Lean Six Sigma in Research:

Process Improvement, Minimizing Waste, CAPAs, and More…

Emma Barkman, MHA, CCRP
Lean Six Sigma Green Belt
Lead Regulatory Research Coordinator
University of Maryland
Greenebaum Comprehensive Cancer Center
Amelia.Barkman@umm.edu

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

UNIVERSITY of MARYLAND
MARLENE AND STEWART GREENEBAUM COMPREHENSIVE CANCER CENTER

LEAN SIX SIGMA INTENT

The organization will execute a phased, full deployment of Lean Six Sigma (LSS) to accelerate Business Transformation by ***creating a culture of continuous, measurable improvement*** that ***eliminates non value-added activities*** and improves quality and responsiveness for patients and customers.

LEAN SIX SIGMA PROCESS IMPROVEMENT

- Improve the effectiveness (quality) of processes by identifying and removing the causes of defects (errors) and variation

- Improve the efficiency of processes by identifying and removing sources of waste within the process

- Improve the effectiveness and efficiency based on outputs that are critical to ***Participants***

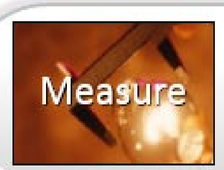
WHAT IS LEAN SIX SIGMA?

- Lean Methods:
  - Remove non-value added waste (TIMWOOD)
  - Therefore, improving speed or process lead time
- Six Sigma Methods:
  - Grounded in the DMAIC methodology
  - Attacks variation
  - As a result, improving quality
- Combined, Lean and Six Sigma
  - Faster cycle times, decreased costs, and improved quality
  - Hence, more satisfied patients

Introducing DMAIC

- The foundational methodology of Lean Six Sigma
- Intentional focus on data

Define: Describe the problem quantifiably, visualize the process, and understand customer needs



Measure: Understand the process and its current performance

Analyze: Identify the true root cause(s) that has the biggest impact on process performance

Improve: Brainstorm and develop improvement solutions to attack root cause(s)

Control: Implement the solutions and *sustain the gains*

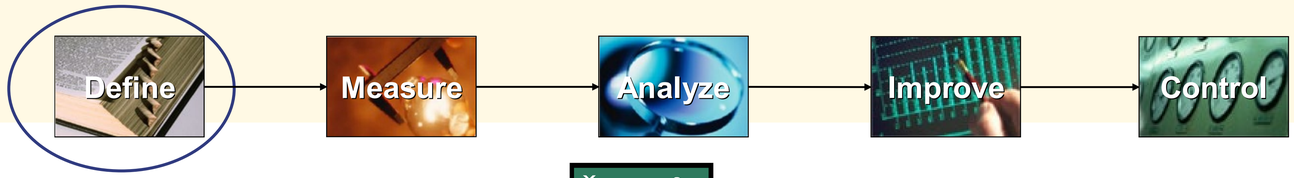
DEFINE

Purpose: To have the team and its sponsor reach agreement on the scope, goals, and financial and performance targets for the project.

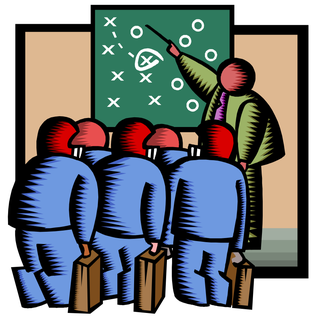
Define:

- Problem Statement
- Goal Statement
- Key Players
- SIPOC Map (Suppliers, Inputs, Process boundaries, Outputs, Customers [patients])
- Process Map

Define



Project Identification & Selection



Team Launch

Solidify Project Charter

PROJECT CHARTER

Business Impact
- Why should we do this? What is the benefit?
- What is the quantified value of the project ($$$)?
- How does this project align with the business strategy?

Opportunity or Problem Statement
- What "pain" are we or our customers experiencing?
- What is wrong or not working?
- Why do we think we can generate the value proposition described in the Business Case?

Goal Statement
- Specifically, what are we going to do and deliver?
- What are our improvement objectives and targets?
- How will success be measured? What specific parameters will be measured? Define Y = f(x)

Project Scope
- What are the boundaries of the initiative (start and end steps of the process)?
- What authority do we have?
- What is not within scope?

Project Plan
- When are we going to complete the work?
- What are the major milestones?

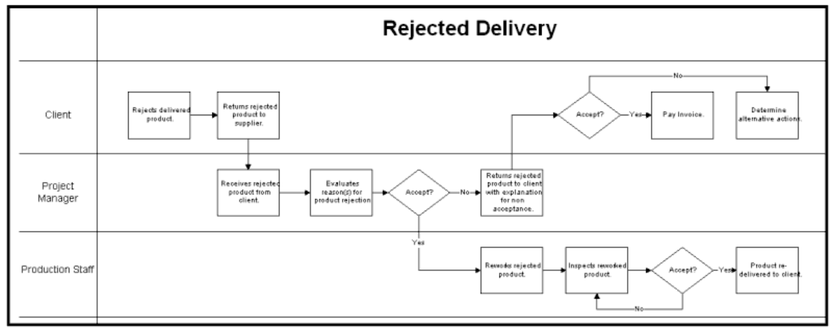
Team Selection
- Who are the team members?
- What is their role?
- How much of their time will be dedicated to the project?

S	I	P	O	C
Supplier	Inputs	Process	Outputs	Customer

Gather VOC/VOB

Process and "Pain" Clearly Defined and Understood

Process Map



Translate to CCRs

Customer Comment	Key Customer Issue	(Quantified) Customer Requirement
"I hate filling out this form."	The form takes too long to complete	The form must take less than five (5) minutes to complete
"Contacting your customer service department is AWFUL"	Wants to talk to the right person quickly	Customer reaches correct person the first time within 30 seconds

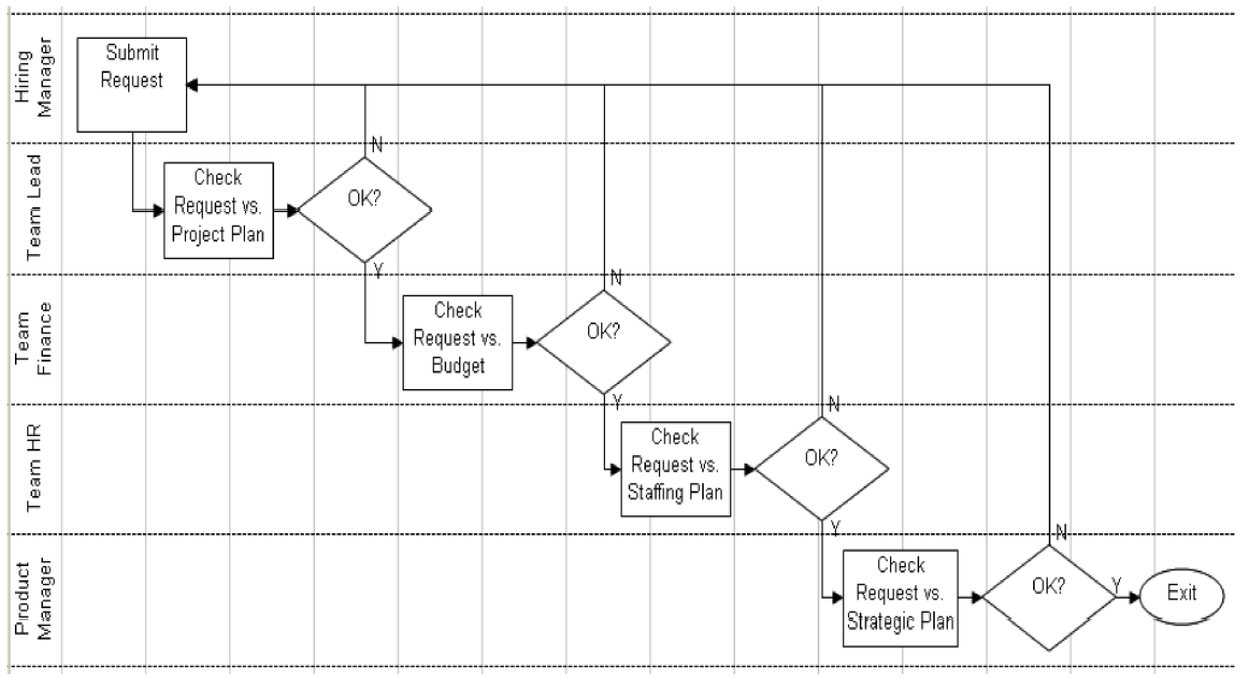
DEFINE - *Exercise*

Define:

- Problem statement
  - Patient appointment request process is not meeting speed, quality, nor cost expectations… Call wait time is 25 minutes
- Goal Statement
  - Decrease call wait time from 25 minutes to 5 minutes within 6 months
- Key Players
  - Voice of Customer/Patient
  - Voice of business
- Process Map

What Is a Process Map?

- A graphical representation of a process flow identifying the steps of the process and opportunities for improvement
- Types of process maps:
  - Top Down Chart
  - Flow Chart
  - Spaghetti Diagram
  - Swim Lane
  - Multi Functional Flow Chart
  - Value Stream Map



MEASURE

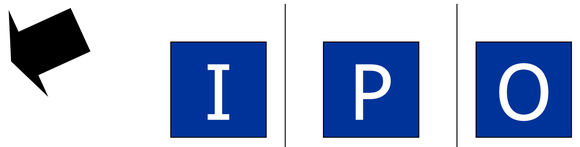
Purpose: To thoroughly understand the current state of the process and collect reliable data on process speed, quality, and costs that you will use to expose the underlying causes of problems

Measure:

- Measurement Systems Analysis & Performance and Capability
- Baseline Statistics
- Measures of Central Tendency
- Control Charts
- List barriers and issues
- Propose quick wins and rapid improvements

Measure

Develop Measures



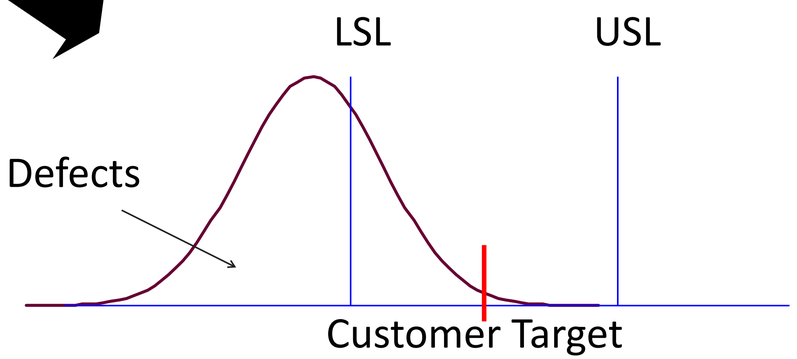
- Based on process and Y=f(X)

Data Collection Plan

Wasteful Energy Habits	Week 1	Week 2	Week 3	Total
Long showers	///	/	//	6
Lights left on	////	///	////	11
Windows left open	//	/		3
AC set below 72°	/	//	//	5
Door left open	𝍸	𝍸	///	13
Total	**15**	**12**	**11**	**38**

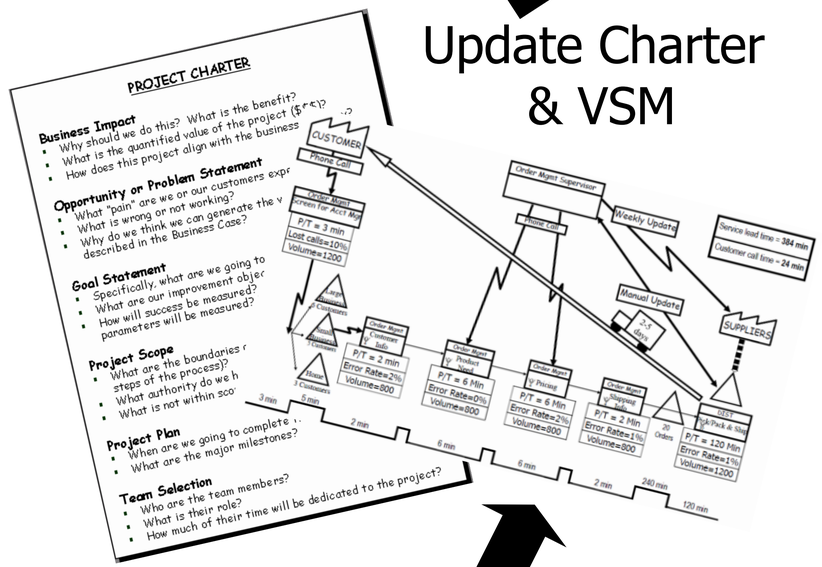
Validate Measurement System

Baseline Process Performance



Current Process Performance Established

Update Charter & VSM



Sigma Quality Level

1. Determine number of defect opportunities per unit	O =	3
2. Determine number of units processed	N =	100
3. Determine total number of defects made	D =	19
4. Calculate Defects per Opportunity	$DPO = \frac{D}{N \times O} =$	0.063
5. Calculate DPMO	DPMO = DPO x 1,000,000 =	63,333
6. Look up the Sigma in the Sigma Table (next slide)	Sigma Quality Level =	~ 3

ANALYZE

Purpose: To pinpoint and verify causes affecting the key input and output variable tied to project goals. “Finding the critical Xs”

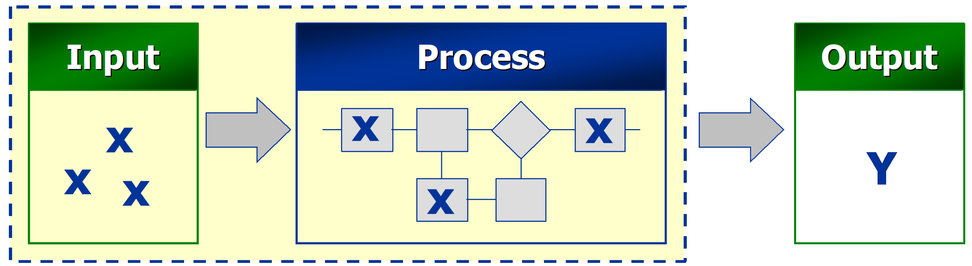
Analyze:

- 5 Why’s
- Fishbone Diagram
- Root Cause Verification
- Pareto Charts
- Proposed Quick Wins / Rapid Improvements
- TIMWOOD

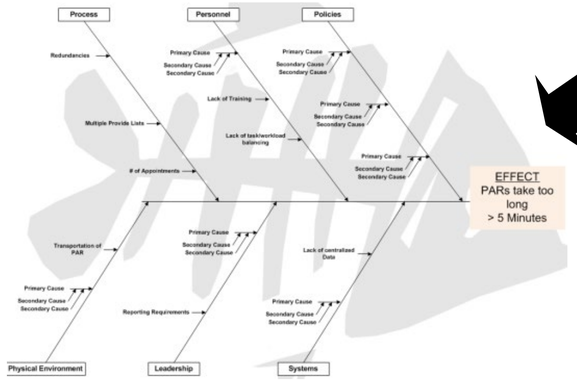
Analyze

Determine Critical X's

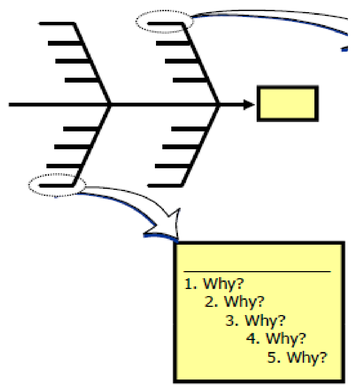
Y = f(X)



C&E Diagram

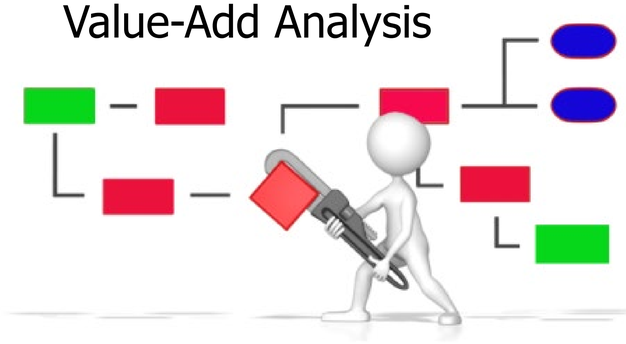


Root Cause ID
5 Why's



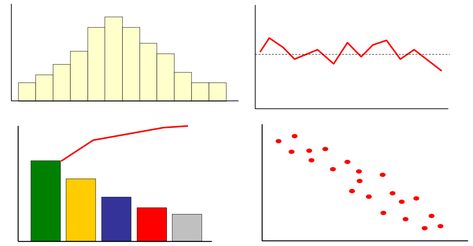
Identify and Remove Waste

Value-Add Analysis

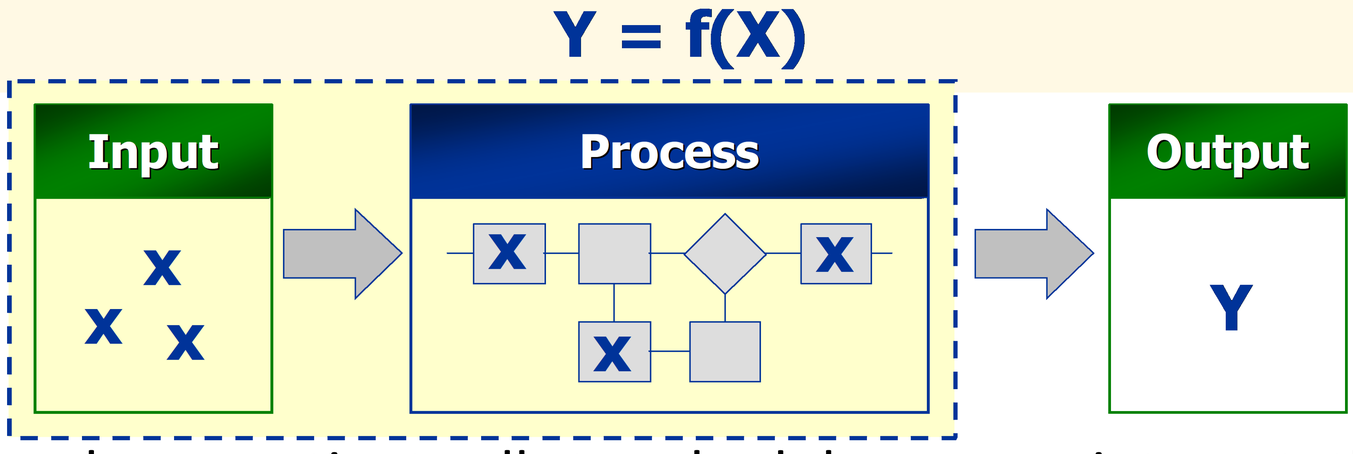


Prioritized Critical Xs
& Root Causes

Data Analysis & Hypothesis Testing



Determining the *"Critical Factors (X's)"*



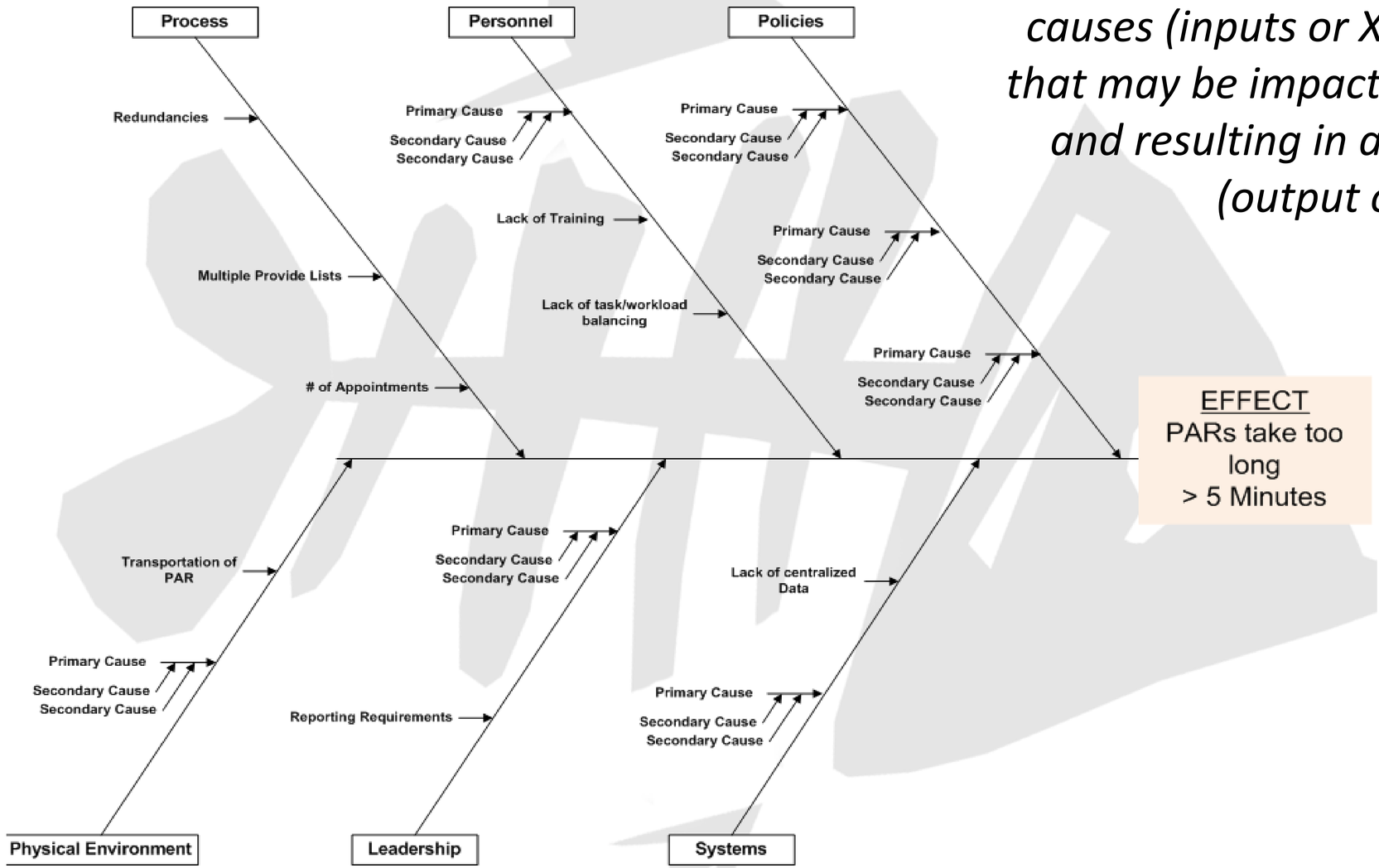
- For example, when a patient calls to schedule an appointment, the wait time to have their appointment scheduled (Y) is a function (f) of:
  - Appointments available
  - # of people answering the phones
  - Representative's knowledge and skills
  - # of people calling at the same time
  - Accuracy of patient information in the "system"

These are just SOME of the X's

- All of these X's can be defined, measured and improved
- The key questions are:
  - What are the critical X's?
  - Which X's need to be improved and controlled to yield a satisfactory result (Y)?

Cause & Effect Diagram

- Also called the Fishbone or Ishikawa Diagram
- Represents the relationship between an Effect (Y) and its potential causes (Xs)

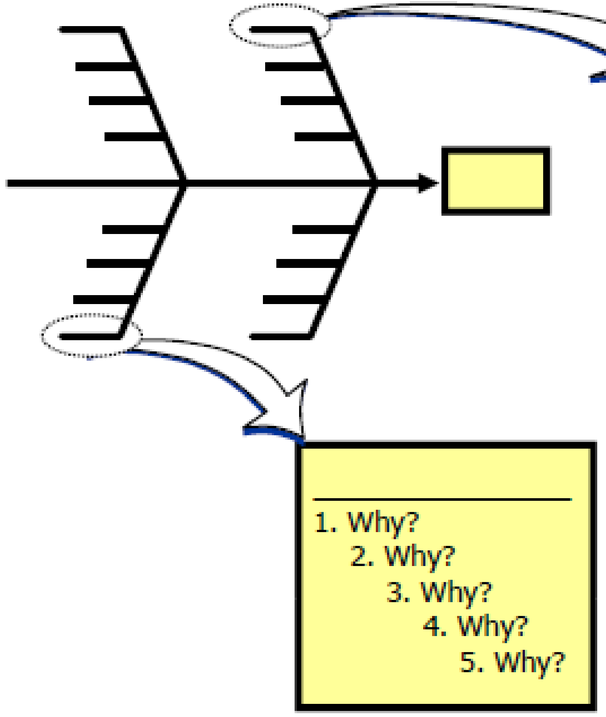


Used to explore all the potential causes (inputs or Xs) of variation that may be impacting the process and resulting in a single effect (output or Y)

Drilling Down to Root Causes
"5 Whys"

- Dive deeper into the "cause" by asking "Why" 5 times
- Get past the surface *symptom* and identify the Root Cause

Ask "Why?" 5 Times



Lean Six Sigma projects take too long

1. Why? Teams don't have time to work on project

2. Why? Other activities have not been cleared from their duties

3. Why? Project Sponsor and other affected managers not aware that they need to make this happen

4. Why? Project Sponsor and other affected managers have not attended Project Sponsor Workshop

5. Why? . . .

Non-Value Add Activities - *WASTE*

1. **T**ransportation (moving material/product from one place to another)
2. **I**nventory (material/product waiting to be processed)
3. **M**otion (excess movement and/or poor ergonomics)
4. **W**aiting (delays caused by shortages, approvals, downtime)
5. **O**verproduction (producing more than is needed)
6. **O**ver-processing (adding more value than the patient is willing to paying for)
7. **D**efects/Rework (correcting mistakes)

Eliminate it
Reduce it
Streamline it
Combine steps

→ TIMWOOD

Value-Add Analysis

- **Participant Value Add** – Steps essential to deliver the product or service according to patient requirements. Three criteria:
  1. Transforms the item or service toward completion
  2. Patient cares (would be willing to pay for it)
  3. Done right the first time

- **Non-Value Add Required** – Steps that allow overall greater effectiveness or efficiency in the process or are required due to regulations.

- **Non-Value Add** – **Waste**. Steps that do not qualify as Value Add or Non-Value Add

IMPROVE

Purpose: To learn from pilots of the selected solution(s) and execute full-scale implementation

Improve:

- Develop “To-Be” Process Map
- Implement Pilot Plan, Develop Approved Solution(s) and Detailed Implementation Plan
- Develop Implementation Risk Analysis and Mitigation Plan
- Estimate Operational and Financial Benefits

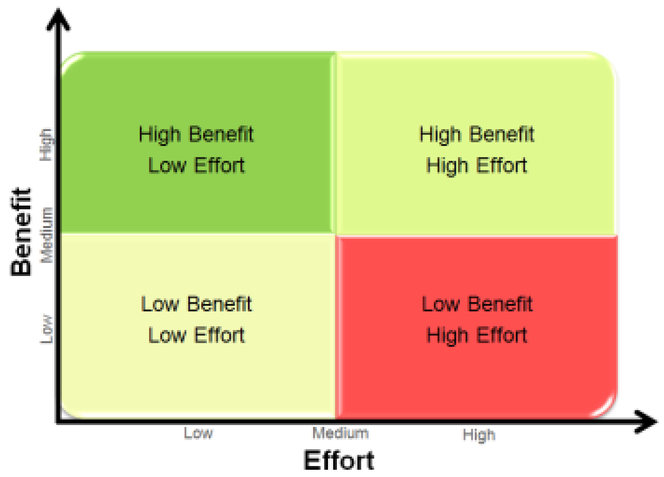
Improve

Generate Solutions
Idea Generation Techniques

- Brainstorming
- Six Thinking Hats
- Problem Reversal
- Idea Box
- Random Word
- Mind-Mapping
- Lateral Thinking
- Twenty Questions
- Candid Comments
- Musical Chairs
- Building on Ideas
- Challenge Assumptions
- Solution Mapping
- Many Others

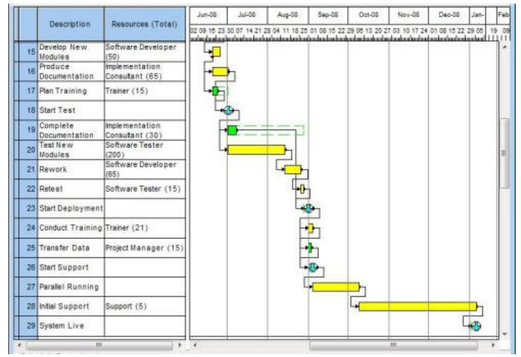
Narrow Solutions

Prioritize & Select Solutions



Pilot the Solutions

Implementation Plan



	Description	Resources (Total)
15	Develop New Modules	Software Developer (50)
16	Produce Documentation	Implementation Consultant (65)
17	Plan Training	Trainer (15)
18	Start Test	
19	Complete Documentation	Implementation Consultant (30)
20	Test New Modules	Software Tester (200)
21	Rework	Software Developer (65)
22	Retest	Software Tester (15)
23	Start Deployment	
24	Conduct Training	Trainer (21)
25	Transfer Data	Project Manager (15)
26	Start Support	
27	Parallel Running	
28	Initial Support	Support (5)
29	System Live	

Solutions generated, prioritized, and piloted

CONTROL

Purpose: To complete project work and hand off improved process to process owner, with procedures for maintaining the gains

Control:

- Corrective and Preventive Actions (CAPA)
- Revise Process Documentation
- SOPs and Training Plans
- Plan for Transition to Process Owner
- Risk Analysis and Mitigation
- Goal Achievement

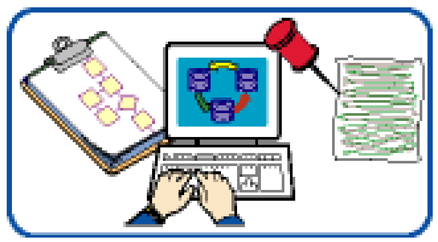
Control

Sustaining the Gains

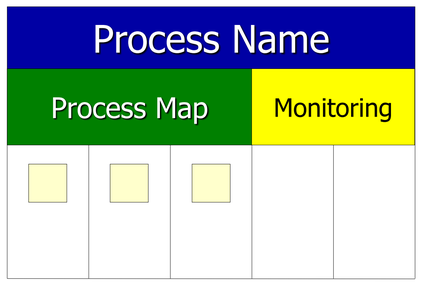
New process in control
Control plan in place
Transitioned to "owner"

Transition Ownership

Documentation/SOP's



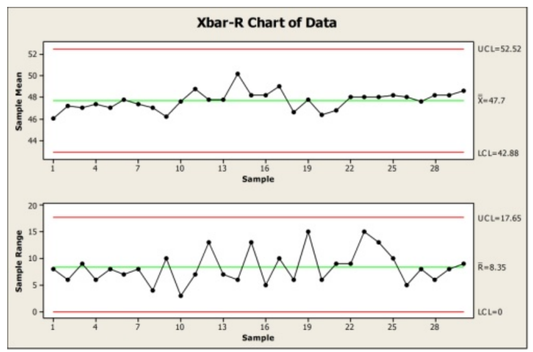
Process Control Plan



Poka-Yoke

日本

Control Charts



ELEMENTS OF PROCESS IMPROVEMENT: CAPA

CAPA Defined:

- Corrective Action: Action to eliminate the cause of a detected nonconformity or other undesirable situation.
- Preventive Action: Action to eliminate the cause of a potential nonconformity or other undesirable situation.

Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent reoccurrence.

CAPA planning may involve writing new SOP's or Work Instructions to address deficiencies and/or editing existing SOP's/WI.

When creating corrective action plans, the individual(s) involved in the issue will be engaged to assist in identifying corrective action steps they can agree to and implement.

ELEMENTS OF PROCESS IMPROVEMENT: CAPA

FDA Regulatory Expectations:

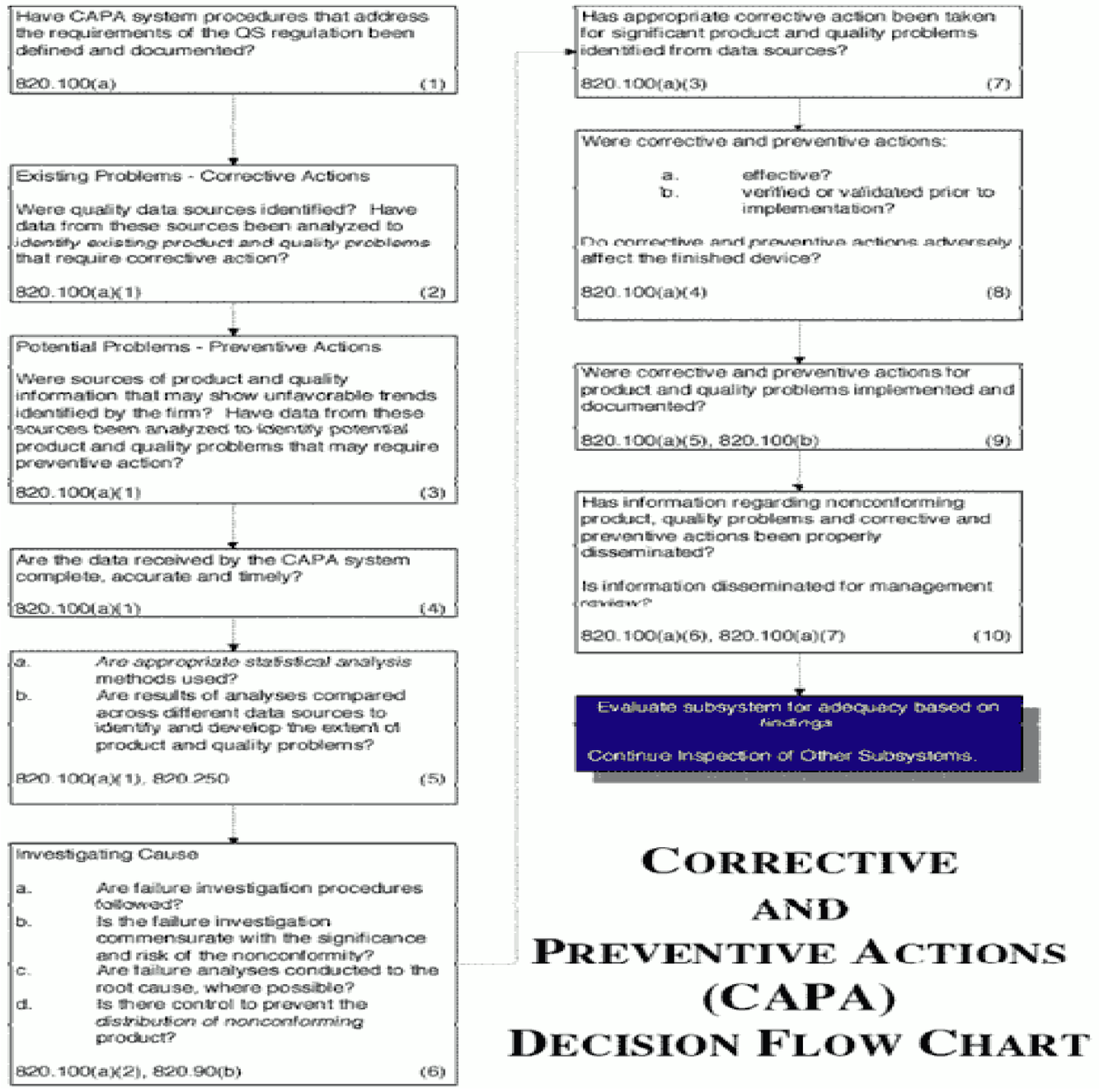
- Do you have a well designed plan?
- Have you done what was planned?
- Did you check for the presence of errors?
- Did errors that matter occur and were you able to identify them?
- When errors occurred, how were they handled to ensure subject protection and data integrity?
- Was an appropriate CAPA promptly instituted, communicated, tracked and revised as needed?
- Did you document this process so that it is transparent to regulatory authorities?

KEY STEPS IN CONTROL / CAPA

The key steps in control and your CAPA are:

- Develop supporting methods and documentation
- Launch implementation
- Lock in performance gains
- Monitor implementations
- Develop process control plans and hand off control to the process owner
- Audit the results
- Finalize the project
- Validate performance and financial results

CAPA DECISION FLOW CHART



LEAN SIX SIGMA IN CLINICAL RESEARCH

- Lean Six Sigma (LSS) accelerates transformation by creating a culture of continuous, measurable improvement that eliminates non-value added activities and improves quality and responsiveness for patients and participants.

- The complexity of research, high costs, and delays has an impact on patients and the public.

- Need for more effective and efficient research

- Lean Six Sigma and Process Improvement projects
  - Standardize performance metrics
  - Drug discovery
  - IRB approval
  - Clinical trial activation
  - Minimize deviations

Improving Clinical Trial Activation Using Lean Six Sigma Methodology

Amelia Schmidt, MHA, CCRP; Theresa Cummings, RN, MS, CCRP; Jennifer Richards, MS, CCRP

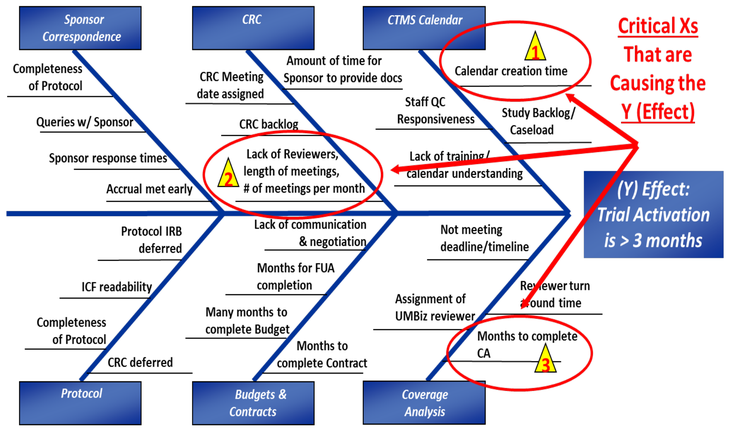
Background

Clinical trial activation at an Academic Institution involves a multitude of stakeholders that include but are not limited to the hospital, the University, and the financial departments of both. Lean Six Sigma (LSS) methodology accelerates business transformation by creating a culture of continuous, measurable improvement that eliminates non value-added activities and improves quality and responsiveness for patients and customers.

The experience at the University of Maryland Greenebaum Comprehensive Cancer Center revealed that delays and barriers throughout the trial activation process lead to considerable time loss in activating our site and opening a study to accrual. This has led to lower patient accrual, termination as a participating site and wasteful use of resources.

In a series of root cause analyses conducted at UMGCCC by a LSS green belt, we determined the following were the most significant and impactful contributors to delayed trail activation: lack of Scientific Review Committee (SRC) meetings; delay in calendar creation in our online Clinical Trial Management System (CTMS); Sponsor un- responsiveness leading to a delay in IRB submission; and delayed completion of the Coverage Analysis and finalization of budgets and contracts.

Figure 1: Fishbone Diagram identifying main causative factors



Goals

- To improve efficiency of trial activation
- To reduce median activation time by 40%
- Protocol assigned and reviewed by SRC within 4 weeks of site approval
- Lower calendar creation time in the CTMS to less than 8 days

Methods

- Implemented a 3rd SRC meeting per month and added more members and reviewers to the committee. Added a regulatory resource and dedicated CRC coordinator to accommodate this.
- Improved Calendar creation process in the CTMS system by revising the work flow to improve, define, and minimize steps and time involved in the process.
- Education of all CRO staff of the revised study activation timeline.
- Assessed and communicated the obstructions that were found using LSS Methodology. These findings were communicated to Hospital and University management that are overseeing Coverage Analysis and Budget and Contract negotiation.

Results

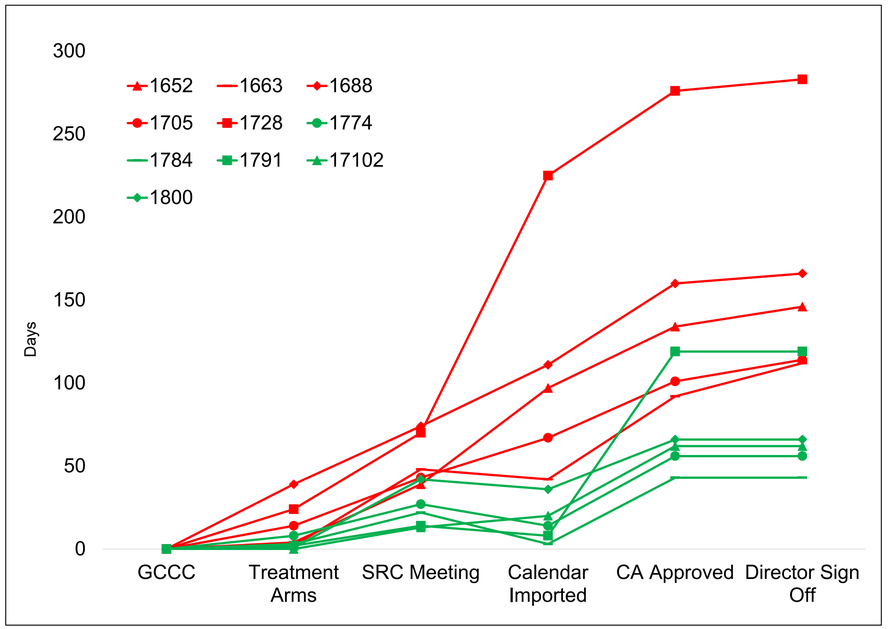
Before implementing LSS:

	Mean	Median
SRC Review	57.2	54
CTMS Calendar	84.4	97
CA Approval	124.8	118
IRB Submission	150	152

After implementing LSS :

	Mean	Median
SRC Review	23.6	22
CTMS Calendar	16.2	14
CA Approval	69.2	62
IRB Submission	69.2	62

Figure 2: Timeline of study activation when comparing protocols



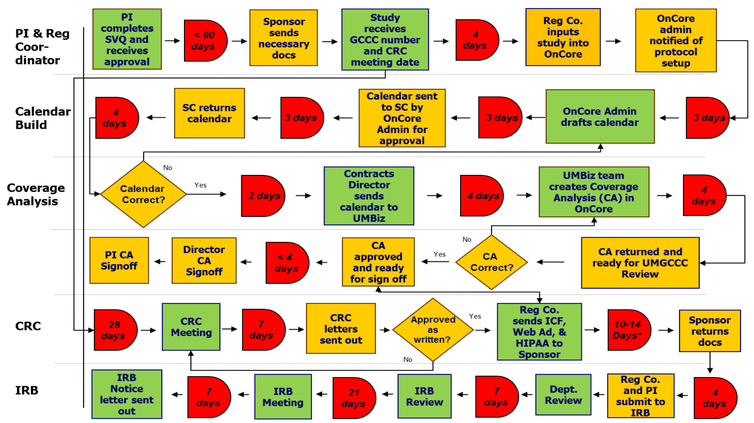
Conclusion

Using Lean Six Sigma Methodology and the DMAIC process, we defined, measured, analyzed, improved, and continue to control underlying causes, waste, and barriers. In doing this, we identified and implemented two process improvement initiatives to improve study activation timelines and were able to improve the speed, quality, and cost of study start up. In addition, we established two new methods of communication and training of staff to increase transparency and "buy-in" to Six Sigma methodology across the team.

Implementation of a third SRC meeting eliminated the immediate backlog of new clinical trial reviews and allowed more time for the possibilities of re-reviews and emergency use protocols while still providing time slots for full reviews.

Through 10 Root Cause Analyses, UMGCCC built process maps, conducted baseline statistics, performed measures of central tendencies, and created pareto charts. In doing this, a significant difference was seen in the trial activation timeline.

Figure 3: "To Be" Process Map



Future Directions

This work demonstrates that LSS Methodology can be applied to operational issues in clinical research, including clinical trial activation. Ensuring the research team within a designated cancer center includes a staff with LSS experience/certification ensures the resources and knowledge exist to apply the methodology effectively. Sharing results with key stakeholders outside of the research office is critical to allow visibility to the outcome of the problems identified. Future directions for GCCC include performing a quarterly review of randomly selected trials. This allows UMGCCC leadership to perform risk analysis and mitigation, establish/modify goals and review results for further revision of process documentation as needed.

Green (CVA); Amber (NVA-R); Red (NVA)

1688GCC"Current State" Process map

PI & Reg Coor-dinator

PI completed SVQ [05/25/2016]

71 days

Sponsor sent necessary docs [8/4/2016]

GCCC number and CRC meeting date [8/4/2016]

39 days

Reg Co. inputs study into OnCore [9/12/2016]

Contracts Dir. Informed of OnCore completion [9/12/2016]

2 days

Calendar Build

Calendar requested by Contracts Dir. [9/14/2016]

3 days

Nimblify returns calendar [9/17/2016]

3 days

Calendar sent to SC by OnCore Spec. for approval [9/20/2016]

9 days

63 days

MCA

OnCore Spec. requested update from SC [9/29/2017]

SC replied as WIP [9/30/2017]

15 days

OnCore Spec. requested update from SC (CC'd TC) [10/14/2017]

17 days

OnCore Spec. requested update from SC (CC'd TC) [10/31/2017]

23 days

SC returned calendar with no queries [11/22/2016]

5 days

Calendar imported [11/23/2016]

Con. Dir. Creates R vs. SOC [11/28/2016]

2 days

MCA Submitted to UMBiz [11/30/2016]

18 days

MCA Assigned to reviewer [12/18/2016]

23 days

MCA returned and ready for UMGCCC Review [1/10/2017]

MCA approved and ready for sign off [1/11/2017]

7 days

Director MCA Signoff [1/17/2017]

PI MCA Signoff [1/17/2017]

CRC

74 days

CRC Meeting [10/17/2016]

8 days

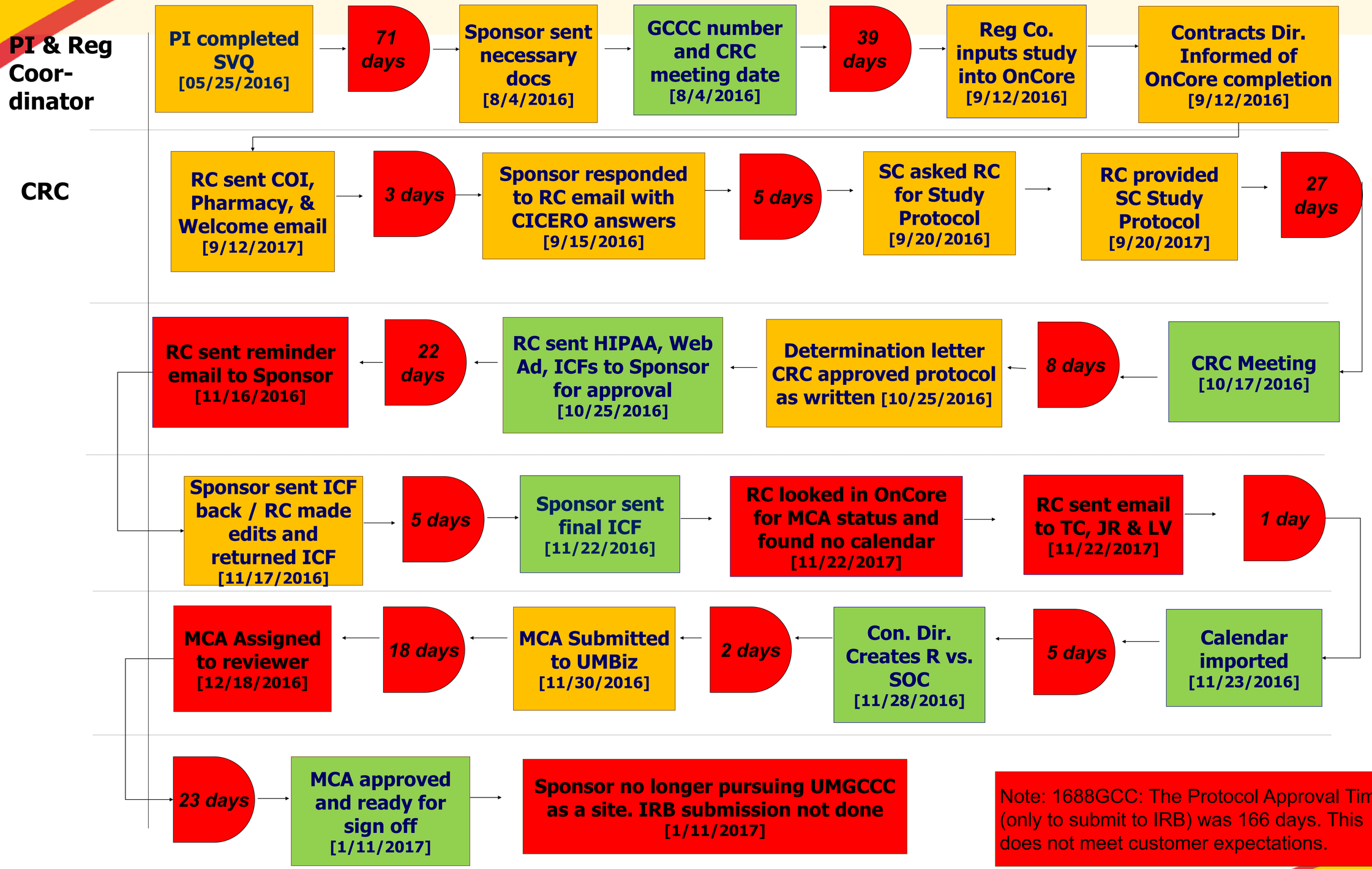
Determination letter CRC approved protocol as written [10/25/2016]

78 days

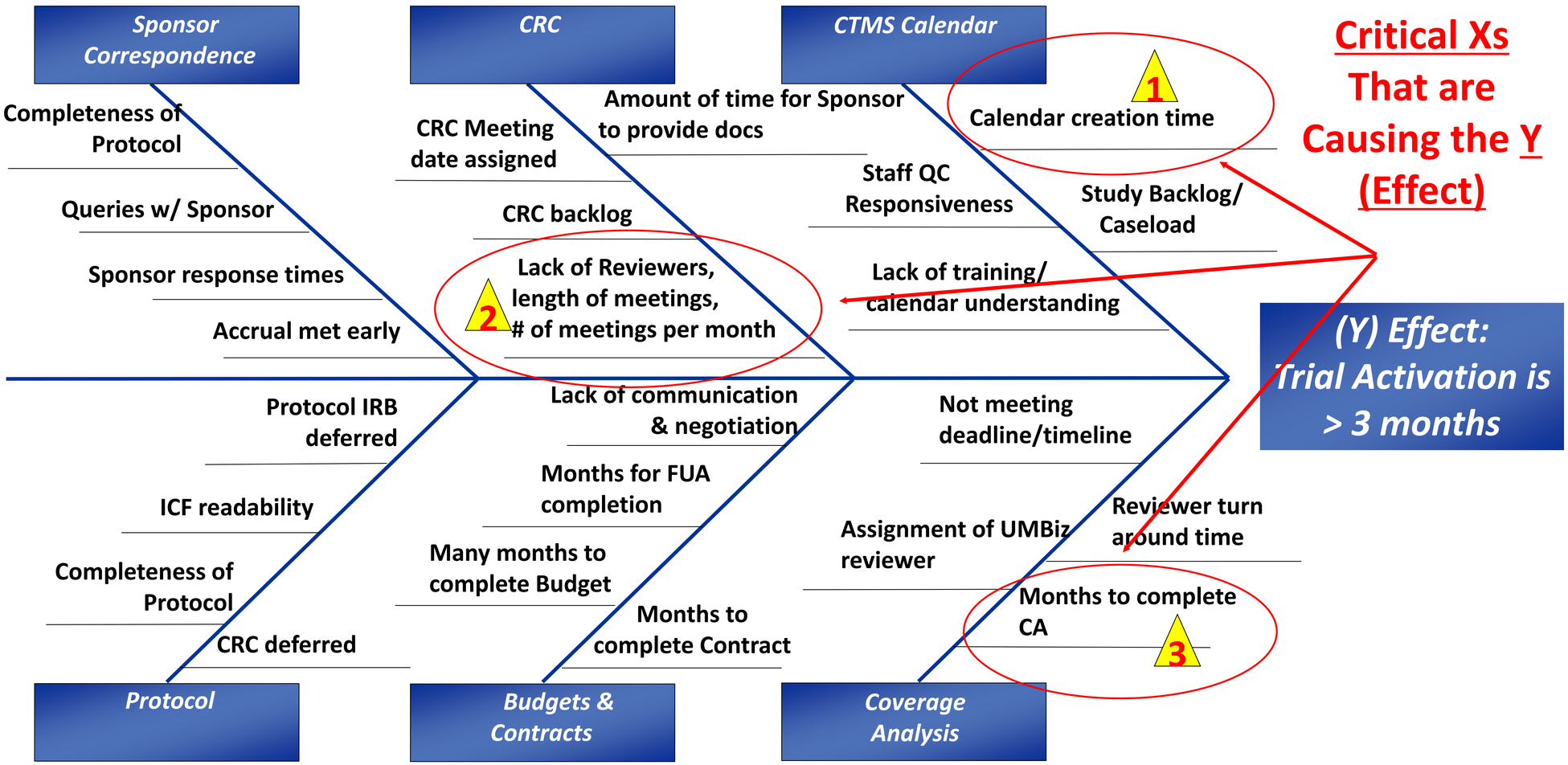
Reg Co. sent ICF, Web Ad, & HIPAA to Sponsor [1/11/2017]

Green (CVA); Amber (NVA-R); Red (NVA)

1688GCC"Current State" Regulatory Process Map



Note: 1688GCC: The Protocol Approval Time (only to submit to IRB) was 166 days. This does not meet customer expectations.


Sponsor Correspondence
CRC
CTMS Calendar
Completeness of Protocol
Queries w/ Sponsor
Sponsor response times
Accrual met early
Protocol IRB deferred
ICF readability
Completeness of Protocol
CRC deferred
Amount of time for Sponsor to provide docs
CRC Meeting date assigned
CRC backlog
Lack of Reviewers, length of meetings, # of meetings per month
Lack of communication & negotiation
Months for FUA completion
Many months to complete Budget
Months to complete Contract
Staff QC Responsiveness
Calendar creation time
1
Study Backlog/ Caseload
Lack of training/ calendar understanding
Not meeting deadline/timeline
Assignment of UMBiz reviewer
Reviewer turn around time
Months to complete CA
3
2
Protocol
Budgets & Contracts
Coverage Analysis
Critical Xs That are Causing the Y (Effect)
(Y) Effect: Trial Activation is > 3 months

Improving Clinical Trial Activation Using Lean Six Sigma Methodology

Amelia Schmidt, MHA, CCRP; Theresa Cummings, RN, MS, CCRP; Jennifer Richards, MS, CCRP

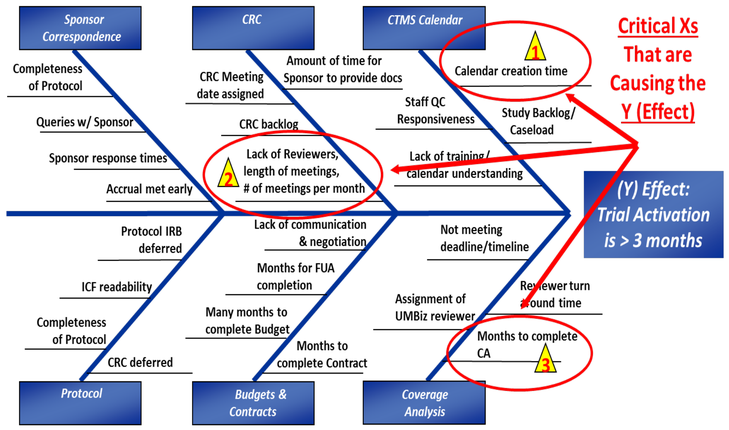
Background

Clinical trial activation at an Academic Institution involves a multitude of stakeholders that include but are not limited to the hospital, the University, and the financial departments of both. Lean Six Sigma (LSS) methodology accelerates business transformation by creating a culture of continuous, measurable improvement that eliminates non value-added activities and improves quality and responsiveness for patients and customers.

The experience at the University of Maryland Greenebaum Comprehensive Cancer Center revealed that delays and barriers throughout the trial activation process lead to considerable time loss in activating our site and opening a study to accrual. This has led to lower patient accrual, termination as a participating site and wasteful use of resources.

In a series of root cause analyses conducted at UMGCCC by a LSS green belt, we determined the following were the most significant and impactful contributors to delayed trail activation: lack of Scientific Review Committee (SRC) meetings; delay in calendar creation in our online Clinical Trial Management System (CTMS); Sponsor un- responsiveness leading to a delay in IRB submission; and delayed completion of the Coverage Analysis and finalization of budgets and contracts.

Figure 1: Fishbone Diagram identifying main causative factors



Goals

- To improve efficiency of trial activation
- To reduce median activation time by 40%
- Protocol assigned and reviewed by SRC within 4 weeks of site approval
- Lower calendar creation time in the CTMS to less than 8 days

Methods

- Implemented a 3rd SRC meeting per month and added more members and reviewers to the committee. Added a regulatory resource and dedicated CRC coordinator to accommodate this.
- Improved Calendar creation process in the CTMS system by revising the work flow to improve, define, and minimize steps and time involved in the process.
- Education of all CRO staff of the revised study activation timeline.
- Assessed and communicated the obstructions that were found using LSS Methodology. These findings were communicated to Hospital and University management that are overseeing Coverage Analysis and Budget and Contract negotiation.

Results

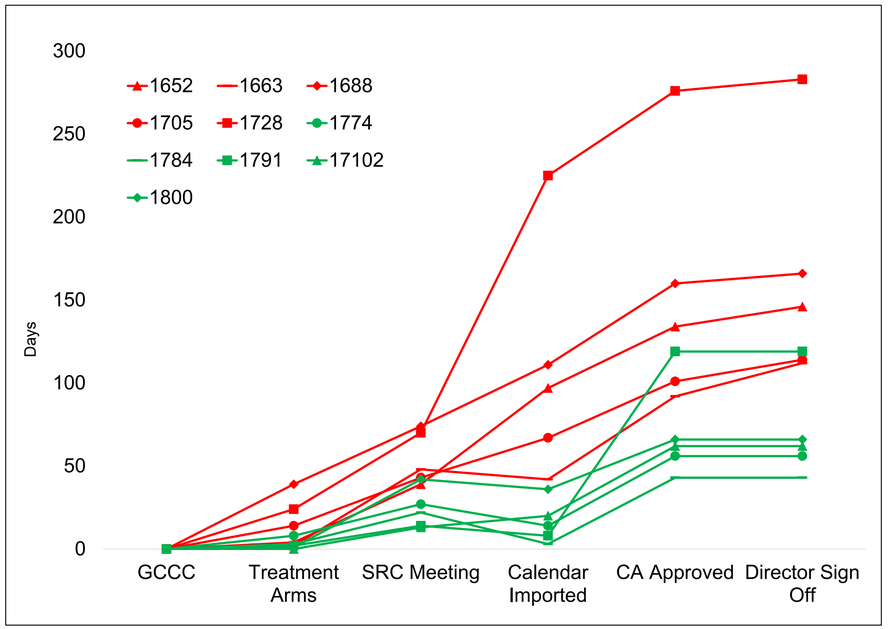
Before implementing LSS:

	Mean	Median
SRC Review	57.2	54
CTMS Calendar	84.4	97
CA Approval	124.8	118
IRB Submission	150	152

After implementing LSS :

	Mean	Median
SRC Review	23.6	22
CTMS Calendar	16.2	14
CA Approval	69.2	62
IRB Submission	69.2	62

Figure 2: Timeline of study activation when comparing protocols



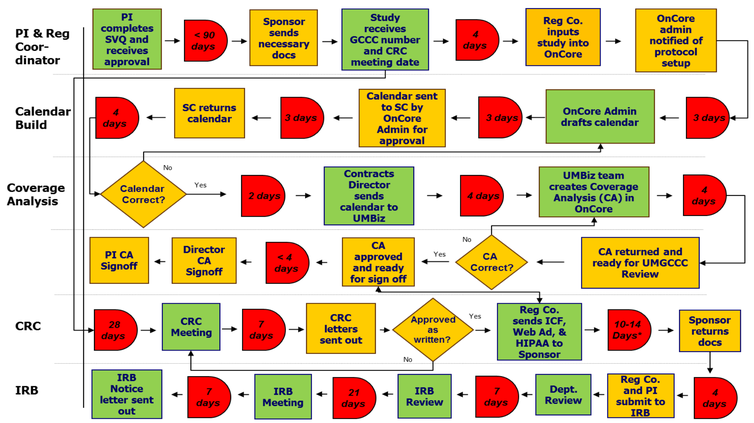
Conclusion

Using Lean Six Sigma Methodology and the DMAIC process, we defined, measured, analyzed, improved, and continue to control underlying causes, waste, and barriers. In doing this, we identified and implemented two process improvement initiatives to improve study activation timelines and were able to improve the speed, quality, and cost of study start up. In addition, we established two new methods of communication and training of staff to increase transparency and "buy-in" to Six Sigma methodology across the team.

Implementation of a third SRC meeting eliminated the immediate backlog of new clinical trial reviews and allowed more time for the possibilities of re-reviews and emergency use protocols while still providing time slots for full reviews.

Through 10 Root Cause Analyses, UMGCCC built process maps, conducted baseline statistics, performed measures of central tendencies, and created pareto charts. In doing this, a significant difference was seen in the trial activation timeline.

Figure 3: "To Be" Process Map

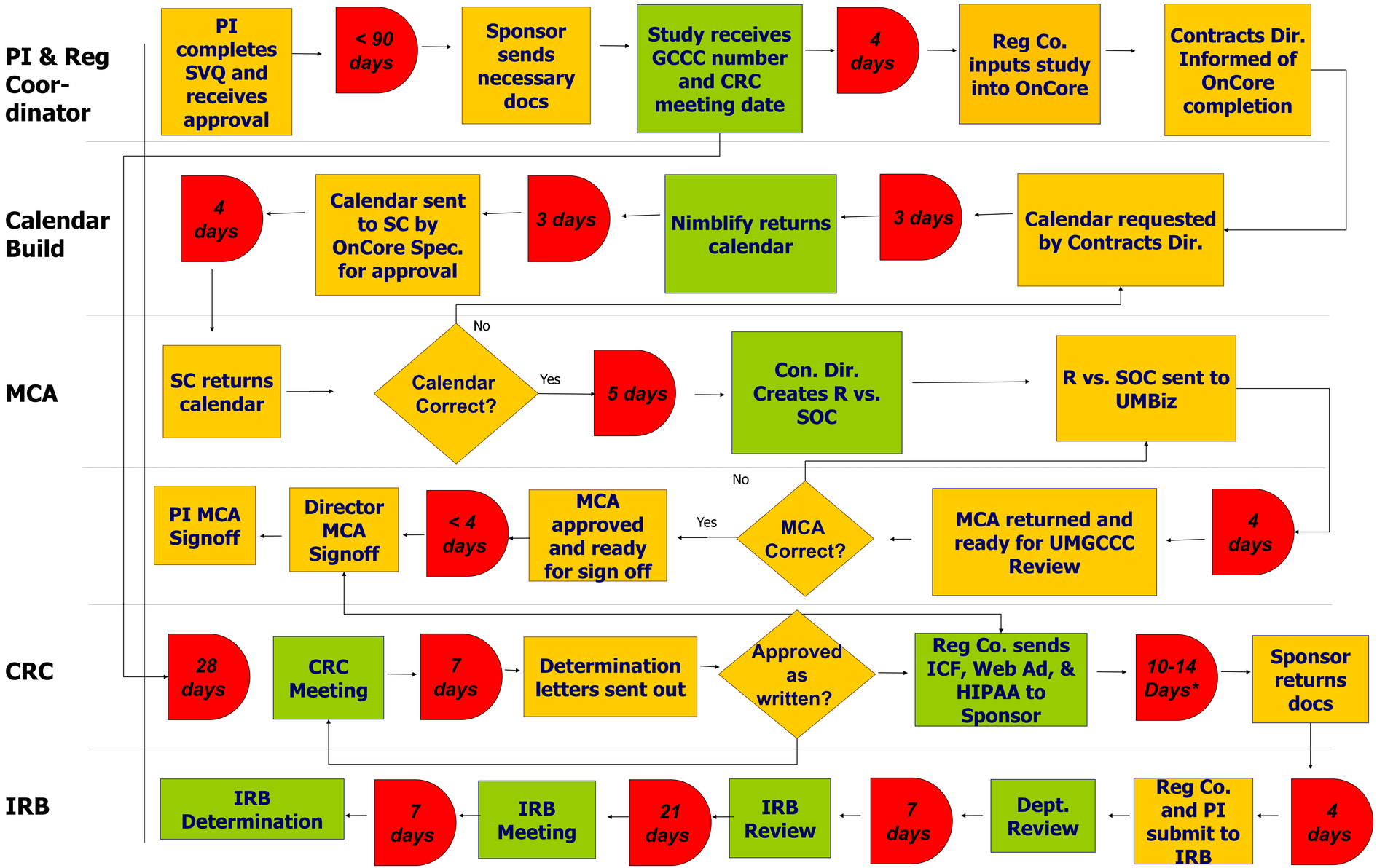


Future Directions

This work demonstrates that LSS Methodology can be applied to operational issues in clinical research, including clinical trial activation. Ensuring the research team within a designated cancer center includes a staff with LSS experience/certification ensures the resources and knowledge exist to apply the methodology effectively. Sharing results with key stakeholders outside of the research office is critical to allow visibility to the outcome of the problems identified. Future directions for GCCC include performing a quarterly review of randomly selected trials. This allows UMGCCC leadership to perform risk analysis and mitigation, establish/modify goals and review results for further revision of process documentation as needed.

Note: Following SOPs and Work Instruction Guidelines, the Study Start up Process will take 28 days.

"To Be" Process Map



Improving Clinical Trial Activation Using Lean Six Sigma Methodology

Amelia Schmidt, MHA, CCRP; Theresa Cummings, RN, MS, CCRP; Jennifer Richards, MS, CCRP

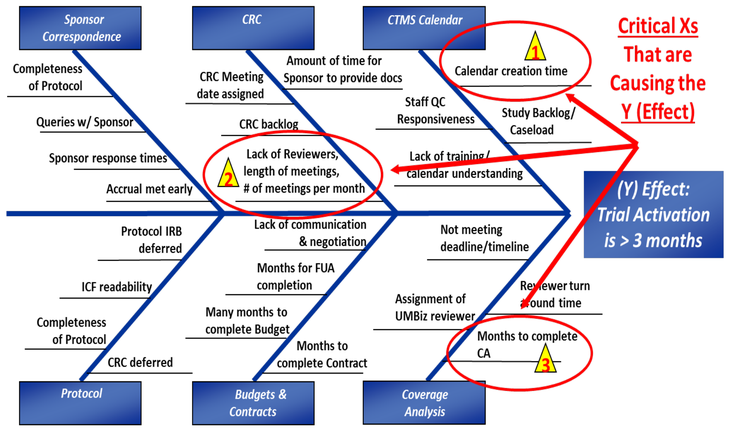
Background

Clinical trial activation at an Academic Institution involves a multitude of stakeholders that include but are not limited to the hospital, the University, and the financial departments of both. Lean Six Sigma (LSS) methodology accelerates business transformation by creating a culture of continuous, measurable improvement that eliminates non value-added activities and improves quality and responsiveness for patients and customers.

The experience at the University of Maryland Greenebaum Comprehensive Cancer Center revealed that delays and barriers throughout the trial activation process lead to considerable time loss in activating our site and opening a study to accrual. This has led to lower patient accrual, termination as a participating site and wasteful use of resources.

In a series of root cause analyses conducted at UMGCCC by a LSS green belt, we determined the following were the most significant and impactful contributors to delayed trail activation: lack of Scientific Review Committee (SRC) meetings; delay in calendar creation in our online Clinical Trial Management System (CTMS); Sponsor un- responsiveness leading to a delay in IRB submission; and delayed completion of the Coverage Analysis and finalization of budgets and contracts.

Figure 1: Fishbone Diagram identifying main causative factors



Goals

- To improve efficiency of trial activation
- To reduce median activation time by 40%
- Protocol assigned and reviewed by SRC within 4 weeks of site approval
- Lower calendar creation time in the CTMS to less than 8 days

Methods

- Implemented a 3rd SRC meeting per month and added more members and reviewers to the committee. Added a regulatory resource and dedicated CRC coordinator to accommodate this.
- Improved Calendar creation process in the CTMS system by revising the work flow to improve, define, and minimize steps and time involved in the process.
- Education of all CRO staff of the revised study activation timeline.
- Assessed and communicated the obstructions that were found using LSS Methodology. These findings were communicated to Hospital and University management that are overseeing Coverage Analysis and Budget and Contract negotiation.

Results

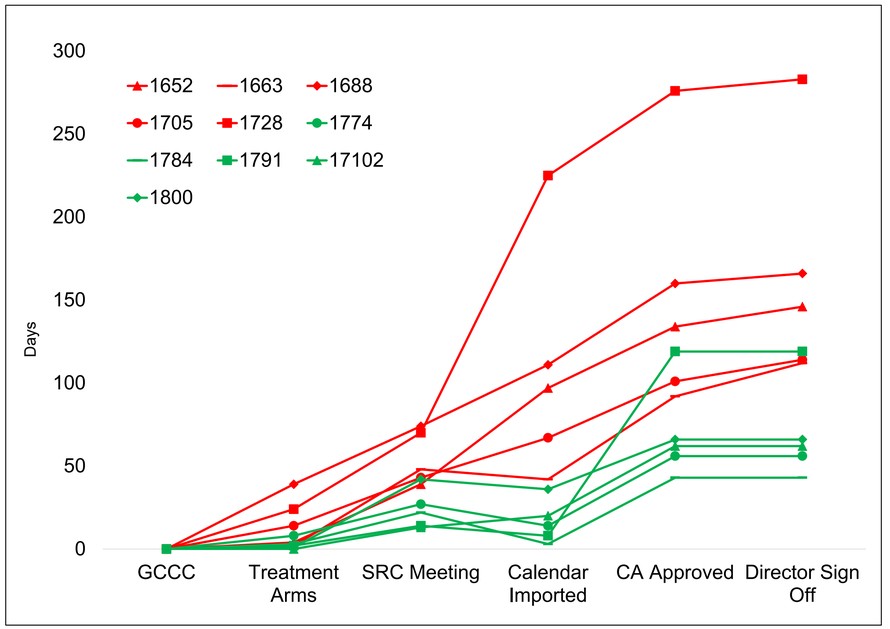
Before implementing LSS:

	Mean	Median
SRC Review	57.2	54
CTMS Calendar	84.4	97
CA Approval	124.8	118
IRB Submission	150	152

After implementing LSS :

	Mean	Median
SRC Review	23.6	22
CTMS Calendar	16.2	14
CA Approval	69.2	62
IRB Submission	69.2	62

Figure 2: Timeline of study activation when comparing protocols



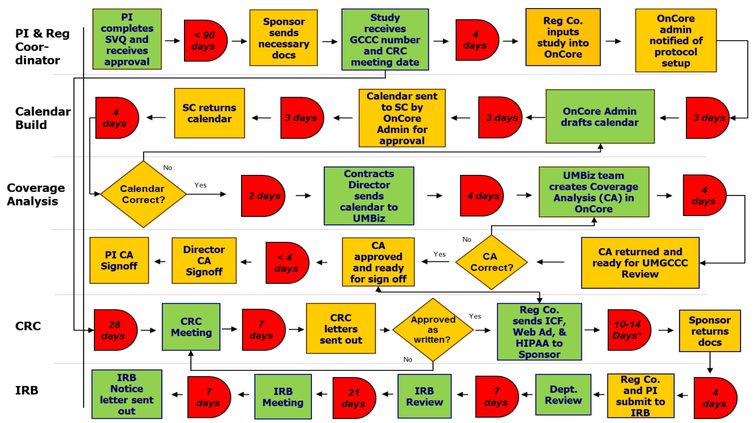
Conclusion

Using Lean Six Sigma Methodology and the DMAIC process, we defined, measured, analyzed, improved, and continue to control underlying causes, waste, and barriers. In doing this, we identified and implemented two process improvement initiatives to improve study activation timelines and were able to improve the speed, quality, and cost of study start up. In addition, we established two new methods of communication and training of staff to increase transparency and "buy-in" to Six Sigma methodology across the team.

Implementation of a third SRC meeting eliminated the immediate backlog of new clinical trial reviews and allowed more time for the possibilities of re-reviews and emergency use protocols while still providing time slots for full reviews.

Through 10 Root Cause Analyses, UMGCCC built process maps, conducted baseline statistics, performed measures of central tendencies, and created pareto charts. In doing this, a significant difference was seen in the trial activation timeline.

Figure 3: "To Be" Process Map



Future Directions

This work demonstrates that LSS Methodology can be applied to operational issues in clinical research, including clinical trial activation. Ensuring the research team within a designated cancer center includes a staff with LSS experience/certification ensures the resources and knowledge exist to apply the methodology effectively. Sharing results with key stakeholders outside of the research office is critical to allow visibility to the outcome of the problems identified. Future directions for GCCC include performing a quarterly review of randomly selected trials. This allows UMGCCC leadership to perform risk analysis and mitigation, establish/modify goals and review results for further revision of process documentation as needed.

Minimizing Clinical Trial Deviations Through Lean Six Sigma and a CRO Compliance Committee

Amelia Schmidt, MHA, CCRP; Jill Kessler, MS, CCRP; Theresa Cummings, RN, MS, CCRP

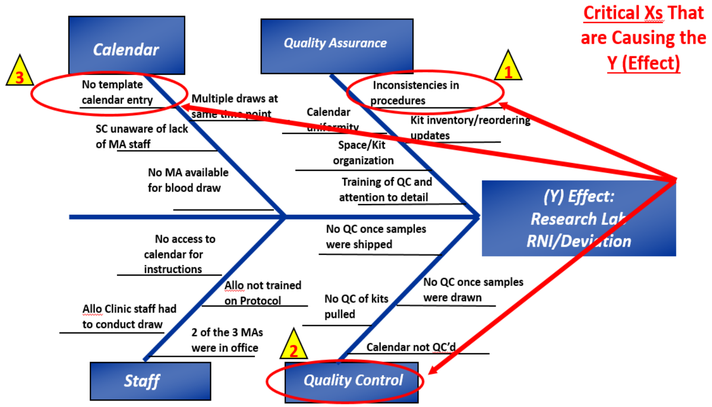
Purpose

The University of Maryland Greenebaum Comprehensive Cancer Center Clinical Research Office (UMGCCC CRO) Compliance Committee reported an abundance of re-occurrences and similar occurrences of clinical trial deviations deriving from research specimen collections and sample management.

The purpose of this project was to analyze and determine the root causes of lab and sample deviations, to improve sample collection, and minimize research lab errors and deviations.

In a root cause analyses conducted at UMGCCC by a Lean Six Sigma Green Belt, we determined the following were the most significant and impactful contributors to sample management deviations: inconsistent performance of procedures, lack of quality control processes, inconsistent usage of the calendar of events, and staffing of the lab and medical assistant teams.

Figure 1: Fishbone Diagram identifying main causative factors



Goals

- The immediate goal of this project was to determine the root causes of sample collection RNIs and deviations.
- To improve lab collection and minimize research lab errors and deviations
- The long term goal of this analysis is to reduce the sample management error rate by at least 50% in the next 6 months by implementing solutions for deviations.

Methods

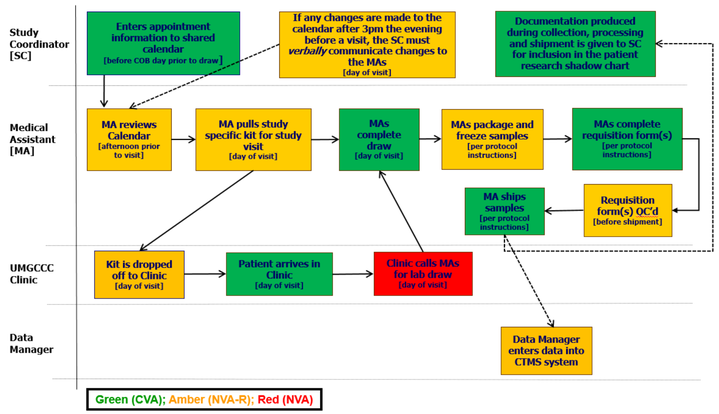
- **Define:** Using Lean Six Sigma (LSS), we identified and defined the problem statement that the amount of deviations in 9 months (n=55) was too high and set a goal to minimize the errors by 50% in 6 months.
- **Measure:** Created a "current state" process map of the lab and sample collection process. Through creating the process map, we were able to look at the path of sample collection and define cost value added, no value added but required, and no value added processes.
- **Analyze:** By creating a fishbone diagram, we were able to identify the effect (Y): research lab deviations and then identify the Critical (X): root causes. We were then able to prioritize the root causes and propose quick wins and rapid improvements.
- **Improve:** Through prioritizing the root causes, we then were able to prioritize a list of solutions. We created a "future state" process map of sample collection and came up with a pilot plan.
- **Control:** In the control phase, we revised process documentation, updated SOPs and training plans, and planned to transition sample management to the process owner. These improvements were implemented in April 2019 and is currently an active project. The re-evaluation date is set for October 2019.

Priority	Solutions
1	**Solution A:** Update SOPs and Work Instructions The SOPs and work instructions should be updated and implemented to put policies into place to ensure reduced errors and deviations. Edits should be made to Calendar procedures, Kit inventory, Kit reordering and Kit organization, etc.
2	**Solution B:** Quality Control training of MAs and SCs Implement Quality Control and importance of attention to detail training. Lab deviations can be prevented through QC checks.
3	**Solution C:** Calendar updates Create a template for SCs to use when entering in new appointments. Color code the calendar to reflect the status of the appointment. Make edits to calendar to reflect when appointment is complete.
4	**Solution D:** Create Lab Management Position Work with HR and Associate Director of Administration to create a Lab Manager position. Currently, the MAs do not have management to help train and streamline the lab collection process.
5	**Solution E:** Create plan for unexpected staff shortage Implementation of a plan when a MA is OOO or unable to help. Grant the clinic access to calendar if their assistance is needed.

Results

- Updated the Research Specimen & Procedure Management SOP
- Implemented quality control training
- Updated the processes for calendar entry of research specimen collection requirements
- Provided supporting evidence and documentation that a Clinical Lab Coordinator management position was necessary for the CRO. This position was filled and the coordinator took over as the "process owner"

Figure 3: "Future State" Process Map



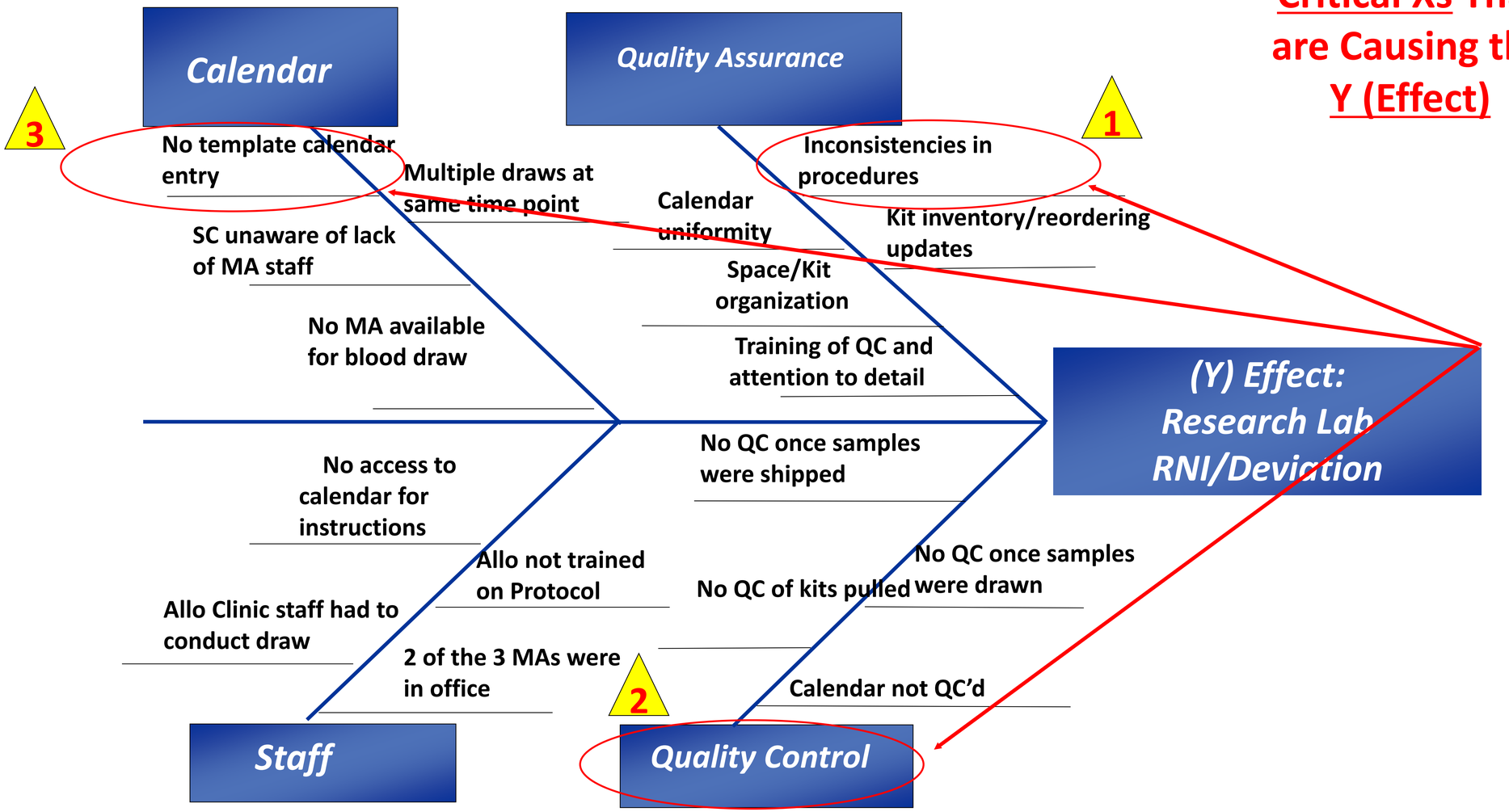
Conclusions

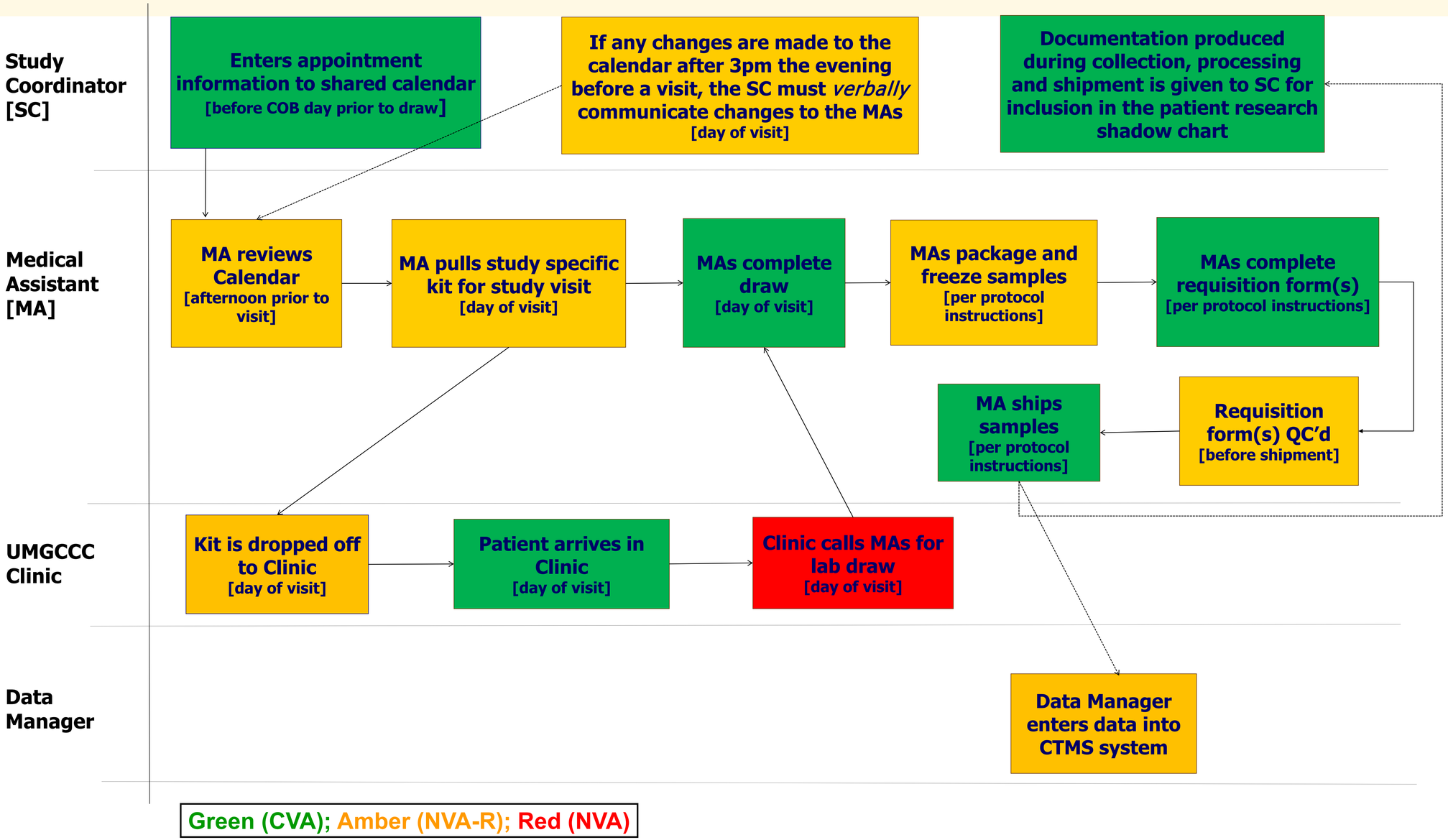
This work demonstrates that LSS methodology can be applied to operational issues in clinical research, including clinical trial deviations. By identifying root causes and prioritizing solutions, the UMGCCC CRO Compliance Committee was able to review and discuss the deviation report descriptions, brainstorm causes for deviations, discuss possible solutions for deviations, and mitigate strategies to be relayed by the CRMO leader representative.

Future directions for GCCC include creating a monthly compliance report and quarterly reviews of research specimen and management deviations. This will allow UMGCCC leadership to perform risk analysis and mitigation, establish/modify goals and review results for further revision of process documentation as needed.

This Poster was supported through the Maryland Department of Health's Cigarette Restitution Fund as well as the National Cancer Institute Cancer Center Support Grant (P30) # CA134274-04

Critical Xs That are Causing the Y (Effect)




Study Coordinator [SC]
Enters appointment information to shared calendar [before COB day prior to draw]
If any changes are made to the calendar after 3pm the evening before a visit, the SC must *verbally* communicate changes to the MAs [day of visit]
Documentation produced during collection, processing and shipment is given to SC for inclusion in the patient research shadow chart
Medical Assistant [MA]
MA reviews Calendar [afternoon prior to visit]
MA pulls study specific kit for study visit [day of visit]
MAs complete draw [day of visit]
MAs package and freeze samples [per protocol instructions]
MAs complete requisition form(s) [per protocol instructions]
MA ships samples [per protocol instructions]
Requisition form(s) QC'd [before shipment]
UMGCCC Clinic
Kit is dropped off to Clinic [day of visit]
Patient arrives in Clinic [day of visit]
Clinic calls MAs for lab draw [day of visit]
Data Manager
Data Manager enters data into CTMS system
Green (CVA); Amber (NVA-R); Red (NVA)

Minimizing Clinical Trial Deviations Through Lean Six Sigma and a CRO Compliance Committee

Amelia Schmidt, MHA, CCRP; Jill Kessler, MS, CCRP; Theresa Cummings, RN, MS, CCRP

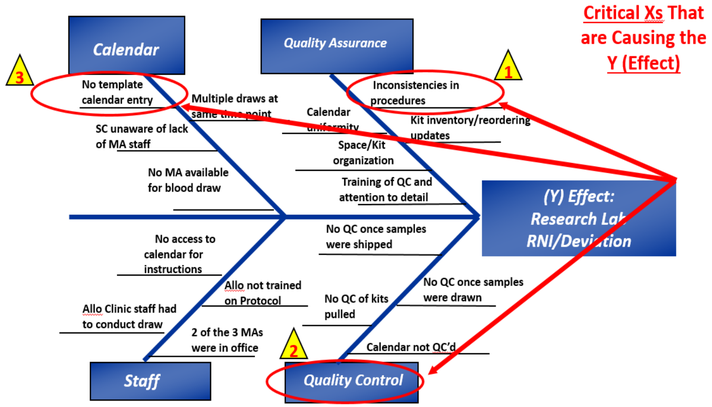
Purpose

The University of Maryland Greenebaum Comprehensive Cancer Center Clinical Research Office (UMGCCC CRO) Compliance Committee reported an abundance of re-occurrences and similar occurrences of clinical trial deviations deriving from research specimen collections and sample management.

The purpose of this project was to analyze and determine the root causes of lab and sample deviations, to improve sample collection, and minimize research lab errors and deviations.

In a root cause analyses conducted at UMGCCC by a Lean Six Sigma Green Belt, we determined the following were the most significant and impactful contributors to sample management deviations: inconsistent performance of procedures, lack of quality control processes, inconsistent usage of the calendar of events, and staffing of the lab and medical assistant teams.

Figure 1: Fishbone Diagram identifying main causative factors



Goals

- The immediate goal of this project was to determine the root causes of sample collection RNIs and deviations.
- To improve lab collection and minimize research lab errors and deviations
- The long term goal of this analysis is to reduce the sample management error rate by at least 50% in the next 6 months by implementing solutions for deviations.

Methods

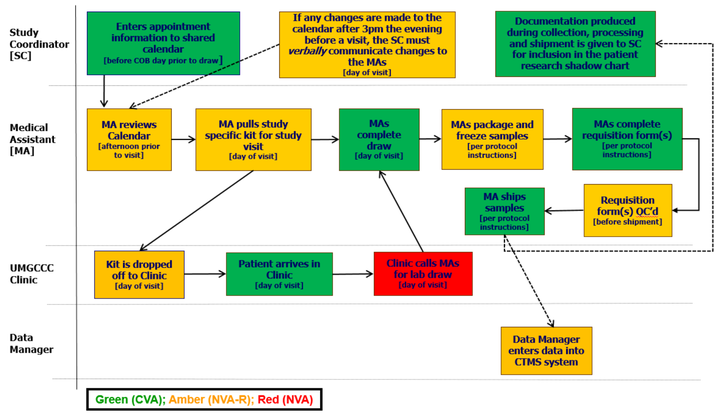
- **Define:** Using Lean Six Sigma (LSS), we identified and defined the problem statement that the amount of deviations in 9 months (n=55) was too high and set a goal to minimize the errors by 50% in 6 months.
- **Measure:** Created a "current state" process map of the lab and sample collection process. Through creating the process map, we were able to look at the path of sample collection and define cost value added, no value added but required, and no value added processes.
- **Analyze:** By creating a fishbone diagram, we were able to identify the effect (Y): research lab deviations and then identify the Critical (X): root causes. We were then able to prioritize the root causes and propose quick wins and rapid improvements.
- **Improve:** Through prioritizing the root causes, we then were able to prioritize a list of solutions. We created a "future state" process map of sample collection and came up with a pilot plan.
- **Control:** In the control phase, we revised process documentation, updated SOPs and training plans, and planned to transition sample management to the process owner. These improvements were implemented in April 2019 and is currently an active project. The re-evaluation date is set for October 2019.

Priority	Solutions
1	**Solution A:** Update SOPs and Work Instructions The SOPs and work instructions should be updated and implemented to put policies into place to ensure reduced errors and deviations. Edits should be made to Calendar procedures, Kit inventory, Kit reordering and Kit organization, etc.
2	**Solution B:** Quality Control training of MAs and SCs Implement Quality Control and importance of attention to detail training. Lab deviations can be prevented through QC checks.
3	**Solution C:** Calendar updates Create a template for SCs to use when entering in new appointments. Color code the calendar to reflect the status of the appointment. Make edits to calendar to reflect when appointment is complete.
4	**Solution D:** Create Lab Management Position Work with HR and Associate Director of Administration to create a Lab Manager position. Currently, the MAs do not have management to help train and streamline the lab collection process.
5	**Solution E:** Create plan for unexpected staff shortage Implementation of a plan when a MA is OOO or unable to help. Grant the clinic access to calendar if their assistance is needed.

Results

- Updated the Research Specimen & Procedure Management SOP
- Implemented quality control training
- Updated the processes for calendar entry of research specimen collection requirements
- Provided supporting evidence and documentation that a Clinical Lab Coordinator management position was necessary for the CRO. This position was filled and the coordinator took over as the "process owner"

Figure 3: "Future State" Process Map



Conclusions

This work demonstrates that LSS methodology can be applied to operational issues in clinical research, including clinical trial deviations. By identifying root causes and prioritizing solutions, the UMGCCC CRO Compliance Committee was able to review and discuss the deviation report descriptions, brainstorm causes for deviations, discuss possible solutions for deviations, and mitigate strategies to be relayed by the CRMO leader representative.

Future directions for GCCC include creating a monthly compliance report and quarterly reviews of research specimen and management deviations. This will allow UMGCCC leadership to perform risk analysis and mitigation, establish/modify goals and review results for further revision of process documentation as needed.

This Poster was supported through the Maryland Department of Health's Cigarette Restitution Fund as well as the National Cancer Institute Cancer Center Support Grant (P30) # CA134274-04

REFERENCES

- Garrett, Kelly. “Welcome to Green Belt Training.” MHA 510. Mount St. Mary’s University, Frederick, MD. May 2016. Lecture

- George, Michael L. The Lean Six Sigma Pocket Toolbook: A Quick Reference Guide to Nearly 100 Tools for Improving Process Quality, Speed, and Complexity. New York: McGraw-Hill, 2005. Print.

- Daudelin, Denise H., et al. “Applying Process Improvement Methods to Clinical and Translational Research: Conceptual Framework and Case Examples.” *Clinical and Translational Science*, vol. 8, no. 6, 2015, pp. 779–786., doi:10.1111/cts.12326.

CAPA Resources

- http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM337109.pdf
- https://wwwapp1.bumc.bu.edu/ocr/ClinicalResearchNewsletter/article.aspx?article=349
- https://www.allianceforclinicaltrialsinoncology.org/main/cmsfile?cmsPath=/Public/Annual%20Meeting/files/Audit%20Prep-Audit%20Findings%20and%20CAPA%2011-2014.pdf

QUESTIONS?

THANK YOU!