



BENCHMARKING CLINICAL OPERATIONS

Discussion Document

March, 2005



Agenda

- Audio-Conference Housekeeping (5 min)
- Presentation of Speaker (5 min)
- Main Presentation -- with lively discussions (60-70 min)
- Any Additional Q&A's (10 min)



Audio-Conference Participation

- Please note your questions for the end of the presentation
 - We don't have all the answers (feel free to contribute)
 - Please do NOT reveal any proprietary information
- Questions
 - There will be time at the end of the presentation or contact us with any requests for additional information.
(rmcdaniel@vantageptconsult.com)
 - Please identify yourself (affiliation and name) before contributing
 - We'll try to repeat the questions for the entire audience



The Speaker - Keith Ortiz

- Partner at VantagePoint Consulting Group
 - Management consulting firm based in NJ
 - Specialize in process improvement, performance measurement, change management, and IT effectiveness
 - All staff have 15+ years industry and consulting experience
 - Senior staff out of Booz Allen, PA Consulting, Ernst&Young, PWC, First Consulting Group
 - Focus in Pharma with some Biotech: high concentration of projects with Finance, IT, Clinical (our backgrounds)
- Focused on Clinical Operations improvements
- 20 years consulting in pharma (Booz, PA-Consulting)
- Specializes in industry alliances and forums
- Provides analytically-based approaches to improvement projects



Main Presentation - Discussion Topics

- Benchmarking Defined (for this audio-conference)
- Reasons for Benchmarking
- Where to Begin
- What to Expect



Clinical Operations Benchmarking

- Pharmaceutical / Biotech Clinical Operations
- Includes Internal and CRO operations
- From Clinical Plan to Filing (Ph I-IV)
- Cycle Time, Cost & Quality
- Portfolio & Project Benchmarks
- Trial Design Innovations (e.g., Adaptive Trials)

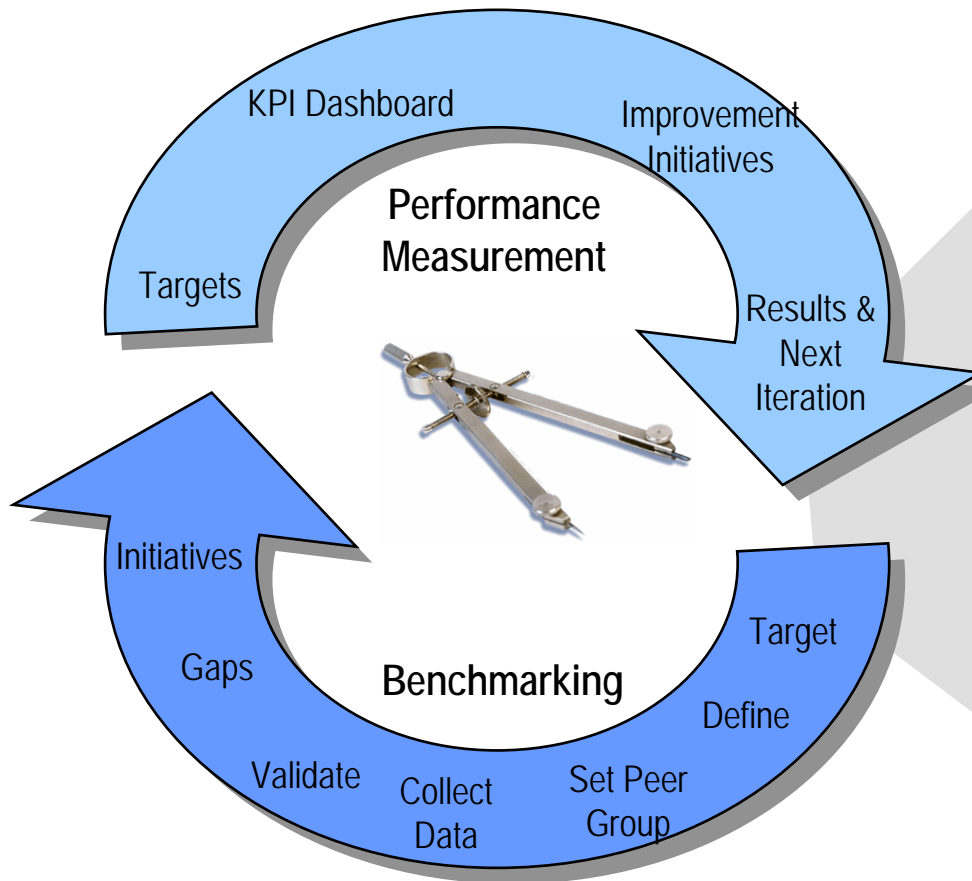


Why Benchmarking

- More and more pressure to “do more with less”
 - Focus investments in areas with greatest return
 - Estimate investment returns for known problem areas
 - Inform Continuous Improvement Initiatives / Dashboards
 - Justify need for level of resources
 - Decide Internal Operations vs. CRO’s (or vs. Other Internal Ops)
 - Establish stretch targets for overall organization performance
- Establish “the dialog” with peers in the industry to share non-proprietary insights
- Licensing partners more and more demanding objective evidence of operational efficiency (in addition to effectiveness)



Benchmarking And Performance Measurement



These tools enable management to drive change:

- Develop credible performance improvements based on objective analysis
- Set targets and standards of performance tied to competitive realities
- Understand current performance and improvement opportunities
- Estimate improvement potential
- Accelerate adoption of best practices
- Instill focus and culture of high-performance in the organization

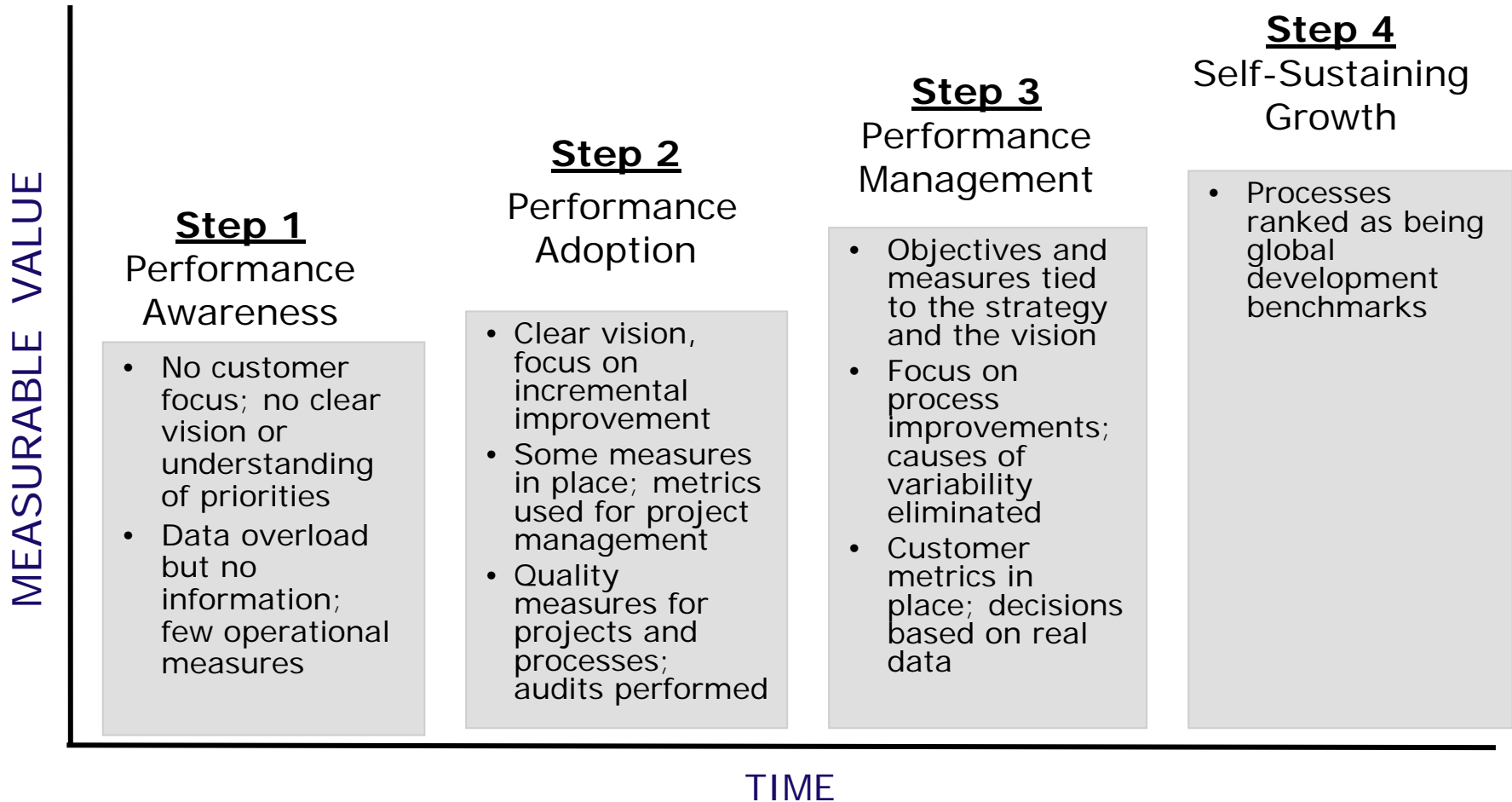


Clinical Benchmarking Maturity Levels ...

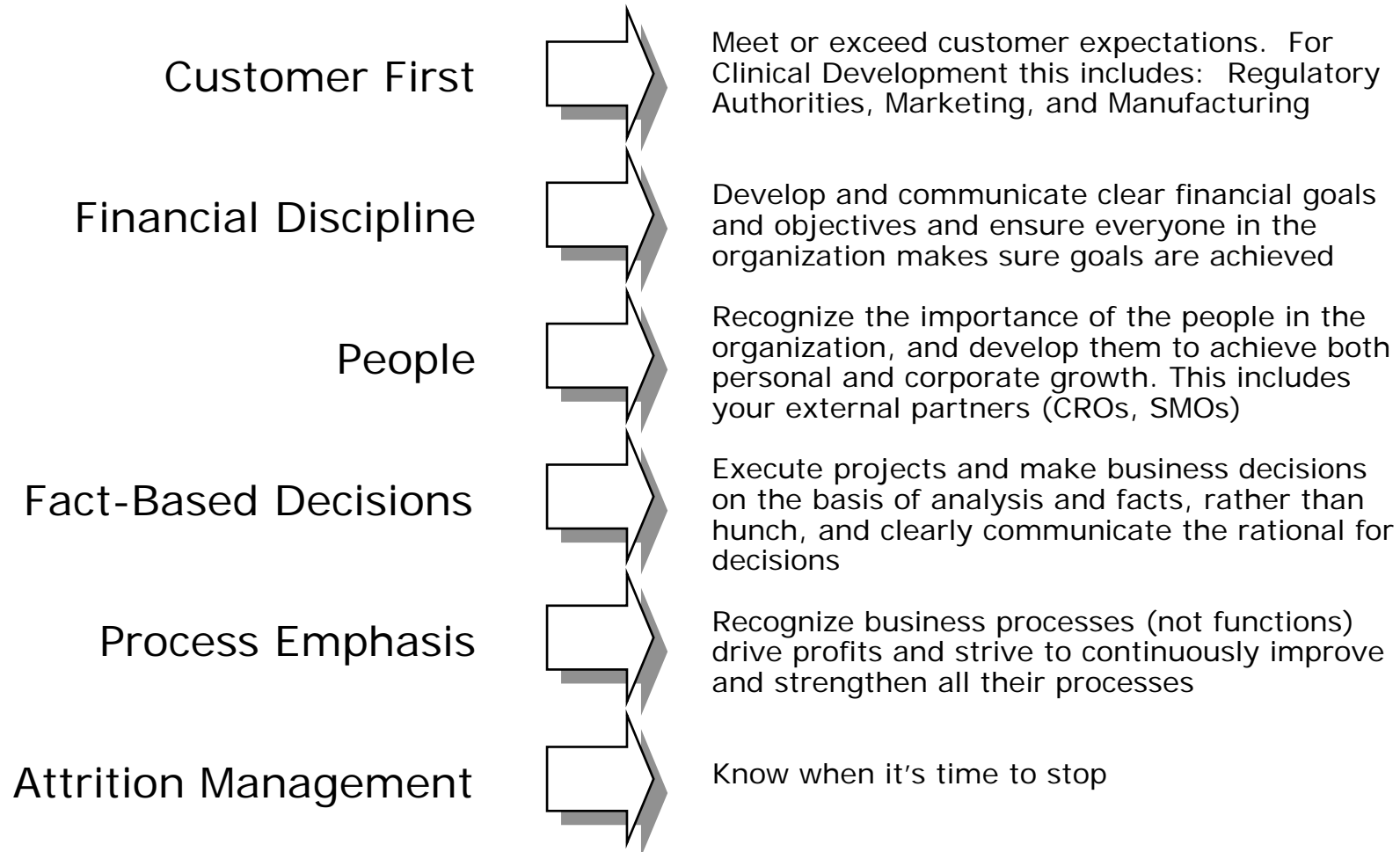
Maturity	Characterized by...	Benefits
First Study (Year 1)	<ul style="list-style-type: none"> Limited scope Data challenges Development of methodology – measures, validation Establishment of peer-group Cultural acceptance 	<ul style="list-style-type: none"> Define measures Create awareness for performance improvement Get early benefits from “low hanging fruit” Develop baseline Begin to instill performance management culture Enhance understanding of drivers of performance
Follow On Study (Year 2)	<ul style="list-style-type: none"> Improving data collection - baseline Perfecting the methodology Moving beyond the numbers Enhancing acceptance Adopting external ideas Implementing initiatives 	<ul style="list-style-type: none"> Define competitive position – areas of strength and weakness Identify best known methods Clearly distinguish impacts of controllable and non-controllable factors; Incorporate benchmarking into business initiatives Shared understanding of key performance drivers
Subsequent Years (Year 3 +)	<ul style="list-style-type: none"> Expanding scope Automating data collection Establishing formal targets Institutionalizing the practice 	<ul style="list-style-type: none"> Development of strategies to step-change performance Performance reporting Incorporation into target setting and reward mechanisms Performance gaps closed Measurable improvement tracked Mastery of change implementation



...Performance Measurements progress in step

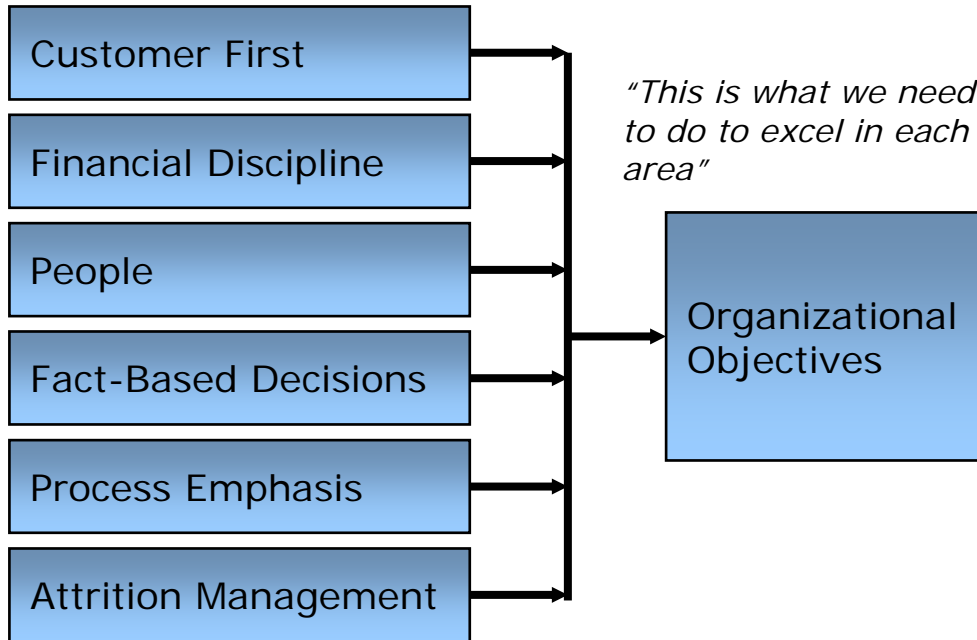


Cost, cycle time and quality are just part of the equation





Where to Begin...



Performance Improvement Worksteps

Step 0
How Big?

- Measure Performance & Current Practices
- Compare Performance & Practices
- Analyze High-Level Opportunities
- Develop Initiatives / Recommendations

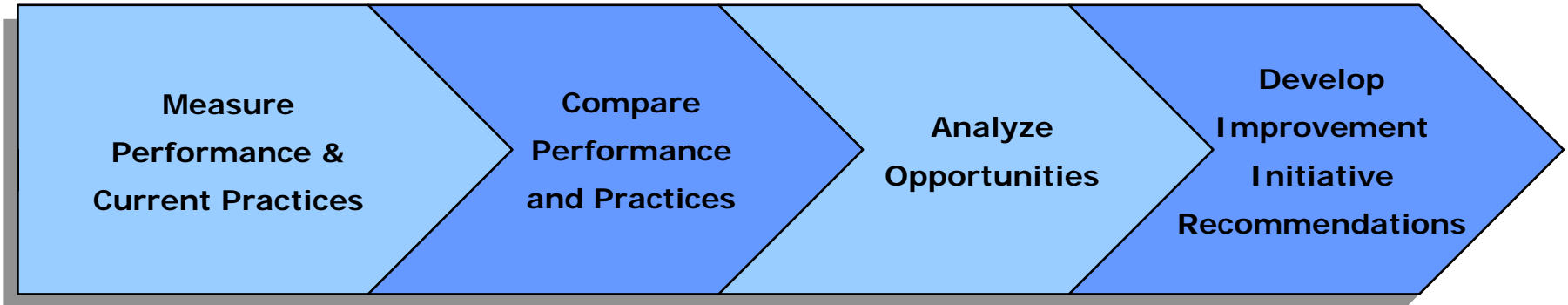
Step 1
What to Do?

Step 2
How to Do It?

Step 3
Do It!



Step 0 - How Big is the Opportunity?



- Measure current costs, cycle times
- Measure service levels / quality
- Capture current practices

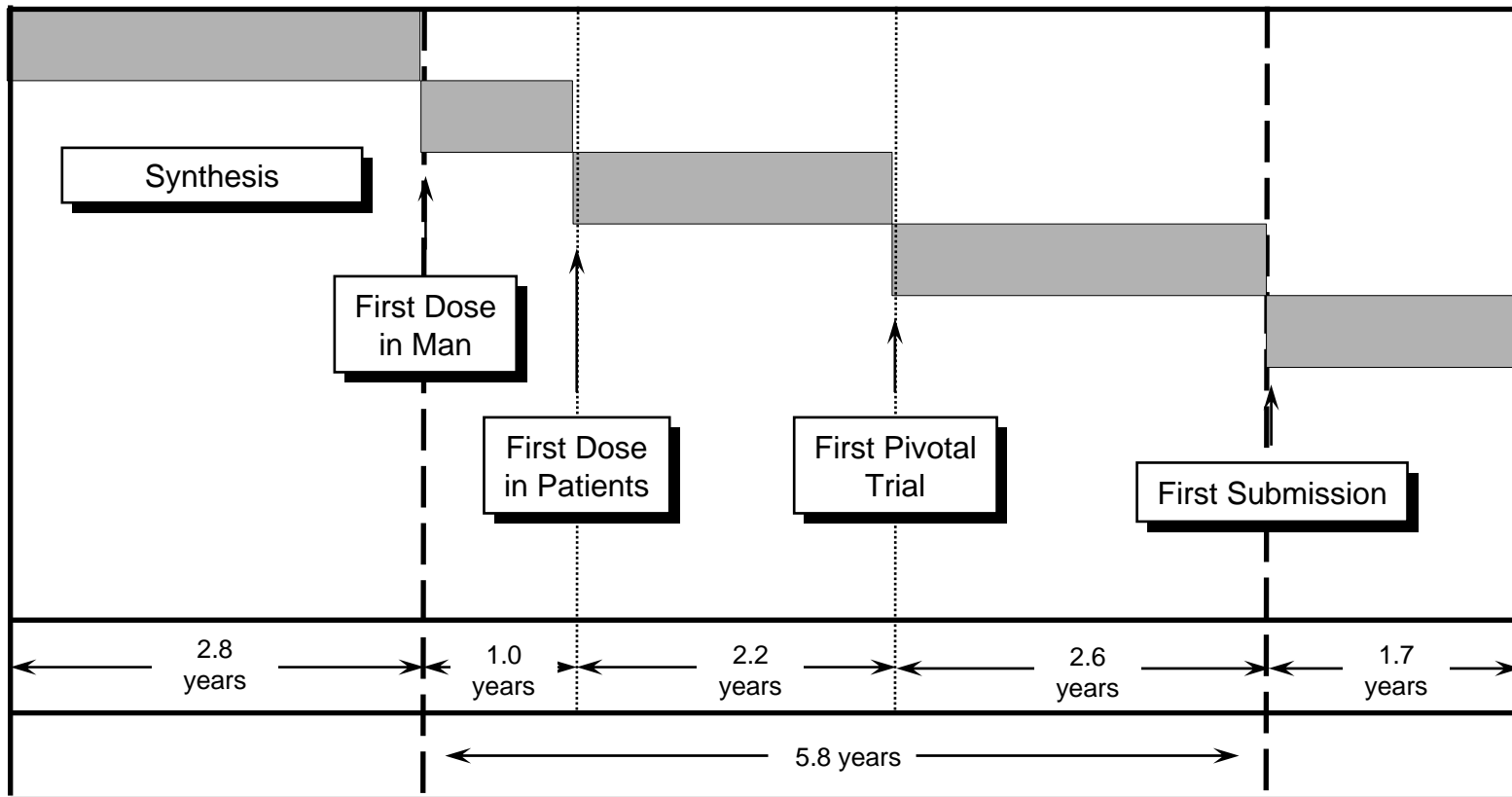
- Compare costs, cycle times against "best in class"
- Assess practices and capabilities
- Identify opportunities for improvement

- Define processes driving performance gaps
- Quantify the opportunity
- Develop consensus

- Identify root causes inhibiting performance
- Develop recommendations for specific changes
- Validate recommendations



Maturity Level 0 - Illustrative Example, Cycle Time



Source: CMR, 1996



Maturity Level 0 - Illustrative Example, Cycle Time

<i>Therapeutic Area</i>	<i>Phase I</i>	<i>Phase II</i>	<i>Phase III</i>	<i>Submission</i>	<i>Overall</i>
All	1.3	2.2	2.6	1.8	7.9
Cardiovascular	1.0	1.8	2.6	2.7	8.1
CNS	1.3	3.0	2.8	3.0	10.1
Antineoplastic	1.1	2.8	3.2	0.9	8.0
Alimentary/ Metabolic	1.1	1.8	3.4	1.0	7.3

Source: CMR, 1996



Benchmarking Clinical Operations

- Published clinical benchmarks focus on time-to-market (e.g., CMR, Best Practices, Parexel, Business Intelligence)
- These benchmarks are typically not “actionable”
 - Not done in conjunction with best practice review
 - No buy-in from senior management on comparability
- Cost data for clinical is harder to obtain
 - No FDA statistics (e.g., filing date boundaries)
 - Multi-tasking and overtime is the norm
 - Costs are spread across internal and external participants
 - “Good planning” is key to cost control, and is difficult to quantify
 - Benchmarking for costs is not institutionalized



Cost Benchmarking - Options to Consider

- Internal Benchmarking
 - Comparisons across multiple clinical studies
 - Comparison with similar internal functions (e.g. clinical development)
 - Contracted services providers (working on sponsor projects)
- External Benchmarking with Peer Group Members
 - Contract service providers (e.g. CROs, CMO's)
 - Pharmaceuticals
 - Biotech



Illustrative Costs and Cycle Time Benchmarks

First Benchmark Study

Identification	Non-Controllables						Metrics	
Product	Novelty / Technology	Therapeutic Area	Geography	Phase	Total Patients	Total Studies	Cycle Time (Months)	Cost (US\$ Millions)
MI34533	MABs	Anti-Infectives	US - Outsourced	1	35	3	15	1.0
MI34533	MABs	Anti-Infectives	US - Outsourced	2	200	5	18	3.0
MI34533	MABs	Anti-Infectives	US - Outsourced	3	15,000	2.1	21	160.0
MI34533	MABs	Anti-Infectives	US - Outsourced	Filing	na	na	6	1.0

Follow-On Benchmark Study

Identification		Non-Controllables						Metrics	
Product	Protocol	Novelty	Therapeutic Area	Geography	Activity	Phase	Median Patients	Cycle Time (Weeks)	Cost (US\$ Thous)
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Protocol Writing	3	10,000	14	75
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Study Start-Up	3	10,000	10	125
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Patient Enrollment	3	10,000	32	150,000
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Data Cleaning	3	10,000	17	450
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Statistical Analysis	3	10,000	10	350
MI34533	Pivotal	MABs	Anti-Infectives	US-Outsourced	Report Writing	3	10,000	14	250

Subsequent Studies

Industry Output Measures designed to measure productivity of clinical staff --

Clinical Staff per Active Protocol				
Active Sites per Clinical Staff				
CRF Pages per Data Management Staff				
Study Reports per Statistician				
Study Reports per Clinical Staff				



Illustrative Findings

Strategy and Planning

- Regular inputs from Regulatory and Marketing critical to success
- Use of initial results to speed-up next stage of development deemed dangerous - led to misleading interpretations and hindered decision making process
- Little ownership of the timeline targets generated a very pessimistic attitude
- Commercialization was the driver - information is made available to project teams on competitor drugs and global market issues

Technology

- Significant focus on use of Internet/intranet for data capture
- Tracking systems used to identify loopholes in data capture and reporting systems
- Common use of publishing technology with focus on dossier submission
- Use of technology was driven and supported from the very top of the business

People and Processes

- Training undertaken in time management, planning and customer focus
- Quality seen to be reflected in in staff, training and levels of experience
- Some resistance to change characterized by poor communication, staff turnover
- Some teams not prepared for change - distinct therapeutic areas differences



Illustrative Recommendations

Strategy and Planning

- Set up clinical operations as Internal CRO
- Establish department to explore “leading edge” technologies and/or methodologies
- Establish clinical operations portfolio / resource management function and responsibilities

Technology

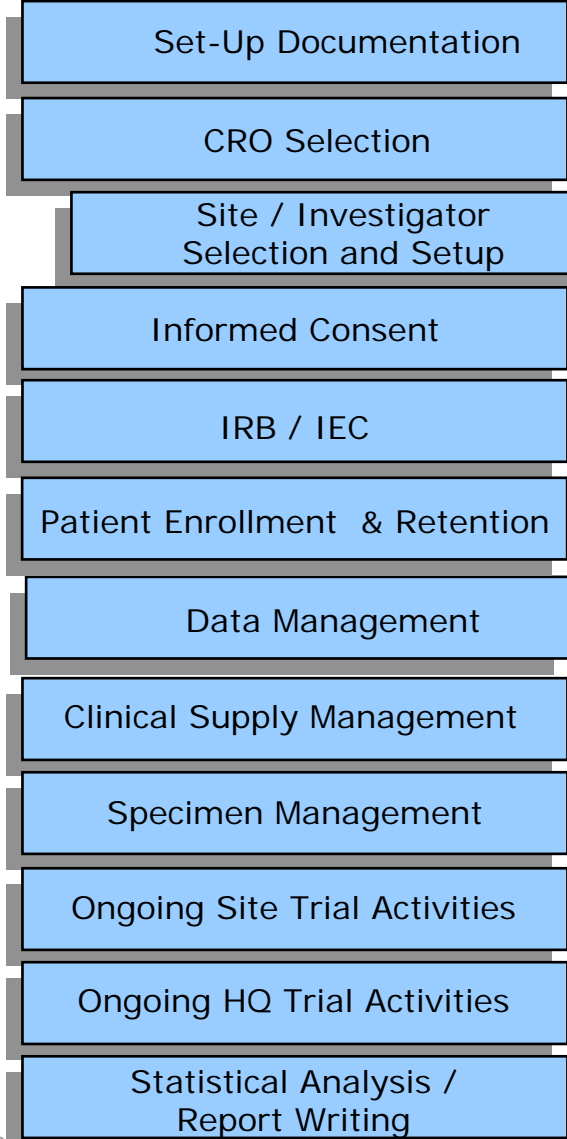
- Reduce Biometrics systems to one - globally
- Consolidate to the corporate document management strategy

People and Processes

- Build centralized Site Management processes and organization
- Process pharmaco-genomics samples in parallel with clinical samples
- Build a cost-effectiveness culture among clinical operations staff
- Implement stage-gates for quality control



Follow-On Benchmarking - Define Processes Rigorously



- Study site / investigator identification
- Pre-study assessment visit
- Site initiation
- Pre-launch training for investigators and study coordinators
- Clinic certification
- Study site budget development / contract negotiations
- Objection handling for the protocol



Controllable vs. Non Controllable Drivers

Controllable

- Automation / Document management
- Processes and organization
- Roles & Responsibilities
- Contracting practices and terms
- CRA turnover

Non Controllable

- Therapeutic area (e.g. oncology vs. cholesterol)
- Scope of the clinical trial (e.g. USA only vs. global)
- Novelty / Technology / Form (e.g., Tablet vs. Injectable) of molecule
- Phase of the clinical trial (I, II, III, IV)

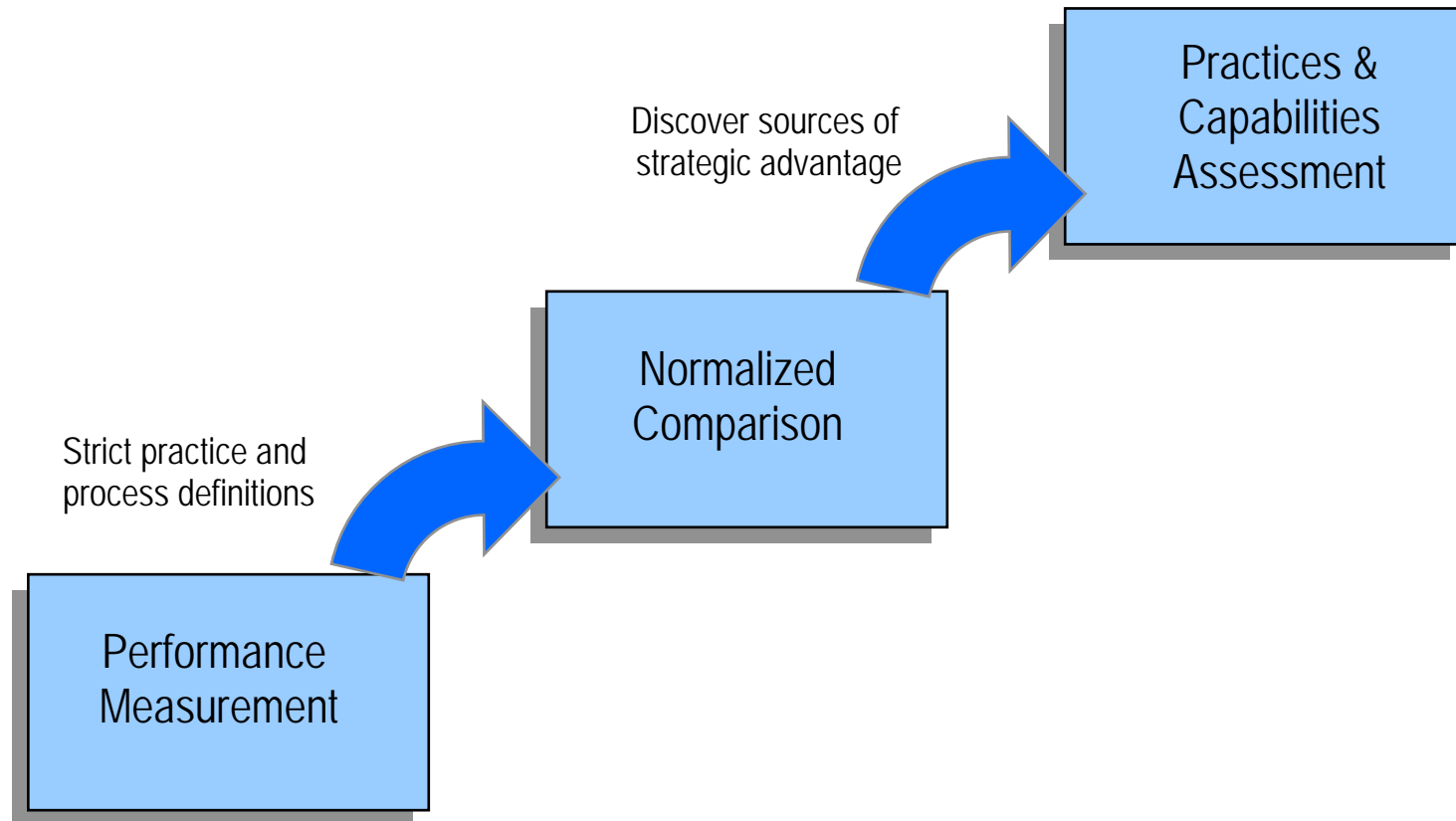


Study-specific Variables

- Protocol Complexity (e.g., Procedures / Patient)
- Use of Affiliated vs. Unaffiliated sites



Normalized Comparisons And Best Practices





Robust Tools For Data Collection

GLOBAL SEMICONDUCTOR FACILITIES BENCHMARK - DATA COLLECTION PACK
Section 4.0 Supplier Information Table

4.1 Who is completing this section?
Name: John Doe
Job title: General Manager
Telephone: 814-867-5309
E-mail address: jdoe@vantagepoint.com

Data Completeness Check
Are all required data fields completed? TRUE

Currency Selector
Please either select or type in the currency unit you are using to report spend:

4.2 Supplier Information
Required data fields are marked in blue

Supplier identifier	Primary service provided	Year supplier first provided services	Total amount paid to supplier	Estimated % of paid amount that is labor	% of paid amount that is material or equipment	Blended hourly labor rate	2003 estimated craft labor hours worked	Comments
1 0001	Full service (maint + repair)	1987	\$US 120,000	90%	10%	\$US 105.00	1,200	Chiller replacement and warranty service
2 0002	Asset repair/replacement	2004	\$US 500,000	30%	70%	\$US		Insulation repairs
3 0003	Asset repair/replacement	2003	\$US 50,000	95%	5%	\$US 90.00		Pump assemblies
4 0004	Commodity supplies	2002	\$US 90,000	0%	100%	\$US		Corrosion testing and repairs
5 0005	Asset repair/replacement	2003	\$US 158,000	90%	10%	\$US	3,500	Vibration analysis and damper installation
6 0006	Specialty parts/equipment	2003	\$US 59,000	80%	20%	\$US	450	Clean Room Janitorial
7 0007	Asset maintenance	1999	\$US 850,000	92%	8%	\$US 14.00		Consumables
8 0008	Commodity supplies	2001	\$US 110,000	0%	100%	\$US		Office cleaning and janitorial
9 0009	Asset maintenance	2000	\$US 580,000	94%	6%	\$US 11.00		Secure shredding
10 0010	Asset maintenance	2003	\$US 158,000	89%	11%	\$US		Chiller repair
11 0011	Asset repair/replacement	2004	\$US 38,000	90%	10%	\$US	120	
12			\$US		100%	\$US		

Please Mark Statement Accuracy
Always True
Mostly True
Mostly Untrue
Always Untrue

Choose from the drop down list in each box - A blank Answer is equivalent to "Always Untrue"

#	Statement	Accuracy
1	Daily Planning & Scheduling	
1.1	A daily maintenance work schedule is created	
1.2	"Squeaky wheel" and favored customers receive priority service	
1.3	There is a systematic, documented way of prioritizing maintenance work	
1.4	Employees are assigned work on an ad hoc basis, through the course of the workday	
1.5	Work is assigned to maintenance technicians by the priority of the work	
1.6	Daily schedule created prior to beginning of work shift based on prioritization of outstanding work requests (i.e. emergency, urgent, routine)	
1.7	Work assigned to craft type as opposed to specific employee	
1.8	All non-emergency work is scheduled	
1.9	The daily work schedule targets 100 - 120% of expected workload	

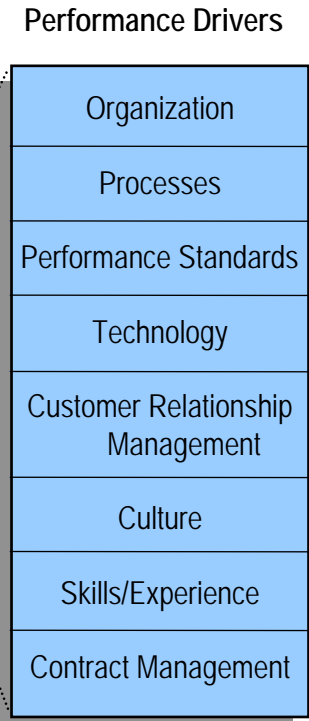
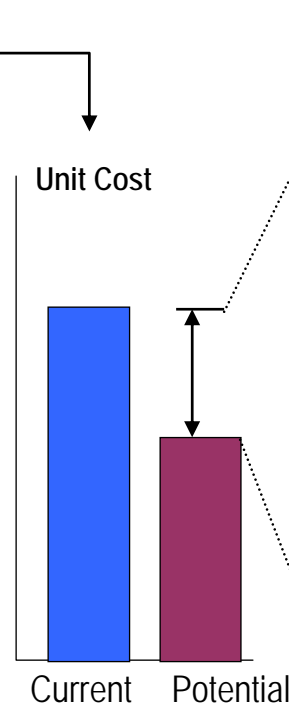
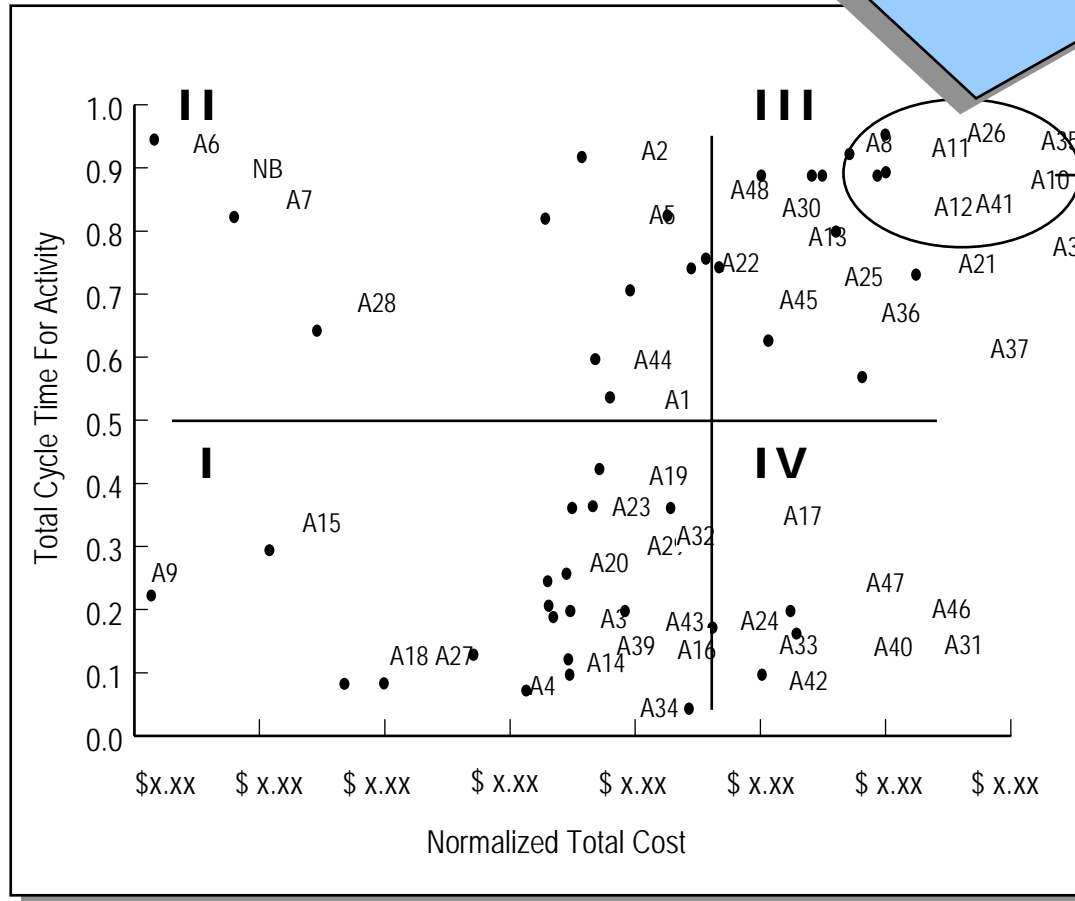
3.5 Activity Allocations

Job Title	% Allocated so far	Total labor hours allocated so far	Labor hours not yet allocated	Non-Fab Activities		Fab Activities						
				Office building maintenance	Office space cleaning	Mechanical systems	Electrical systems	Ultra Pure Water Systems	Industrial Waste Systems	Bulk Chemical Delivery Systems	Sub-Fab Systems Maintenance	
Boiler Mechanic	100.0%	2,200	-			1,540						
Class 3 Boiler Operator	100.0%	2,130	-			1,600						
Class 3 Boiler Operator	100.0%	2,130	-			1,600						
Plant Supervisor	100.0%	2,180	-			1,040						
Shift Supervisor	100.0%	2,080	-			100					1,240	
Class 1 Maintenance Mechanic	100.0%	2,140	-									1,670
Class 1 Maintenance Mechanic	100.0%	2,140	-									1,770
Class 1 Maintenance Mechanic	100.0%	2,140	-			200						1,370
Site Engineer	100.0%	2,080	-			50						500
HVAC Tech Class 4	100.0%	2,220	-	200		1,520						40
HVAC Tech Class 4	100.0%	2,180	-	500		1,230						40
	0.0%	-	-									
	0.0%	-	-									



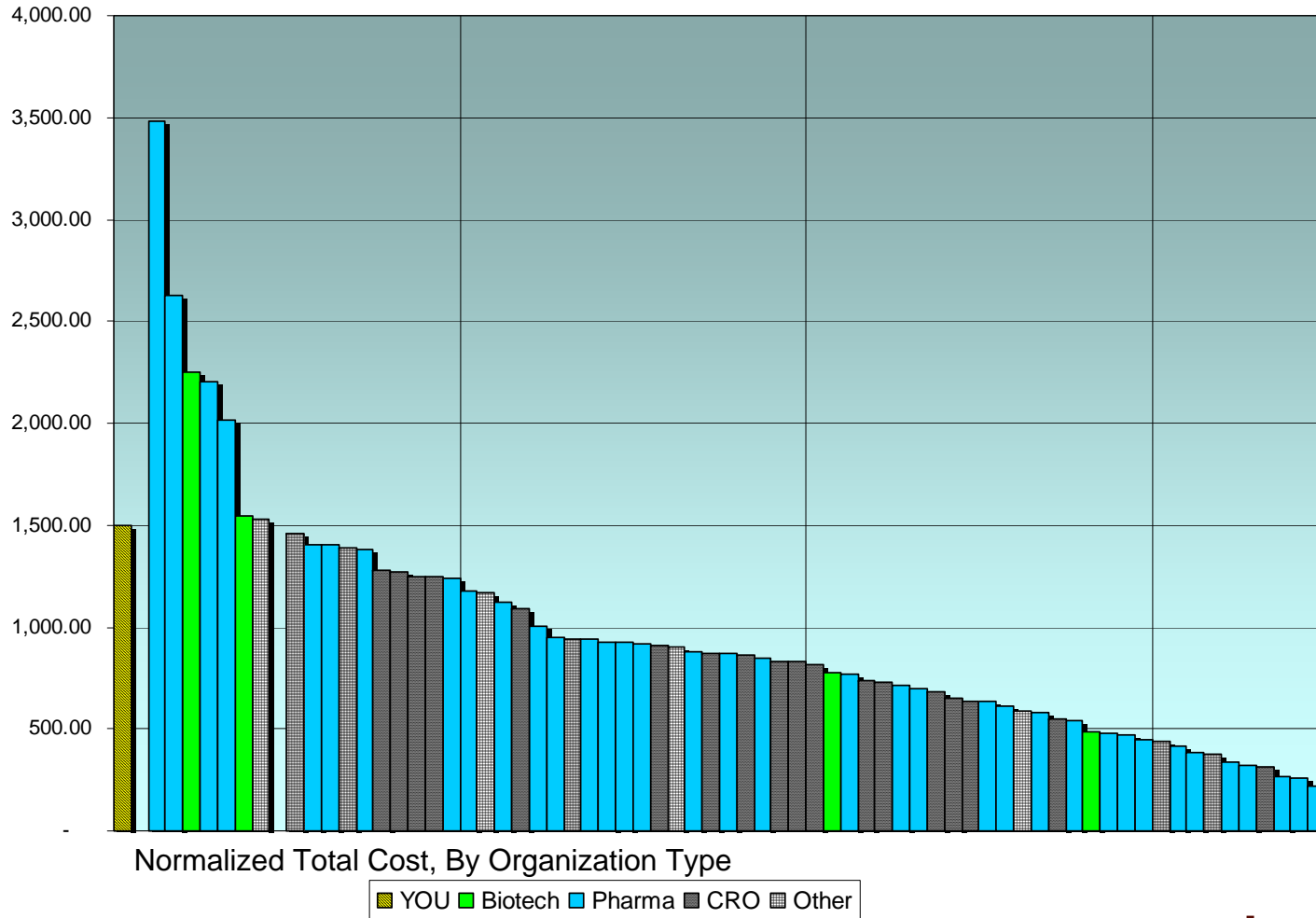
Measurement Frameworks That Explain Trade-Offs

Worst performers are those organizations who have high cycle time AND high total cost for the benchmarked activity





Objective: An Industry Wide Picture





Success Factors

- Maintain confidentiality - to the point of eliminating guessing
- Target your efforts – don't take on too much too soon
- Definition is Key – Consistency in milestones
- Validate data before you calculate results (GIGO)
- Focus on what drives performance – what's behind the numbers
- Involve stakeholders – buy-in and expertise
- Establish the proper peer group
- Define controllable vs. uncontrollable drivers
- Improvement initiatives key part of the collection process
- Challenge the processes not the people



Advantages of Early Adoption

- Ahead of the learning curve
- Strong influence on design, evolution and priorities of the study
- Even a single company “benchmark” creates significant value
 - Build cost structures
 - Identify value vs. non-value added activities
 - Obtain clarity around cost-drivers
 - Develop organizational benchmarking discipline



Benchmarking - What to Expect ... Cycle Time plus ...

	Process Component	Actual (Months)	Target (Months)
Phase I	LPLV to Report Released	> 15	3.8
Phase II, III	Approved Protocol to FPFV	6.3	3.6
	LPLV to Locked Database	5	2.3
	Locked Database to Statistical Analysis	5.5	2.3
	Statistical Analysis to Report Released	> 5	3.2

Full Benchmark Scorecard - Cycle Time, Cost & Best Practice (Illustrative)



Service Area	Cycle Time Lag	Cost	Best Practices	Improvement Opps
Approved Protocol to FPFV	2.8 Months			<ul style="list-style-type: none"> Lack of Centralized Site Set-Up Clinical Supply Packing Delays
LPLV to Locked Database	2.7 Months			<ul style="list-style-type: none"> Lack of EDC Incompatible databases
Locked Database to Statistical Analysis	3.2 Months			<ul style="list-style-type: none"> "Locked" not confirmed Too much manual data entry
Statistical Analysis to Report Released	2+ Months			<ul style="list-style-type: none"> Too much manual intervention Lack of rapid decision making process

- Lead - Top 1/3 of Companies
- In-Line - Middle 1/3 of Companies
- Lag - Bottom 1/3 of Companies