



Defining, Implementing and Tracking Quality Metrics to Effectively Oversee Vendor Performance and Clinical Conduct

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<http://www.metricschampion.org>

- MCC Mission & Goals
- MCC Clinical Trial Performance Metrics
- MCC Quality Scoring Tools
- Additional Programs to Support the Use of MCC Metrics & Quality Tools
- Q & A

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



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

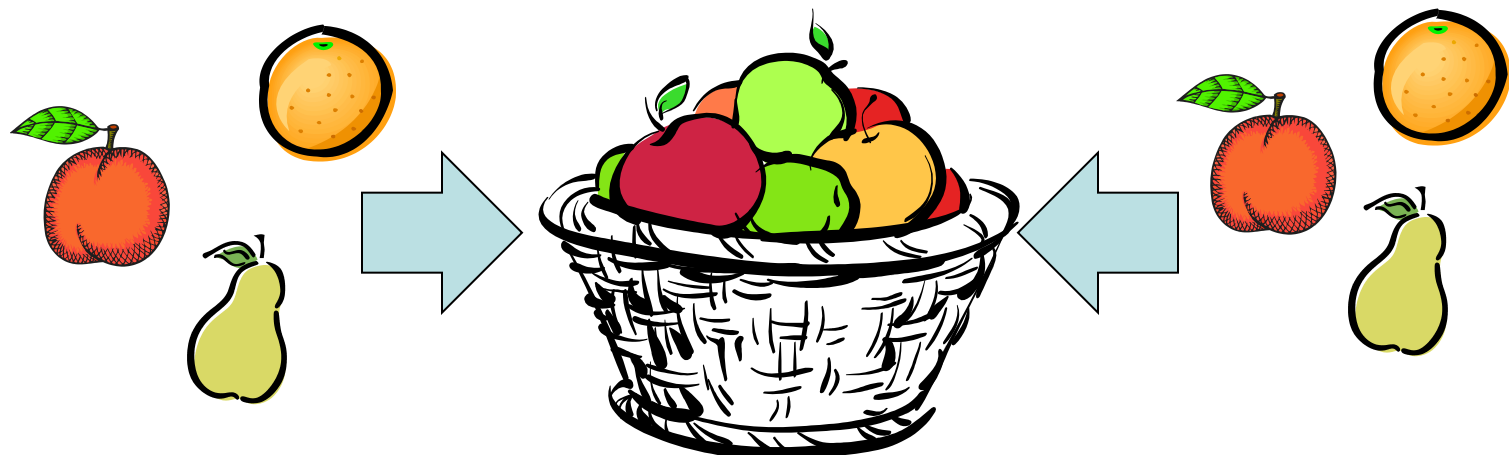
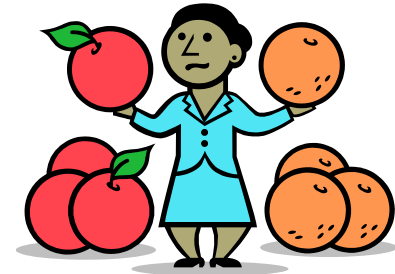
**70+ members
and growing!**

Lack of Standardized Performance Metric Definitions Creates Challenges

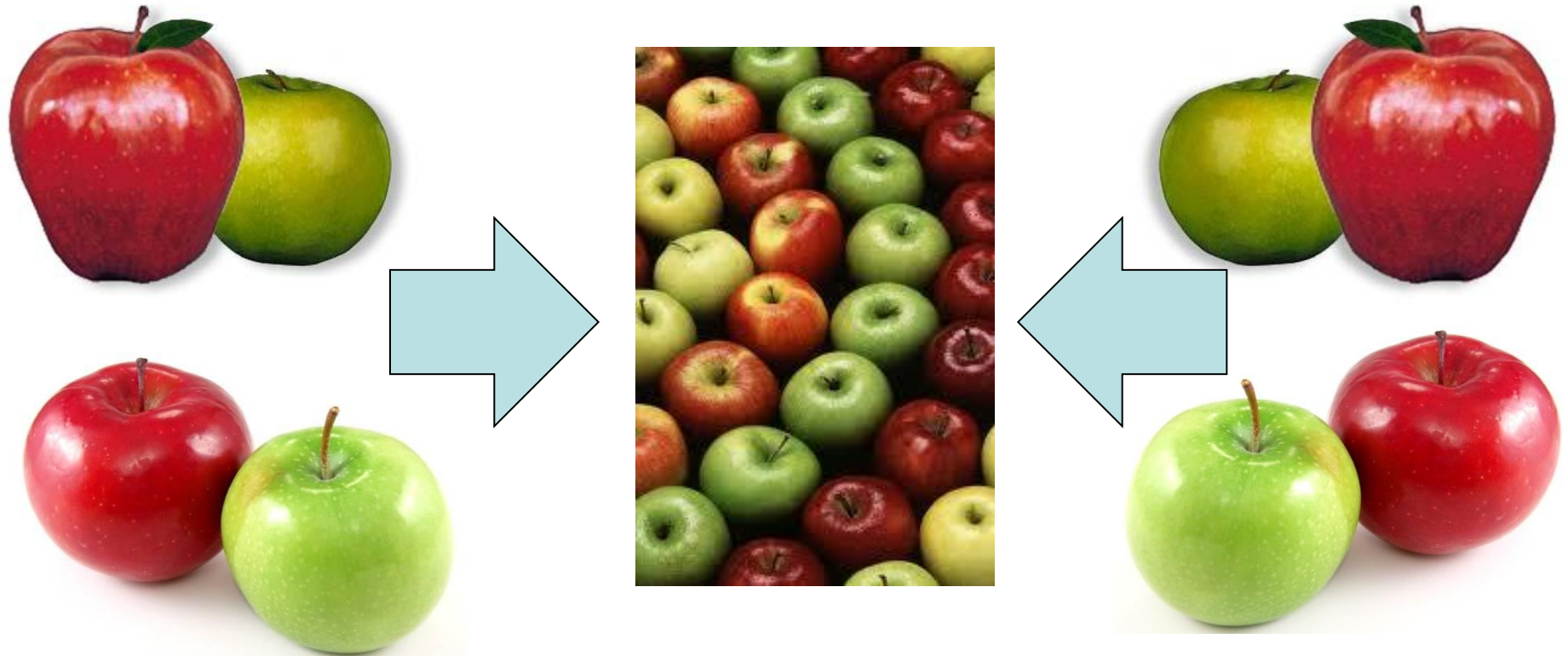


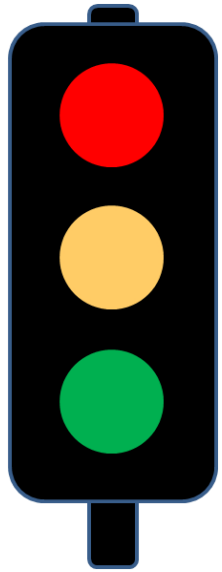
- Sponsors use different service providers
 - Managing metrics across portfolios across service providers is a challenge

- 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





Each set of MCC performance metrics provides a metrics hierarchy:

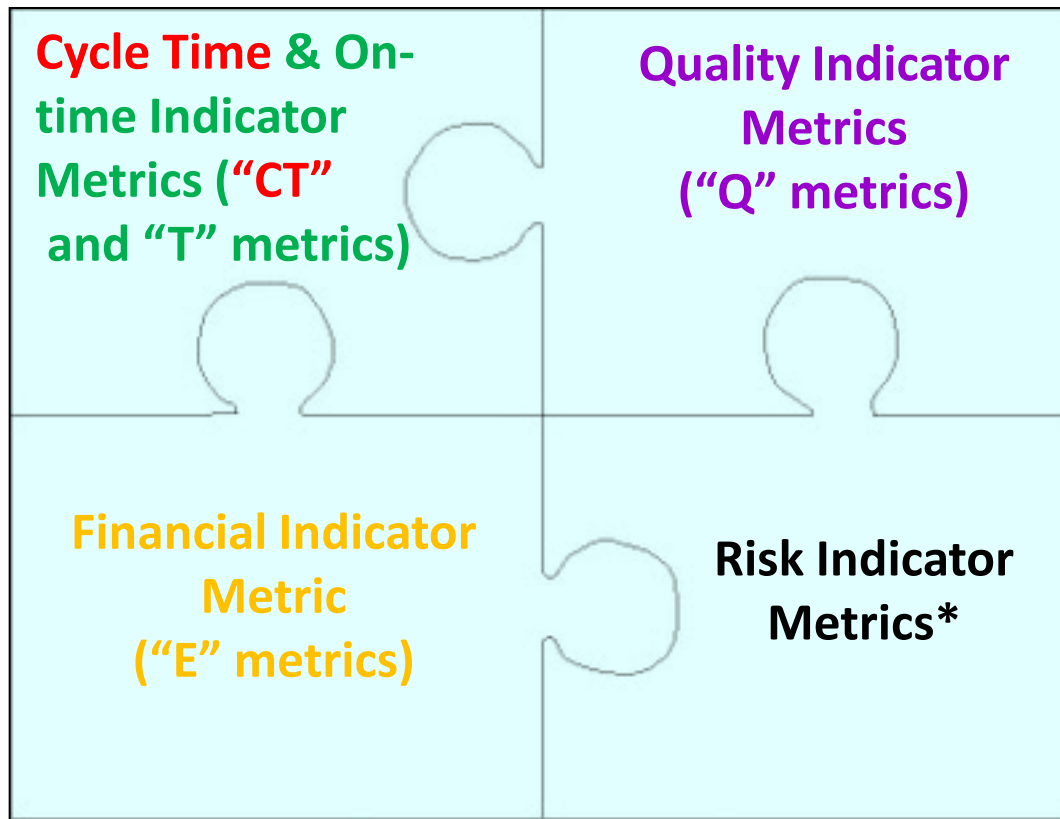
- MCC metrics are performance indicators with defined performance targets
- Most metrics include sub-metrics that should be reviewed when performance does not meet target expectations

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

- 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)

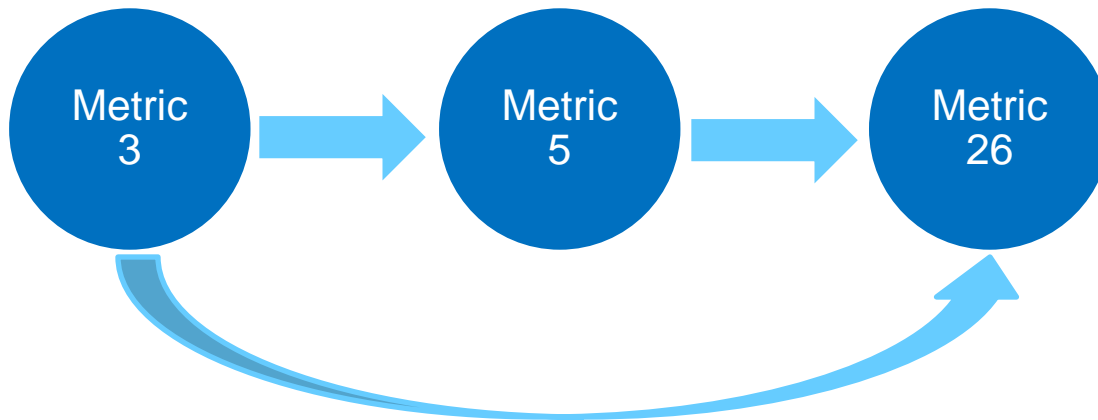
** In development*

- Each Sponsor / Service Provider partnership determines which MCC metrics will be utilized in their own partnerships
- Some MCC metrics are not applicable to all studies
- MCC Workgroups review the metrics definitions in the established MCC Performance Metric sets on a periodic basis and add/delete metrics as needed.



* 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.....



Quality

MCC Quality Tools

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

Benchmarking

MCC Metrics Database

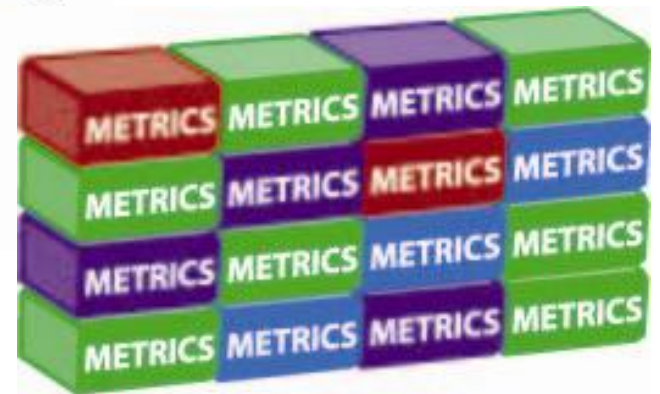
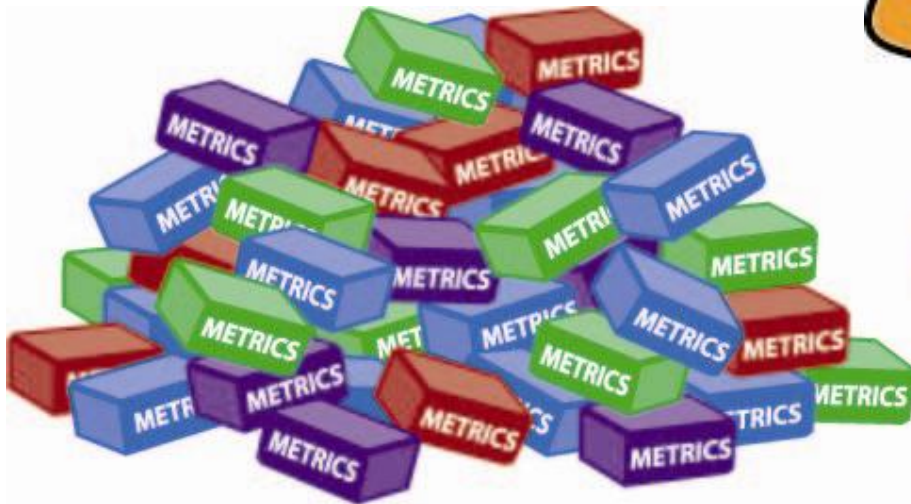
- MCC Members only
- Blinded Comparisons
- Hosted on a Cloud
- **COMING SOON**

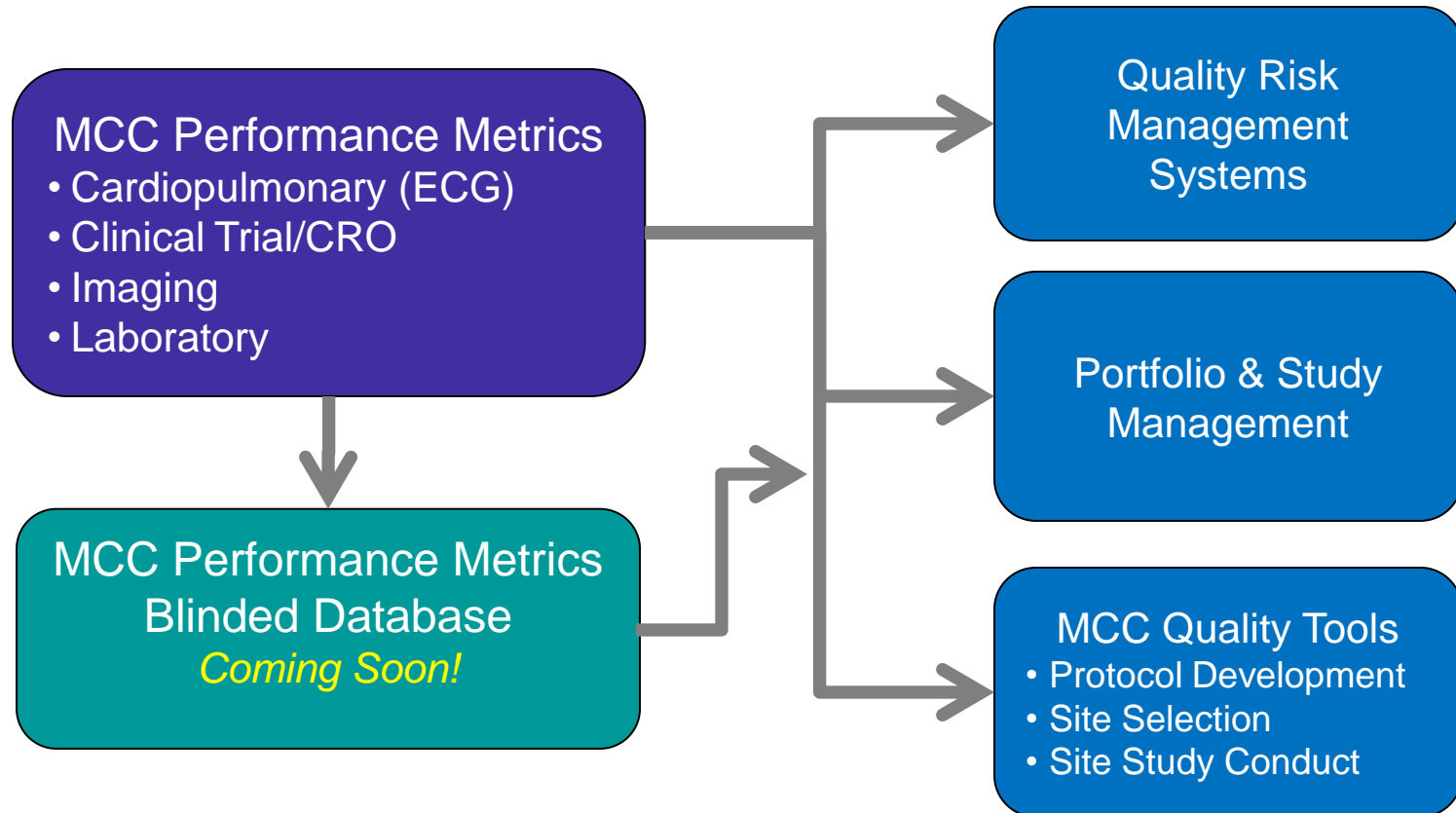
Training

MCC Institute

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

?



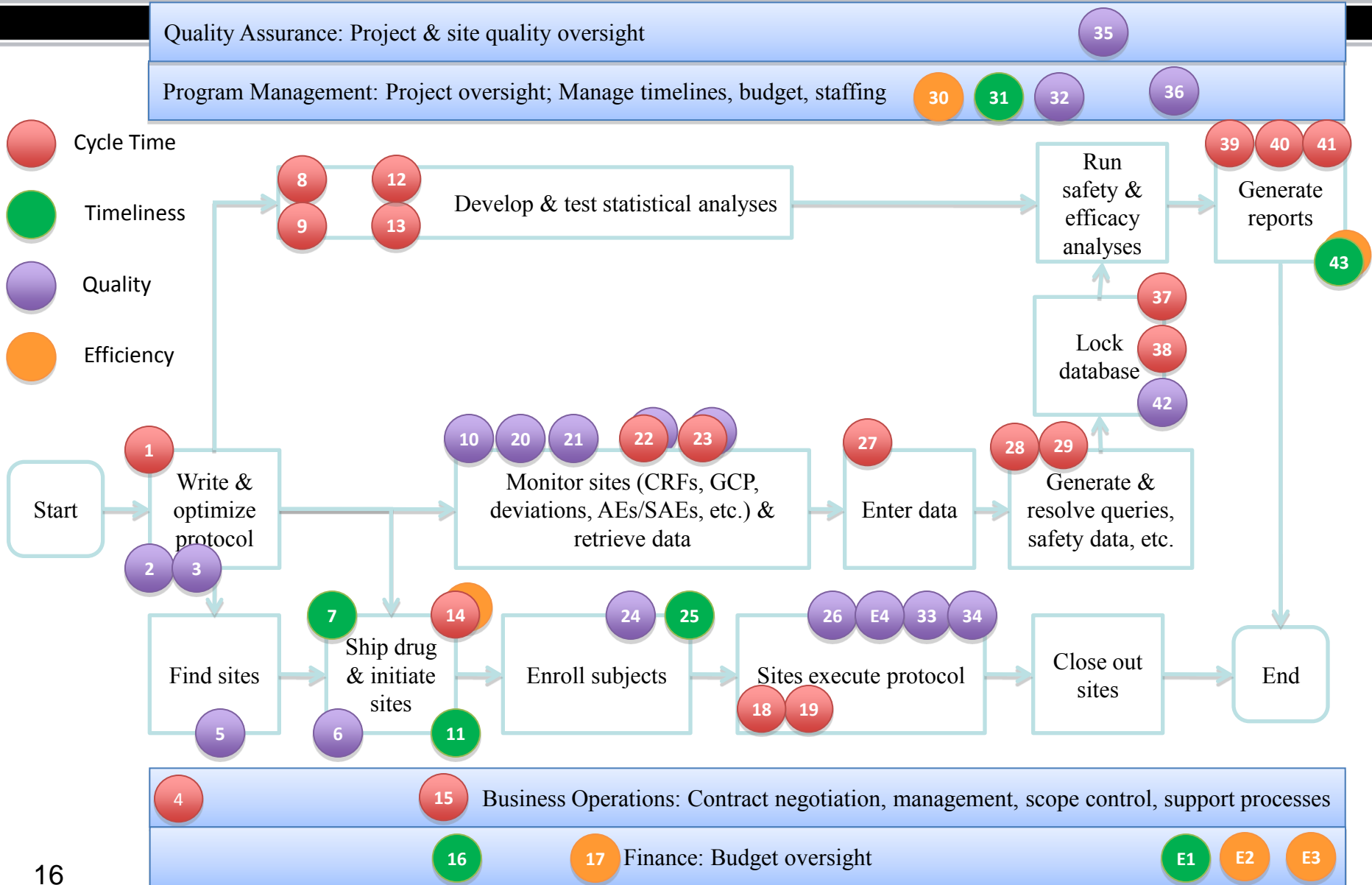


MCC Institute – Training Modules *Coming Soon!*



CLINICAL TRIAL
metrics champion

*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 Study Conduct 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.



QUALITY

- 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

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.

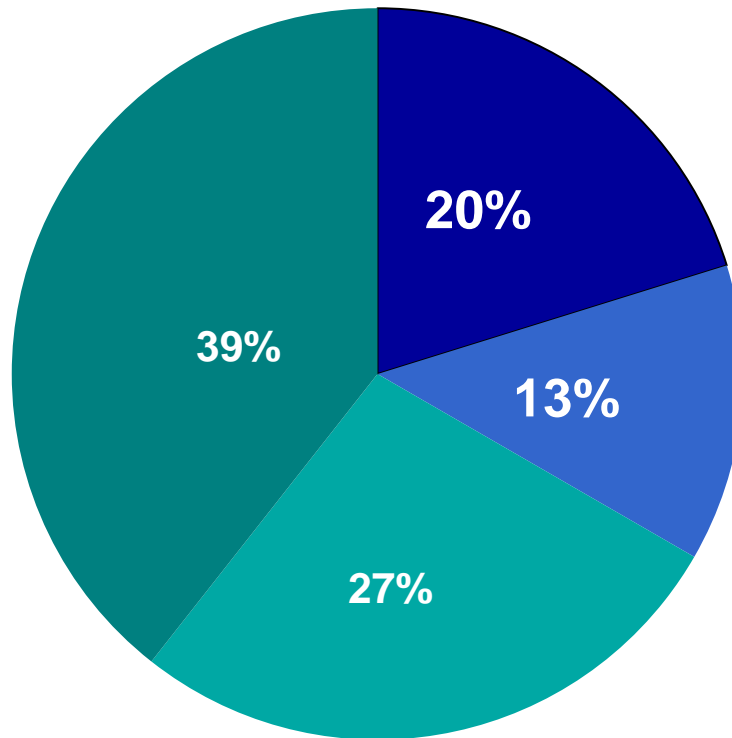
The Quest For Study Start-up Speed Results in Additional Costs!



- 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.



- 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 requirements¹
- Up to 50% of sites enroll one or no patients¹
- 15-20 % of sites never enroll a single patient¹
- Percentage of screened patients retained for the duration of the clinical trial has decreased from nearly 50% in 2001 to less than 25% in 2010²

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

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

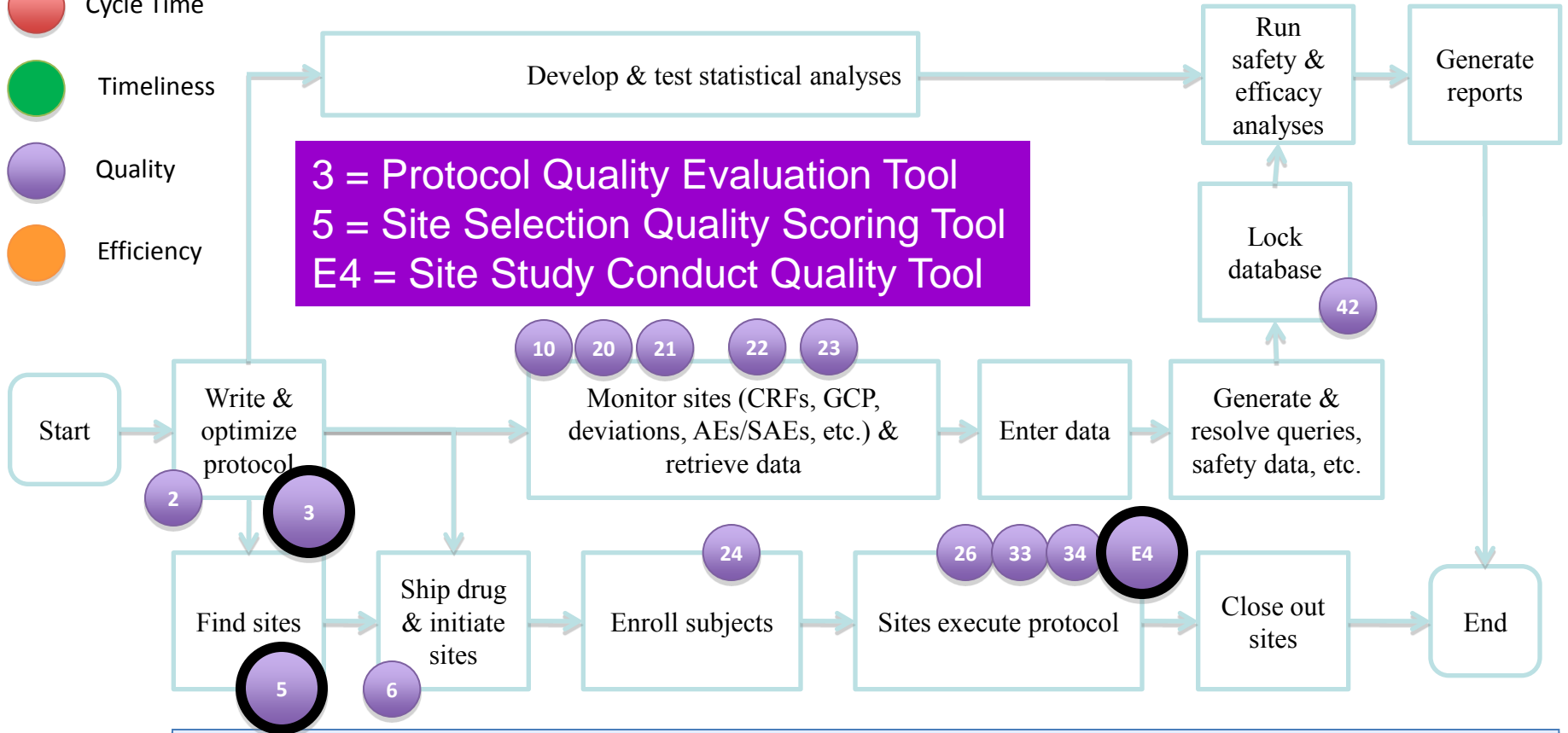
MCC Clinical Trial Performance Metrics Quality Focus

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 Tool



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

Finance: Budget oversight

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

The quality scores shows how well your protocol development processes, site attributes and performance align with the tool's requirements/criteria

- **Goal is to establish a reasonable threshold** which protocols or sites surpass as a measure of quality
- **Focus should not just be on calculating a score** but rather using the tool to assist in rational discussion amongst the teams developing the protocol, selecting sites and/or evaluating performance during study conduct
- **The act of measuring should modify behavior** by providing positive reinforcement for aligning with quality requirements
- **Scores highlight protocols and sites at risk for poor performance:**
 - Can the protocol be implemented at the sites?
 - Are there enough high quality sites selected in country X?
 - Do individual sites need specific training or additional monitoring?

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?

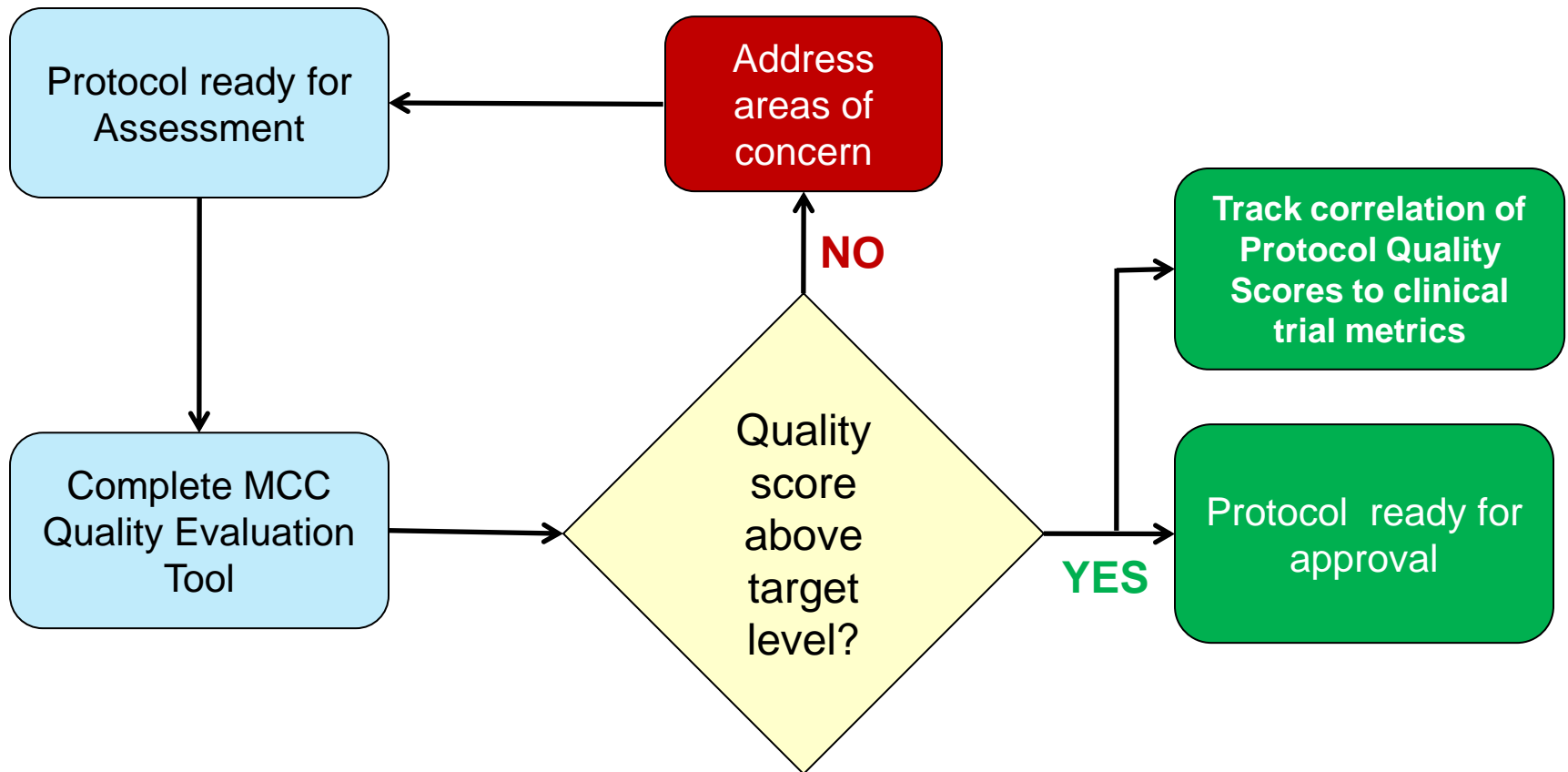
Breadth of Site Interviews

- 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)



Weighted Criteria

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

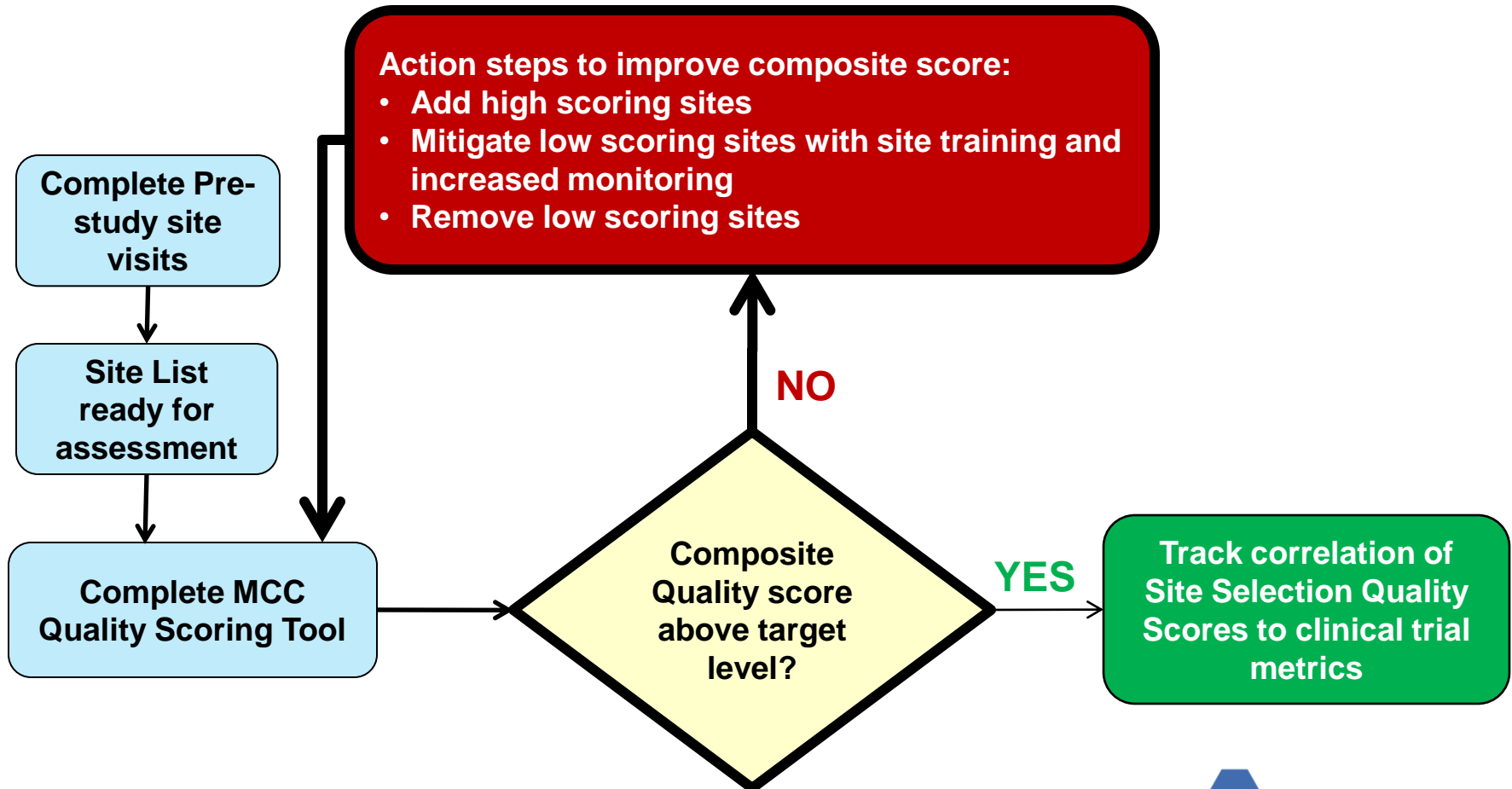
Individual Site Scores

- Each site is rated (Y/N) on a standard set of site quality criteria (8 site selection criteria & 14 site study conduct 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



MCC Site Selection Quality Scoring Tool

The data that you entered up to now has been transferred to this worksheet.
 Now, fill in the answers to the 8 criteria for each site. For each site, enter a "Y" or "N" in columns F through M.
 If a particular criterion is not applicable, this criterion is not included in the scoring; you can enter any value for the site under that criterion (y or n). But you must enter some value to make the calculation work.
 The score for each site will appear in column AB.

If you marked "Do not include this site in calculations" in the Site List worksheet, that's reflected in column AC. However, you can override that decision here by placing a "Y" or "N" in column AD.

Country	Site Name	Key Opinion Leader (KOL)? If you then recommend scoring	Site has unresolved regulatory / audit findings. If you then consider whether to include the site before scoring	Site Scoring Criteria (click on criterion to see a list of useful scoring questions and related MCC metrics)								Site Score	Include this site in selection list? (answer taken from "Site List" Worksheet)
	Criterion Weighting			Demonstrated ability to enroll subjects for this or a similar indication (can meet or beat average enrollment goals; access to recruitment; retention tools and	Facilities/equipment/systems adequate for protocol requirements	Competing trials do not interfere with enrollment at this site or management of the trial by research staff	Standard of care is in line with protocol requirements	Investigator/ sub-investigator/ coordinator with scientific and clinical research background adequate for this indication	Ability to complete start-up activities (budget/contract negotiations, EC approval) within expected country timelines	Demonstrated compliance with sponsor/CRO _ethical, legal, and GCP requirements	Site has a proven ability to produce high quality timely data and is responsive to data queries (paper or EDC)		
				3	2	2	1	3	2	3			
Brazil	1111			N	N	Y	Y	Y	N	Y	N	47%	Y
Brazil	1112			N		Y	Y	Y	Y	N	N	48%	Y
Brazil	1113	Y		N	Y	N	N	Y	Y	N	N	37%	Y
China	1121			Y	N	Y	N	N	N	Y	N	42%	Y
China	1122			Y	N	Y	Y	Y	N	Y	N	63%	Y
China	1123			N	Y	Y	N	Y	N	Y	Y	53%	Y
India	1131			Y	Y	N	Y	Y	Y	Y	Y	74%	Y
India	1132			N	N	N	N	Y	Y	Y	N	42%	Y
Russia	1141			Y	Y	Y	N	Y	N	Y	N	68%	Y
Russia	1142			Y	N	Y	Y	Y	N	Y	Y	79%	Y
Russia	1143			N	Y	N	N	Y	Y	N	N	53%	Y
United States	1151			Y	Y	Y	Y	Y	Y	Y	Y	100%	Y
United States	1152			Y	Y	N	Y	Y	Y	Y	N	74%	Y
United States	1153	Y		N	Y	N	Y	Y	Y	Y	Y	63%	N
United States	1154			Y	Y	Y	Y	Y	Y	Y	Y		Y

Legend: Y (Green), N (Pink)

Navigation: Start Here | SSQ Front Page | SSCE Front Page | SSQ Criteria Weights | SSQ Country List | SSQ Site List | SSQ Site Data | SSQ Scoring

Site received 37% - should it be removed from the site list?

MCC Site Selection Quality Scoring Tool

The data that you entered up to now has been transferred to this worksheet.
 Now, fill in the answers to the 8 criteria for each site. For each site, enter a "Y" or "N" in column F through M.
 If a particular criterion is not applicable, this criterion is not included in the scoring; you can enter any value for the site under that criterion (y or n). But you must enter some value to make the calculation work.
 The score for each site will appear in column AB.

If you marked "Do not include this site in calculations" in the Site List worksheet, that's reflected in column AC. However, you can override that decision here by placing a "Y" or "N" in column AD.

Country	Site Name	Key Opinion Leader (KOL)? If you then recommend whether to include the site before scoring	Site has unresolved regulatory / audit findings. If you then consider whether to include the site before scoring	Criterion 1: Demonstrated ability to enroll subjects for this or a similar indication (can meet or beat average enrollment goals; access to recruitment; retention tools and	Criterion 2: Facilities/equipment/systems adequate for protocol requirements	Criterion 3: Competing trials do not interfere with enrollment at this site or management of the trial by research staff	Criterion 4: Standard of care is in line with protocol requirements	Criterion 5: Investigator/sub-investigator/coordinator with scientific and clinical research background adequate for this indication	Criterion 6: Ability to complete start-up activities (budget/contract negotiations, EC approval) within expected country timelines	Criterion 7: Demonstrates compliance with sponsor/CRO ethical, legal and GCP requirements	Criterion 8: Site has a proven ability to produce high quality timely data and is responsive to data queries (paper or EDC)	Site Score	Include this site in selection list? (answer taken from "Site List" Worksheet)
Criterion Weighting				3	2	2	1	3	2	3	3		
Brazil	1111			N	N	Y	Y	Y	N	Y	N	47%	Y
Brazil	1112			N	Y	Y	Y	Y	Y	Y	N	68%	Y
Brazil	1113	Y		N	Y	N	N	Y	Y	N	N	37%	Y
China	1121			Y	N	Y	N	N	N	Y	N	42%	Y
China	1122			Y	N	Y	Y	Y	N	Y	N	63%	Y
China	1123			N	Y	Y	N	Y	N	Y	N	53%	Y
India	1131			Y	Y	N	Y	Y	Y	Y	N	74%	Y
India	1132			N	N	N	N	Y	Y	Y	N	42%	Y
Russia	1141			Y	Y	Y	N	Y	N	Y	N	68%	Y
Russia	1142			Y	N	Y	Y	Y	N	Y	Y	79%	Y
Russia	1143			N	Y	N	N	Y	Y	Y	N	53%	Y
United States	1151			Y	Y	Y	Y	Y	Y	Y	Y	100%	Y
United States	1152			Y	Y	N	Y	Y	Y	Y	N	74%	Y
United States	1153	Y		N	Y	N	Y	Y	N	Y	Y	63%	N
United States	1154			Y	Y	Y	Y	Y	Y	Y	N	84%	Y

Legend: Y (Green), N (Pink)

Most sites received a "NO" score for criterion 8 (data quality) - study at risk

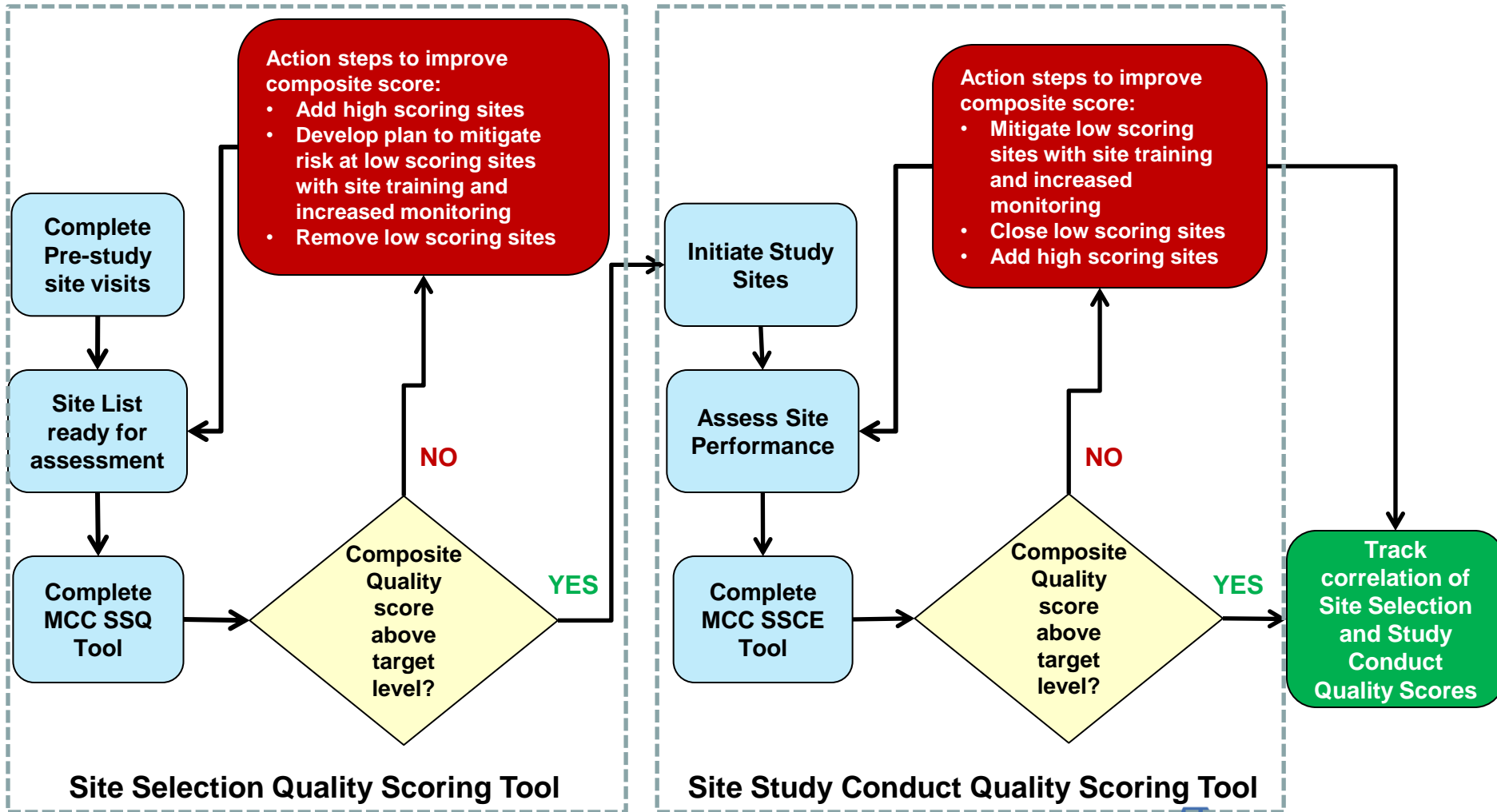
Total number of sites with scoring:	15	<--- This is the Site Selection Score
Total number of sites with scoring selected:	12	
Site Selection Score including all sites:	68%	
Site Selection Score including selected sites only:	75%	

Score by Country:

Country	# sites scored	# sites selected	Site Selection Score	
			All Sites	Selected Sites Only
Brazil	3	2	51%	58%
China	3	3	53%	53%
India	2	1	58%	74%
Russia	3	3	82%	82%
United States	4	3	87%	100%

Score improved to 75% because we removed three low scoring sites

India score improved to 74% because we removed one low scoring site



MCC Clinical Trial Performance Metrics

- Patient enrollment & retention metrics
- Data entry metrics
- Query metrics
- Protocol deviations
- Drug supply metrics
- Audit Findings

MCC Lab Performance Metrics

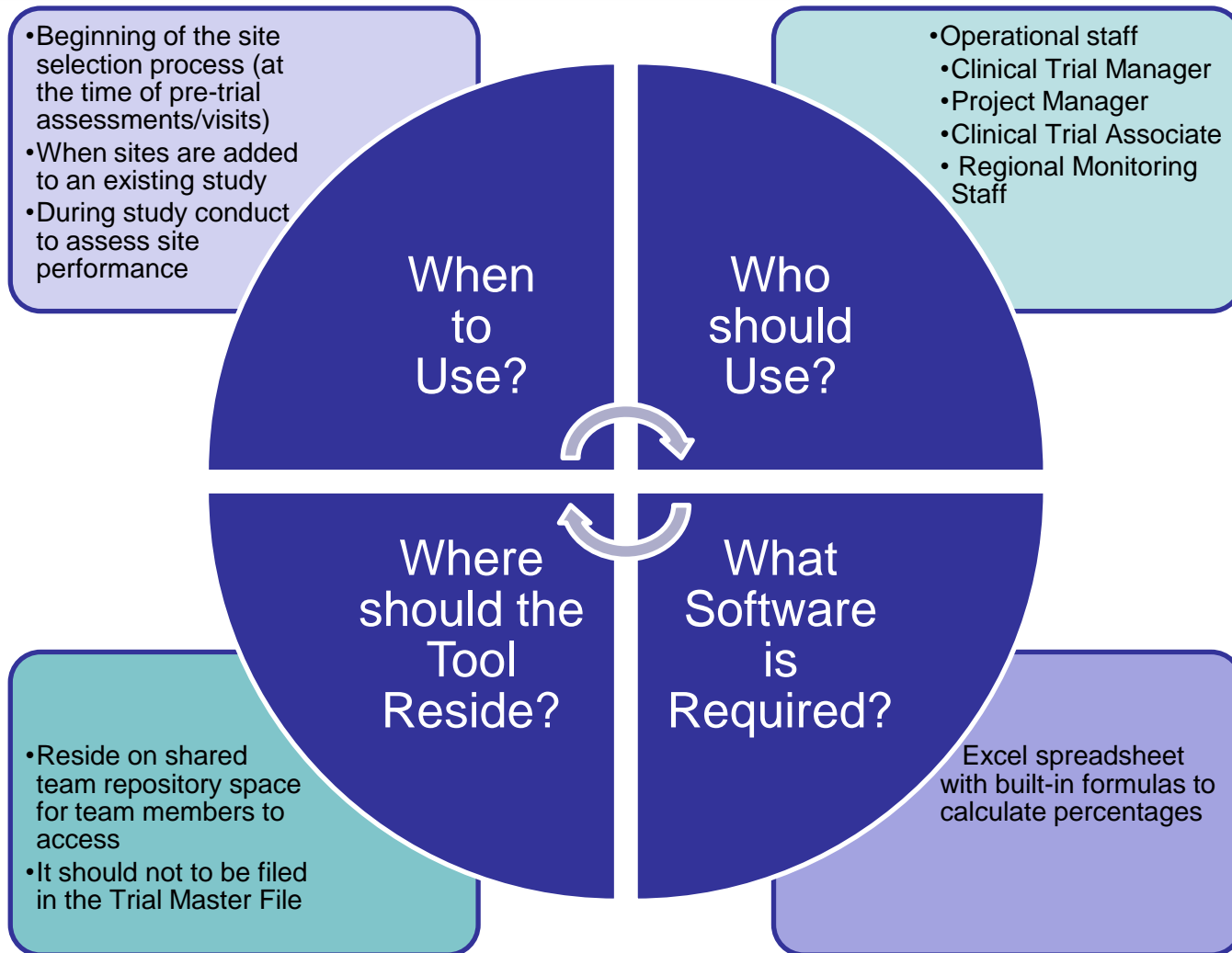
- Sample quality metrics
- Query metrics

MCC ECG Performance Metrics

- Sample collection metrics
- Query metrics
- ECG quality metrics
- Equipment failure metric

MCC Imaging Performance Metrics

- Sample collection metrics
- Query metrics
- Image quality metrics



MCC Monitoring WG provides 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)

Risk-Based Monitoring Approach

Centralized Monitoring

On-Site Monitoring

Remote
Source Data
Verification

Study Data
Outlier
Analysis

Performance
Metrics

MCC
Metrics

Study
Start-Up

High Risk
Sites

MCC Site Selection &
Site Conduct Tool

Performance
Metrics

MCC
Metrics

Quality

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- Protocol Quality Evaluation Tool
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Benchmarking

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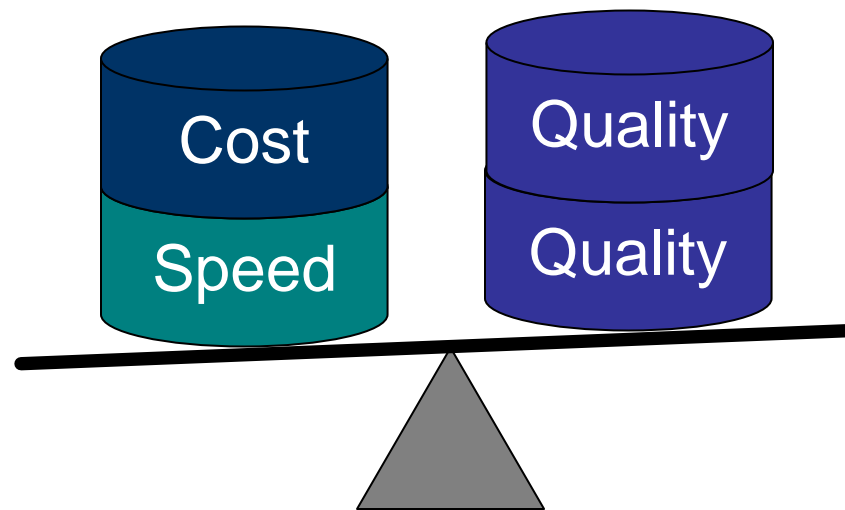
- MCC Members only
- Blinded Comparisons
- Hosted on a Clinical Cloud
- **COMING SOON**

Training

MCC Institute

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

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***