC	LAGGING Indicator
9 - paper	CT	Final Approved Protocol to Final Approved CRF - paper	LAGGING Indicator
10	Q	Monitoring Plan Availability	LEADING Indicator
11	T	% Planned Sites Activated	LEADING Indicator
12 - EDC	CT	Final eCRF to Database "Go Live" - EDC	LAGGING Indicator

Metric #	Metric Type	Metric Title	Metric Indicator
13 - paper	CT	Final CRF to Database "Go Live" - paper	LAGGING Indicator
14	CT	Site Activation to First Patient First Visit	LAGGING Indicator
	E		
15	CT	Change Order execution	LAGGING Indicator
16	T	Timeliness of Invoice payment	LAGGING Indicator
17	E	Budget and pricing accuracy	LAGGING Indicator
18 - EDC	CT	Patient Visit Complete to eCRF data entered - EDC	LEADING Indicator
19 - paper	CT	Patient Visit Complete to CRF data entered - Paper	LEADING Indicator
20	Q	Monitoring Visit Frequency	LEADING Indicator
21	Q	Monitoring Visit Report Completion	LEADING Indicator
22	CT	Documented Monitoring Visit Report Review	LEADING Indicator
	Q		

Metric #	Metric Type	Metric Title	Metric Indicator
23	CT	Monitoring Follow-Up Letter Completion	LEADING Indicator
	Q		
24	Q	Site Productivity	LEADING Indicator
25	T	% subjects enrolled	LEADING Indicator
26	Q	Patient Retention	LEADING Indicator
27 - paper	CT	CRF Pages Received/scanned to Data Entry Complete - Paper	LEADING Indicator
28 - EDC	CT	Generation of Query to update of query response - EDC	LEADING Indicator
29 - paper	CT	Generation of Query to update of query response - paper	LEADING Indicator
30	E	Drug Supply Forecasting	LEADING Indicator
31	T	Variance of Drug Inventory & Resupply	LEADING Indicator
32	Q	Protocol Amendments	LAGGING Indicator
33	Q	Protocol Deviations	LEADING Indicator (if done Quarterly)

Metric #	Metric Type	Metric Title	Metric Indicator
34	Q	Sites Prematurely Terminated	LAGGING Indicator
35	Q	Audit Findings per Site	LAGGING Indicator
36	Q	Issue identification, management and criticality	LAGGING Indicator
37 - EDC	CT	LPLV to Database Lock - EDC	LAGGING Indicator
38 - paper	CT	LPLV to Database Lock - paper	LAGGING Indicator
39	CT	DBL (Database Lock) to final TLG/TFL (Tables, Listings and Graphs/Table Figure Listing)	LAGGING Indicator
40	CT	Final TLGs to First Draft CSR complete	LAGGING Indicator
41	CT	DBL (Data Base Lock) to Final CSR Complete	LAGGING Indicator
42 - paper	Q	Final Database Error Rate	LAGGING Indicator
43	T	Deviation of final TLGs delivered from final agreed target date.	LAGGING Indicator
	E		

## Exploratory Metrics

Metric #	Metric Type	Metric Title	Metric Indicator
E1	CT	Timeliness of Invoice generation following contractual milestones	LAGGING Indicator
E2	E	Determination of project progress versus planned (original contract value)	LEADING Indicator
E3	E	Determination of project progress versus planned (adjusted contract value)	LEADING Indicator
E4	Q	Site Assessment Quality Tool	LEADING Indicator

Anatomy of a MCC Clinical Trial Performance Metric					
Metric #	Metric Type	Metric Title	Category	Metric Indicator	Part of Study
	CT, T, Q or E		Business Operations, Clinical Operations, Data Management, etc.	LEADING or LAGGING Indicator	Study Startup, Conduct and Close-Out
Definition (see Wiki for detailed definitions)			Formula / Example	Reporting Detail	
			Formula: Example:	Site / Country / Study / Therapeutic Area / Portfolio levels	
				Unit of Measure Calendar days, % etc.	
Business Driver(s) / Benefit Statement			Additional Analysis on a "for cause" basis	Reporting Frequency	Threshold Target
Statement about why this metric is important /the reason for utilizing metric. Who / what / why...			List of "drill down" metrics that should be reviewed when the metric is not within established target	Monthly, Quarterly, etc.	Threshold target or acceptable range. Exceeding target triggers additional analysis on a "for cause" basis
Companion Metrics		The term "companion metrics" refers to the concept that many MCC metrics should be examined in combination with other MCC metrics ... together they give you a more complete picture of performance			



# *MCC Quality Tools*



Beginning in Q4 2009, a group of Sponsor and CRO Process Improvement & QM specialists began working together to:

- Encourage the use of the metrics for process improvement
- Help MCC members avoid pitfalls such as sub-optimization
- Develop new approaches to assessing Quality

## **A successful clinical trial is dependent on many factors:**

- Robust, scientifically, ethically sound protocol that can be successfully executed
- Selection of high-performing, GCP compliant sites that contribute timely, accurate and complete data
- Keen oversight of quality execution throughout the life of the trial

***Recent regulatory agency warning letters highlight deficiencies in GCP compliance and sponsor oversight, both which have the potential to compromise high-quality agency submissions.***



The *quality* of something can be determined by comparing a set of inherent characteristics with a set of requirements.

- If those inherent characteristics meet all requirements, high or excellent quality is achieved.
- If those characteristics do not meet all requirements, a low or poor level of quality is achieved

Source: <http://www.praxiom.com/iso-definition.htm>

MCC Process Improvement WG expressed frustrations that many organizations focus on whether clinical trials are being executing in a **timely** manner ...



... but do not measure how **well** tasks are being completed.

# The Quest For Study Start-up *Speed* Results in Additional Costs!

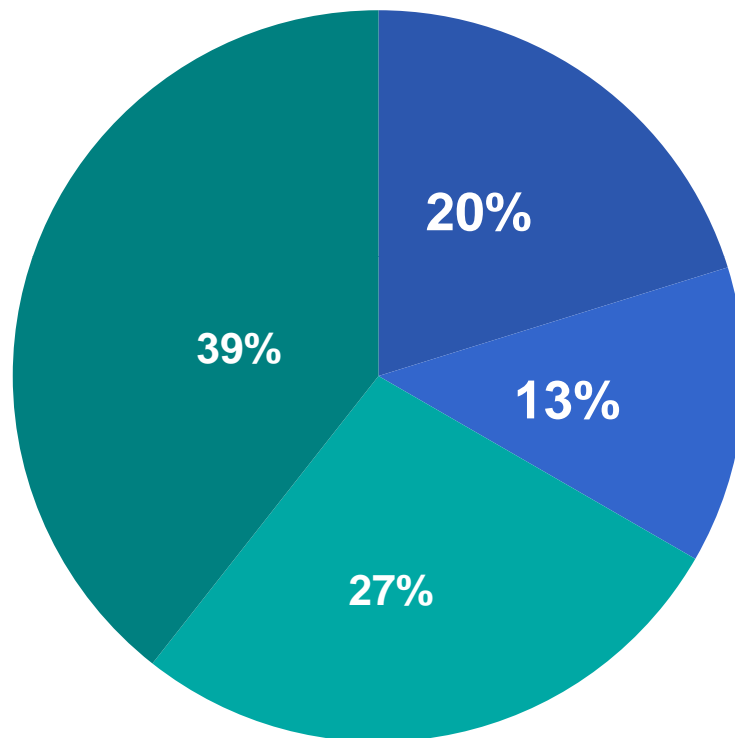


- Poorly designed protocols resulting in:
  - Protocol amendments
  - Collection of extraneous data
  - Poor data quality
  - Poorly designed Case Report Forms (CRFs)
- Inadequate risk identification and mitigation management planning
- Significant rework
- Higher regulatory risk
- Longer time to approval
- Rejected applications

- Nearly 60% of protocols examined required at least one amendment
- 43% of amendments were signed off by the sponsor **before** the first study volunteer had been enrolled
- Each amendment costs nearly \$500, 000 – experts say this number is low for Phase 3 trials!

Source: Getz KA, et al. *Drug Information Journal*. 2011;45(3):265-275.

# Protocols Amendments Are Avoidable



- Completely avoidable amendments
- Somewhat avoidable amendments
- Somewhat unavoidable amendments
- Completely unavoidable amendments

Adapted from Getz KA, et al. *Drug Information Journal*. 2011;45(3):265-275.

- Two-thirds of sites fail to meet patient enrollment requirements<sup>1</sup>
- Up to 50% of sites enroll one or no patients<sup>1</sup>
- 15-20 % of sites never enroll a single patient<sup>1</sup>
- Percentage of screened patients retained for the duration of the clinical trial has decreased from nearly 50% in 2001 to less than 25% in 2010<sup>2</sup>

<sup>1</sup> Getz K. *Applied Clinical Trials*. 2009(February):38-40.

<sup>2</sup> Tufts Center for the Study of Drug Development. Press Release April 26, 2011.

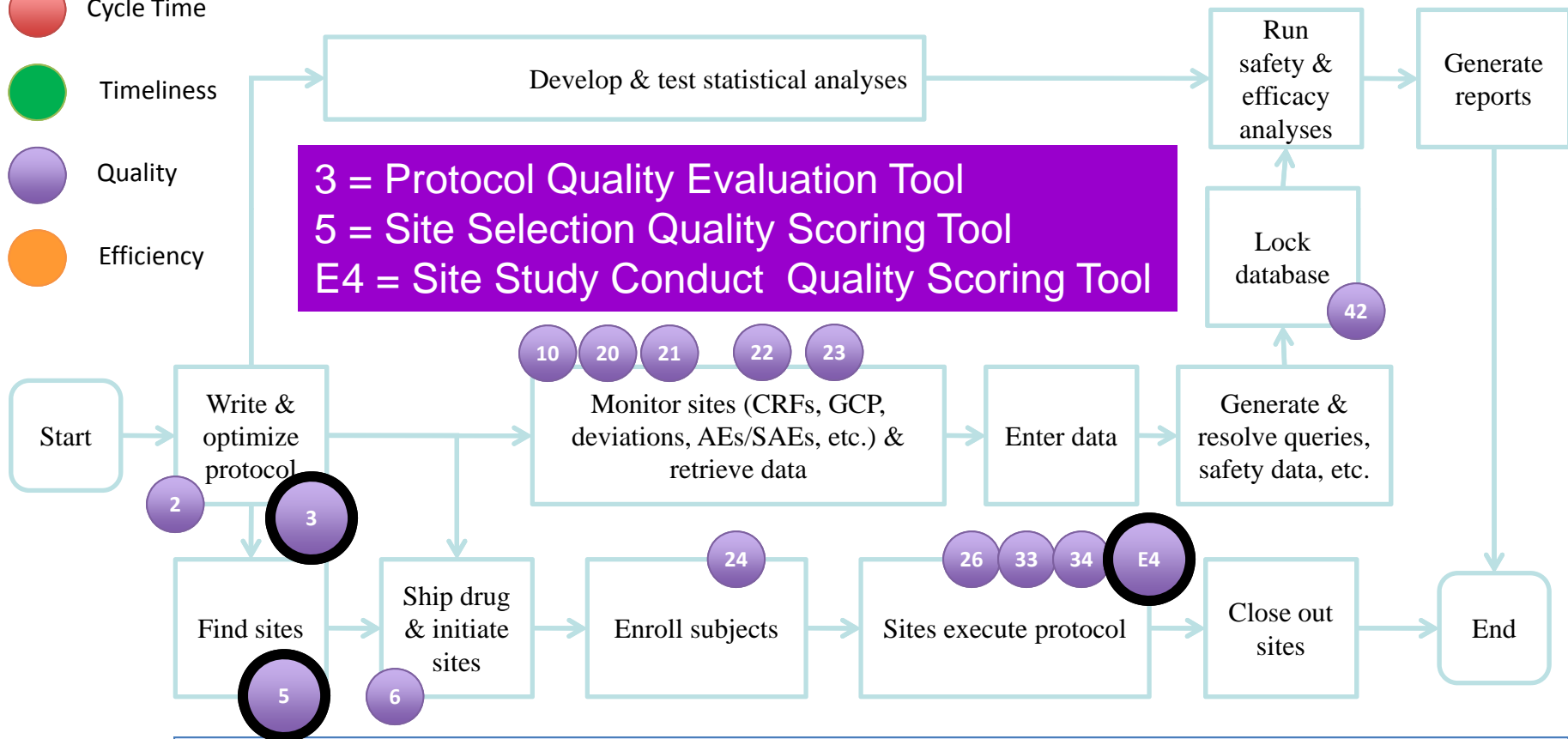
# MCC Clinical Trial Performance Metrics Quality Focus

Quality Assurance: Project & site quality oversight 35

Program Management: Project oversight; Manage timelines, budget, staffing 32 36

- Cycle Time
- Timeliness
- Quality
- Efficiency

3 = Protocol Quality Evaluation Tool  
 5 = Site Selection Quality Scoring Tool  
 E4 = Site Study Conduct Quality Scoring Tool



Business Operations: Contract negotiation, management, scope control, support processes

Finance: Budget oversight

Each **MCC Quality Scoring Tool** contains a set of requirements against which organizations can compare study start-up activities in order to determine a quality score and look for quality improvement opportunities.

*The quality scores shows how well your processes outline site attributes that correlate to performance.*

## Protocol Design

- Was the protocol designed in a robust manner (8 questions)?

## Depth of Site Interviews

- What version of the protocol was used for interviews?
- What type of interviews were conducted?

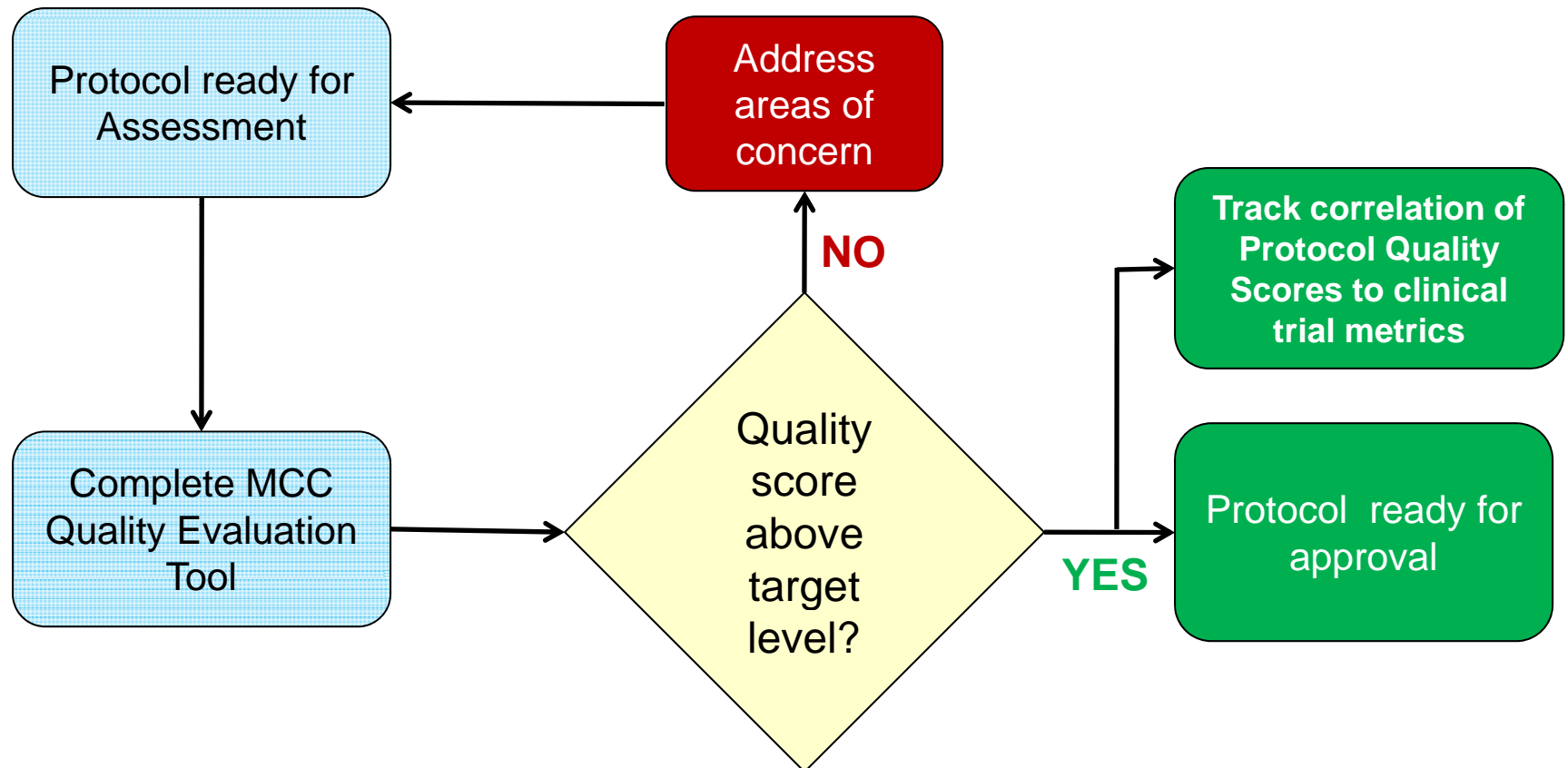
## Breadth of Site Interviews

- How many interviews were conducted in various regions?

## Response to Site Interviews

- How were site suggestions in 7 keys areas incorporated into the protocol?

## Protocol Quality Evaluation Tool (self assessment)



# Site Selection Quality Scoring Tool - Key Features

## Weighted Criteria

- Criteria weighted as to relevance per protocol before beginning scoring process

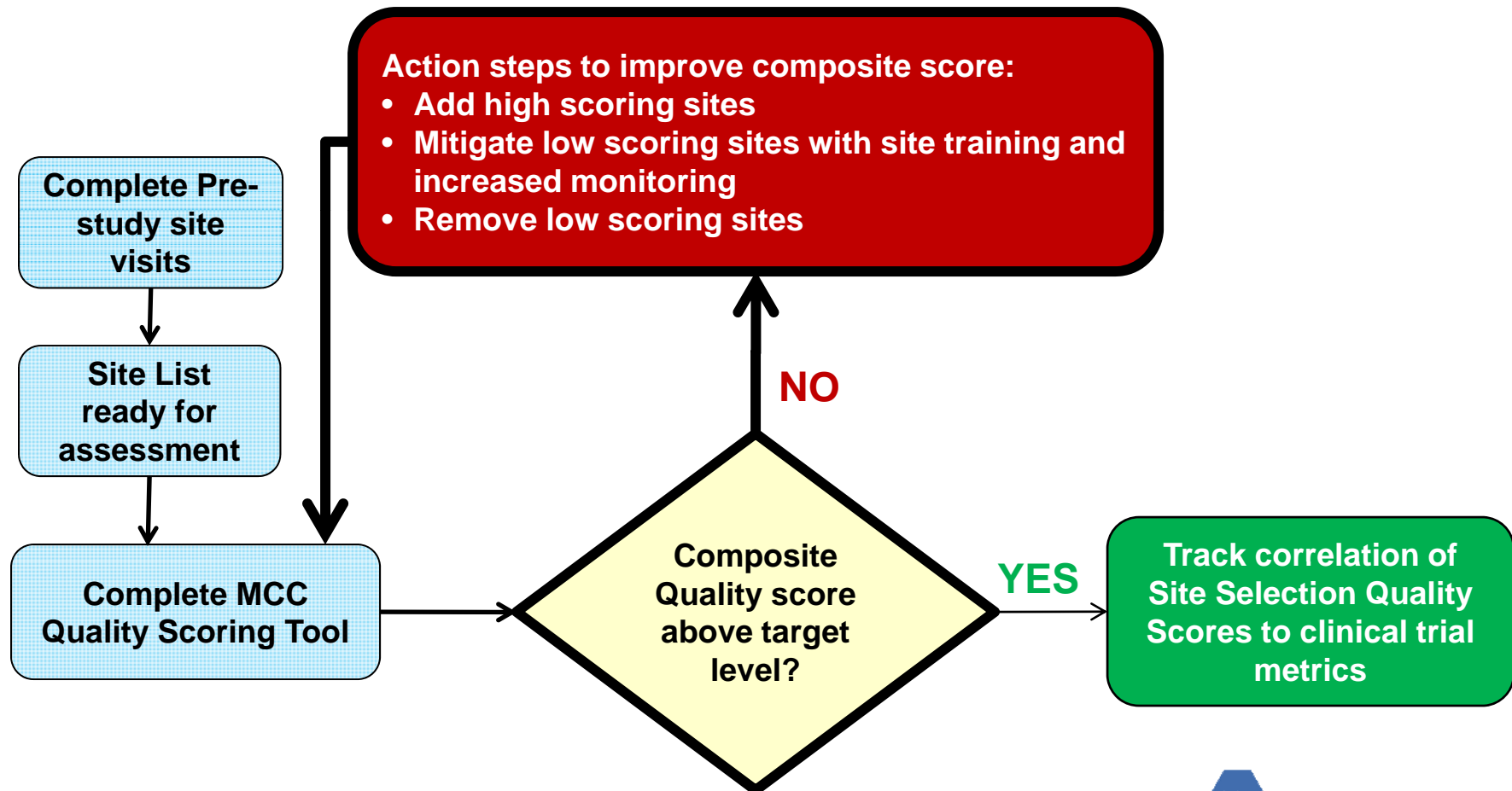
## Individual Site Scores

- Each site is rated (Y/N) on a standard set of eight site quality criteria
- Tool calculates score based on responses

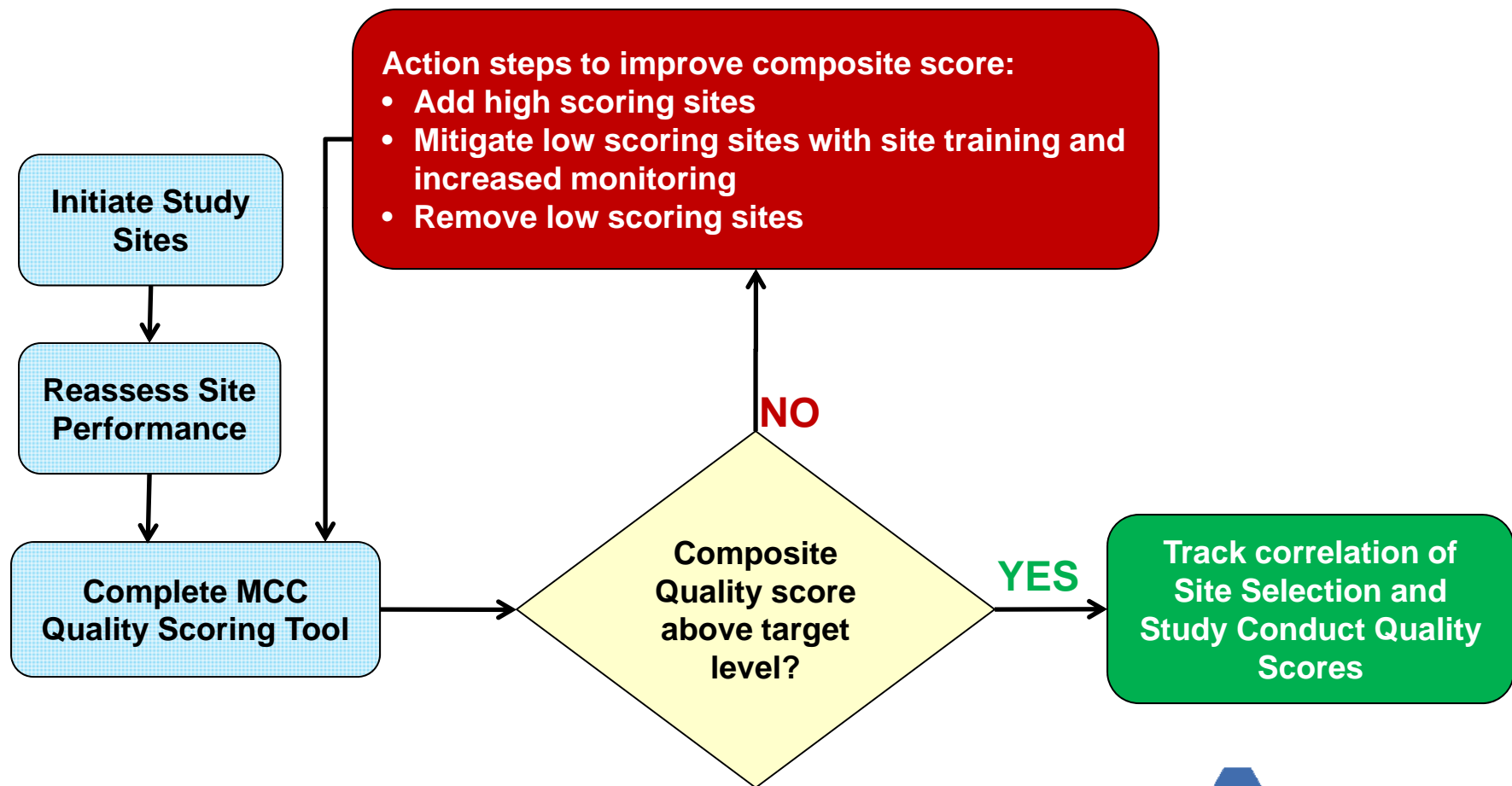
## Country & Site List Composite Scores

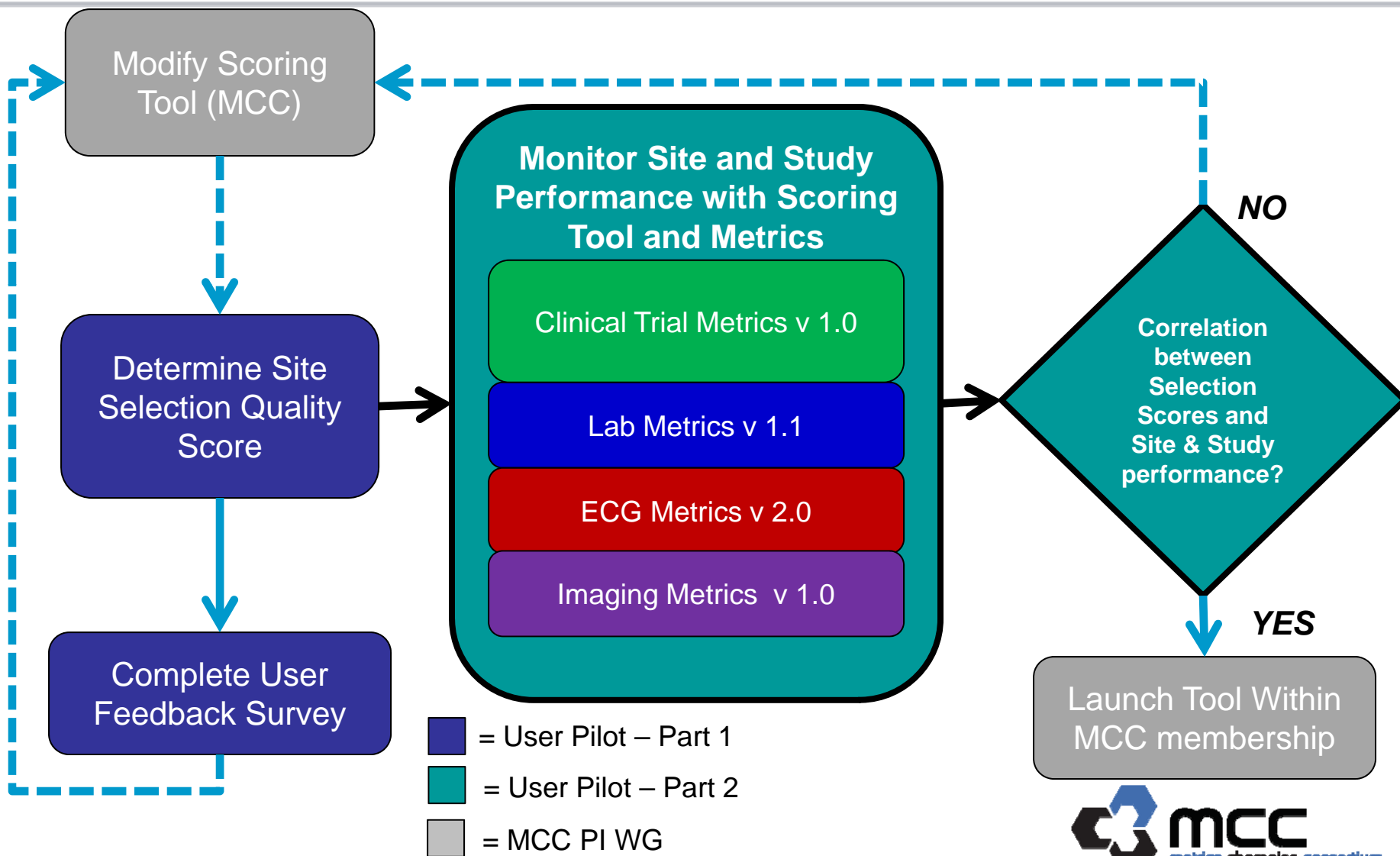
- Individual sites can be excluded from country & site list composite scores
- Composite scores reported for all sites and selected sites only

## Site Selection Quality Scoring Tool



## Site Study Conduct Quality Scoring Tool *(COMING SOON)*







# MCC Lab, ECG and Imaging Portfolio and Study Metrics Can Identify Quality Problems at Sites

## MCC LAB PERFORMANCE METRICS

- Query Metrics
- Sample Quality Metric

## MCC ECG PERFORMANCE METRICS

- Sample Collection Metric
- Query Metrics
- ECG Quality Metrics
- Equipment Failure Metric

## MCC IMAGING PERFORMANCE METRICS

- Sample Collection Metrics
- Query Metrics
- Image Quality Metrics

- Goal is to establish a reasonable threshold which all sites or protocols surpass as a measure of quality
- Focus should not just be on the score - but rather using the tool to assist in rational discussion amongst the team evaluating / selecting sites or developing the protocol
- The act of measuring should modify behavior and highlight sites at risk for poor performance:
  - Has site feedback been incorporated into the protocol?
  - Does a site lack skills and need specific training?
  - Are there enough high quality sites selected in country X?



## Recent Quality Management Guidance

- European Medicines Agency (EMA) Reflection paper on risk based quality management in clinical trials (comment deadline 15 February 2012)
- Food and Drug Administration (FDA) Guidance for Industry Oversight of Clinical Investigations – A Risk-based Approach to Monitoring (posted August 2011)

## Risk-Based Monitoring Approach

Centralized Monitoring

Remote  
Source Data  
Verification

Study Data  
Outlier  
Analysis

Performance  
Metrics

MCC  
Metrics

On-Site Monitoring

Study  
Start-Up

High Risk  
Sites

Performance  
Metrics

MCC Site Selection &  
Site Conduct Tool

MCC  
Metrics



## MCC Monitoring WG *(new)*

- Provide a forum for MCC members to discuss current and new approaches to monitoring
- Explore how MCC Performance Metrics can support Monitoring programs and whether additional metrics need to be added
- Determine whether a MCC monitoring quality evaluation tool can be developed (similar approach to the other MCC process improvement tools)



# New Programs to Support MCC Mission

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## MCC Metrics Blinded Database – *Coming Soon!*

- MCC Executive and Steering Committees working with IBM to design cloud-hosted MCC Metric database
- Database Project Key Features:
  - compare company results to other members (blinded manner)
  - online metric analytic reporting tool
  - ability to “drill down & roll up” to different reporting levels
- MCC member organizations will have the option to participate in the database
- Database will not available to non-MCC member organizations



## MCC Institute – *Coming Soon!*

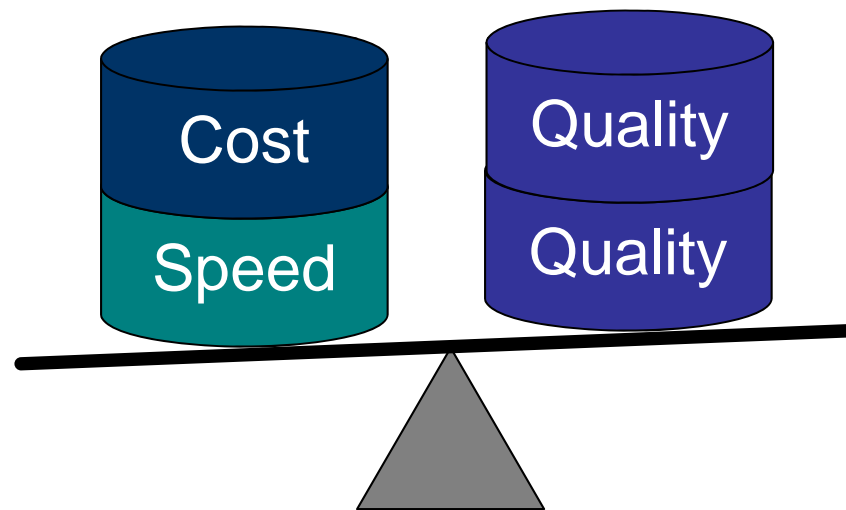
MCC is working with industry experts to develop courses for ***MCC member only*** workshops and online modules designed to help organizations utilize the MCC metrics and tools to their fullest!

Live Workshop & Online Training Modules will include:

- Basic Level (100 level)
- Advanced Levels (200 - 400 levels)\*
- “Ask the Professor” problem-solving sessions

***\* Featuring separate tracks for Senior Managers, Portfolio Managers and Study Managers***

Reducing the time and cost of a task should be balanced with maintaining / improving quality



***MCC Performance Metrics and Quality Tools provide sponsors and service providers with the ability to achieve the right balance***