ASCO's Quality Training Program

Project Title: **Improving Start-Up Times in Oncology Clinical Trials**

Presenter's Name: Leslie Byatt

Institution: University of New Mexico Comprehensive Cancer Center/ New Mexico Cancer Care Alliance

Date: June 29, 2018

Team Members

Project Sponsor: Zoneddy Dayao, MD.

Team Leader: Leslie Byatt, NMCCA Clinical Research Manager.

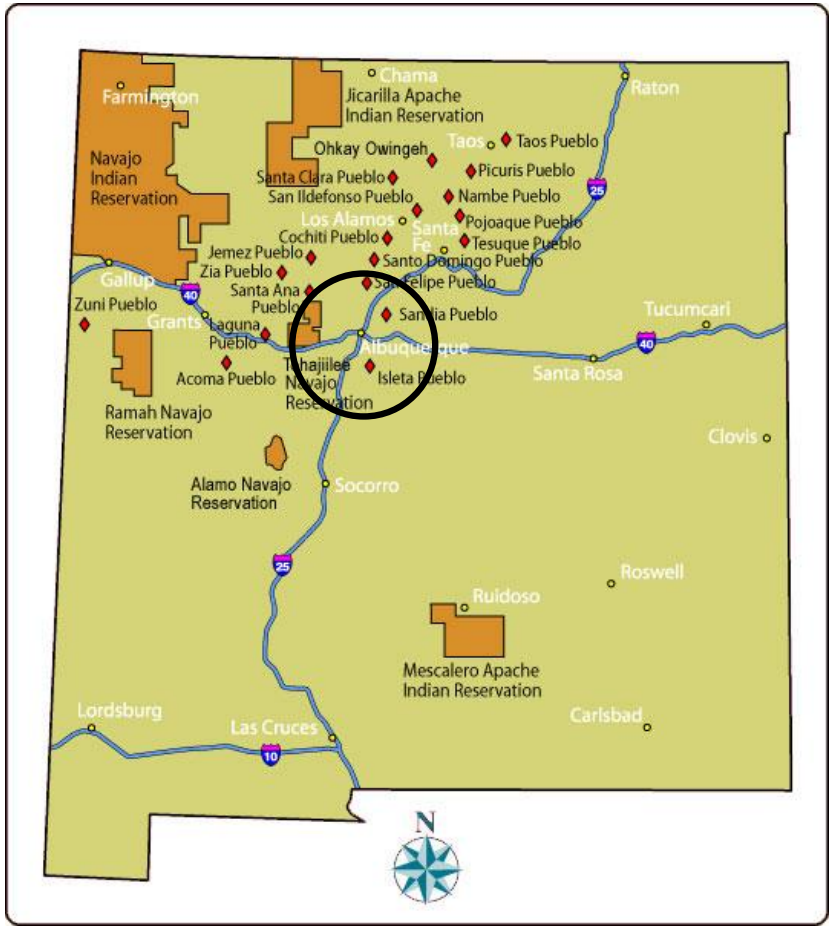
Core Team Member: Kaylee Deutsch, MA, NMCCA Regulatory Supervisor

Focus Group Members: Priscilla Garcia (UNM CCC Data Coordinator) Ebany Martinez-Finlay (UNM CCC Clinical Research Operations Manager), Kelly Vottero (UNM CCC Data Coordinator), Derek Pino (UNMCCC Research Coordinator), Mollie Geske (NMCCA Regulatory Coordinator), Angelina Alvarado (UNM CCC Research Technician), Karwyn Gustafson (UNM CCC Clinical Research Nurse Coordinator)

Institutional Overview



New Mexico: The People We Serve



Rich Multiethnic Diversity

Population: 2,085,528
47% Hispanic
10% American Indian
3% Black / Asian
40% Non Hispanic White

Challenging Geographic, Health and Socioeconomic Disparities

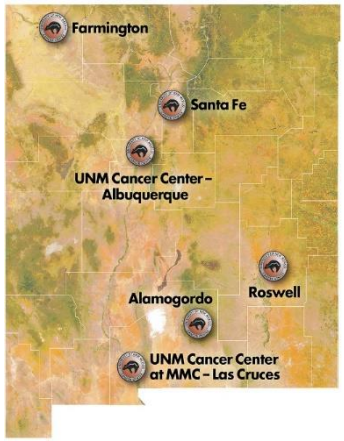
Per Capita Income: 43rd
32/33 New Mexico Counties: Medically Underserved
Poverty Rate: 19% - 36%
Medically Uninsured: 8 – 20%

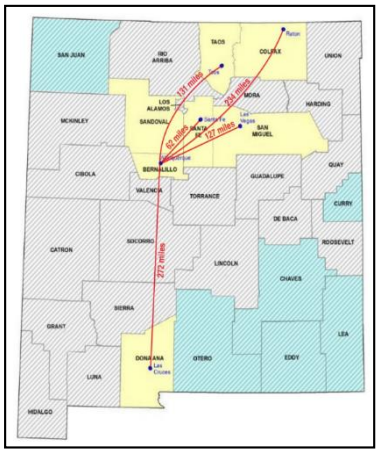
UNMCCC Clinical Facility

UNM Cancer Treatment & Clinical Research Facility

- **Ground Floor:** Radiation Oncology, Radiosurgery, Siemens PETNet Cyclotron Facility & Experimental Radiopharmacy
- **1st Floor:** Laboratory, 3 Surgical Suites, Cancer Imaging, Women's Cancer Screening Clinic, Cancer Registry
- **Education Center**: Video/Virtual Web Links
- **2nd (newly opened) and 3rd Floors:** Multidisciplinary Clinics
- **4th Floor:** Chemotherapy Infusion and Experimental Therapeutics
- **Administration Wing:** Patient Services, Faculty and Staff Offices, Clinical Protocol and Data Management Shared Resource

NMCCA: Statewide Cancer Clinical Trials Network





The New Mexico Cancer Care Alliance (NMCCA)

- Non-profit (501c3) public-private joint venture: UNM CCC, 5 health systems, community oncology clinics, private practices
- Governed by constitution and bylaws creating a single statewide cancer network and integrated infrastructure for the management and oversight of clinical trials
- Based at UNMCCC; UNMCCC Director is Board Chair with authority over all UNM and NMCCA trials

Problem Statement

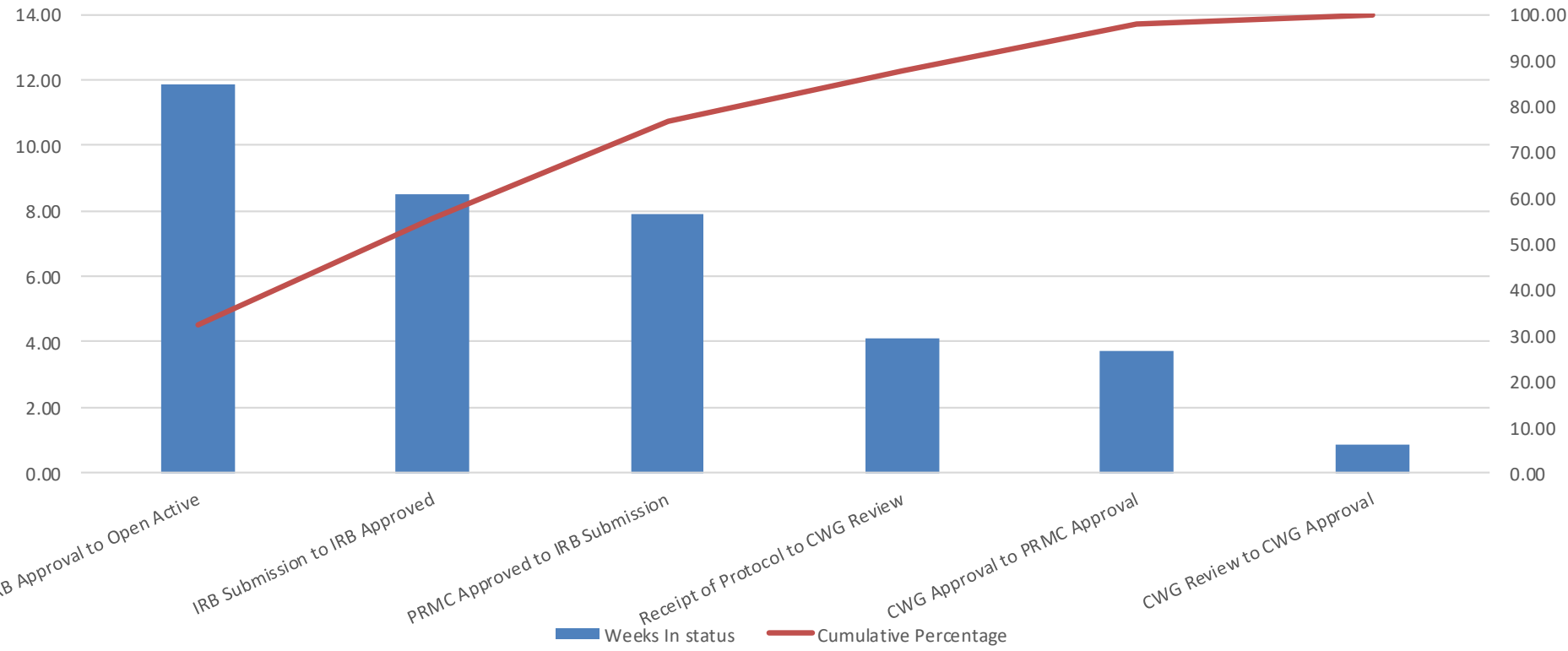
Delays in opening clinical trials impact patient care.

The time to open clinical trials at UNM CCC/ NMCCCA is 33 weeks.

While there are no national benchmarks, average timeline range from 4 -24 weeks.

Diagnostic Data

Weeks from CWG Review to CWG Approval	Weeks from CWG Approval to PRMC Pending	Weeks from PRMC Pending to PRMC Approved	Weeks from PRMC Approved to IRB Submission	Weeks from IRB Submission to IRB Approval	Weeks from IRB Approval to Open Active	Total Weeks from CWG Review to Open Active	
4.08	0.85	3.70	7.90	8.53	11.87	36.93	

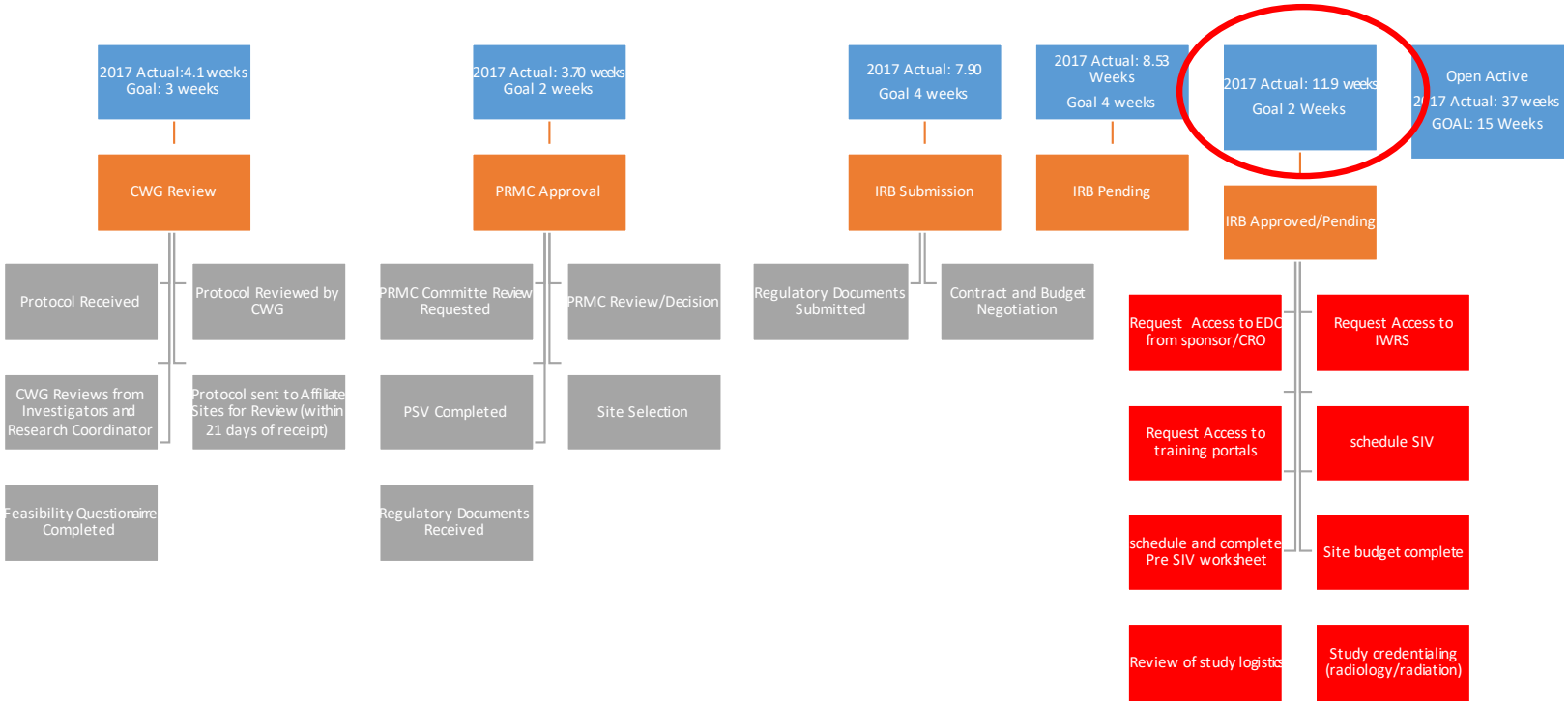


Aim Statement

By June of 2018, NMCCA will establish and implement processes to decrease time from IRB approval to open active by 50% (12 weeks to 6 weeks).

By December of 2018 outcome data should support decrease of 50%.

Process Map: Pre Intervention Work Flow 2017



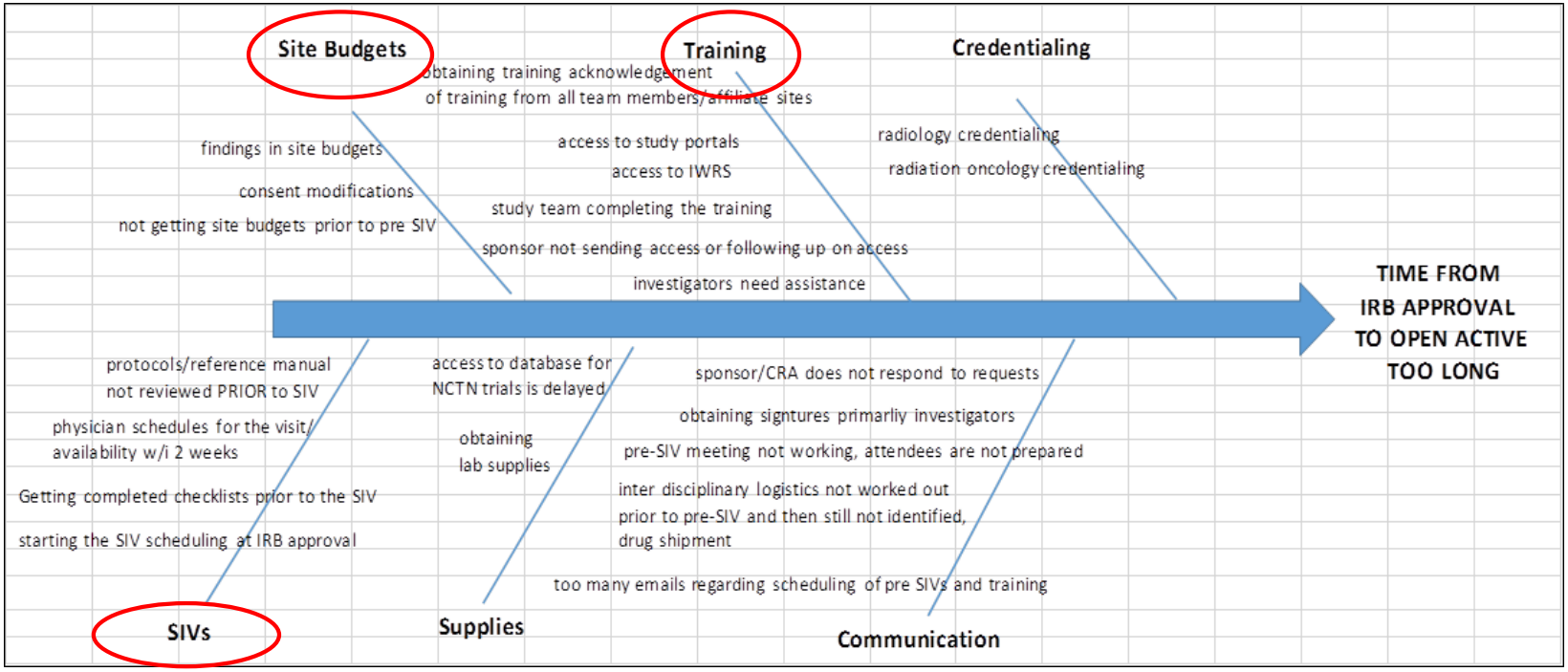
Focus Group

Members: data coordinator, research coordinator , lab technician
regulatory coordinator, research manager

Meeting 1: Identify barriers
A blinded approach to data collection was used.

Meeting 2: Interactive discussion
Top 3 barriers were identified
Strategies were formulated

Cause & Effect Diagram



Measures

- **Measure:** Timeline data for IRB approval to open active from February to June 2018
- **Calculation methodology:** Collected raw data (presented earlier)
- **Data source**: Clinical Trials Management System (E VELOS)
- **Data collection frequency**: Continuous. Reported Quarterly
- **Data quality (any limitations):** All trials included. No subset analysis

2017 Baseline Data: IRB approved to Open/ Active

Weeks from CWG Review to CWG Approval	Weeks from CWG Approval to PRMC Pending	Weeks from PRMC Pending to PRMC Approved	Weeks from PRMC Approved to IRB Submission	Weeks from IRB Submission to IRB Approval	Weeks from IRB Approval to Open Active	Total Weeks from CWG Review to Open Active	
4.08	**0.85**	**3.70**	**7.90**	**8.53**	**11.87**	**36.93**	

Prioritized List of Changes (Priority/Pay –Off Matrix)

Impact	Easy	Difficult
High	• **SHIFTING TASKS EARLIER IN TIMELINE** ○ Study logistics ○ Request of EDC access ○ Credentialing ○ Scheduling of SIV/SIM ○ Scheduling of pre-SIV/SIM ○ Site budget completion • **REGULATORY START UP EMAIL TEMPLATE**	• **PRE SITE INITIATION MEETINGS FOR ALL STUDIES** • **SITE INITIATION MEETING FOR NCORP AND IIT** • **CWG STATUS TIMELINE REPORTS AT EACH MEETING**
Low	• **CREATION OF NMCCA FQ**	

Ease of Implementation

PDSA Plan

Date of PDSA Cycle	Description of Intervention	Results	Action Steps
February 2018	**SHIFTING TASKS EARLIER IN TIMELINE**	Without increased burden on the staff, successfully created a proactive process.	• Continue to monitor task completion. • Reassess in December 2018
February 2018	**REGULATORY START UP EMAIL TEMPLATE**	Effectively started the communication between site and sponsor	After a short trial period the process was implemented by all regulatory coordinators
February 2018	**CREATION OF NMCCA FQ**	This simple tool created the foundation for the regulatory team to work with the sponsors	• Initial tool was updated based on use assessment • Follow up email to staff regarding findings sent post PSVs

PDSA Plan (Test of Change)

Date of PDSA Cycle	Description of Intervention	Results	Action Steps
March 2018	**PRE SITE INITIATION MEETINGS FOR ALL STUDIES**	Team members were not as quick to adapt to this meeting	• Continue to develop the process. • Working with staff to identify needs early
March 2018	**SITE INITIATION MEETING FOR NCORP AND IIT**	This has become a very effective network training method	• Required management to set as a priority. • Identified staff training required.
March 2018	**CWG STATUS TIMELINE REPORTS AT EACH MEETING**	Time consuming task. However, when used it was very useful to working group	• Task will be reassigned. • Fall 2018 will be evaluated against similar tools in use

Materials Developed

NMCCA Pre Site Visit Clinical Trial Feasibility Checklist

(Note: this is not an inclusive list of considerations)

Study: _____ PI: _____ Date Completed: _____

Study Team Contacts	
Name and Contact information for : Project Lead at CRO Project Lead at Sponsor CRA Startup Lead	
Training	
What EDC system will be used	
What study team members will be required to have access?	
Will prior training on the system be recognized?	
What IWRS system will be used	
How will study specific training be accessed?	
When do you think the SIVs	
When will the study team be given this access	
Affiliate Sites	
Sent Site Management Plan	
We may have affiliate sites that are interested in participating. What is the process for getting them started?	
Pharmacy Considerations	
If we use affiliate sites, we will want drug shipped to each site. Do you foresee any issues with this?	

Company Name and Study number: Study Title

Hi Natalie,

Thank you very much for supplying the regulatory document package; my apologies for the delay in my response. Please see attached our study team CVs, MLs, GCP certifications, etc. – if there are too many to send in one email, I will send in separate emails. I will start completing the Site Contact Information form and routing the regulatory documents (FDFs, 1572s, signature pages, etc.) tomorrow.

I would like to let you know about timelines so you have an idea of what to expect. UNMCCC is required to have a Medicare Coverage Analysis completed prior to an internal review of the informed consent. This entails us to send several documents (protocol, budget template, CTA template, and ICF template) out for review against current Medicare standards and requirements. Once this is sent, it takes about 1 week for it to be completed and returned to UNMCCC. It is at that point that I will forward the MCA, site tracked changes ICF, protocol, and IB to our director for her final review. It typically takes her 1 week to review and return the ICF with any further required changes, back to me. When I receive the ICF back from her, I will forward our site tracked changes ICF on for sponsor review and will prepare for the WIRB submission.

The study will be submitted to WIRB following the above-outlined process, and WIRB approval is usually received within 1-2 weeks. Once we submit to WIRB, we will send the Principal Investigator a request for Site Initiation Visit (SIV) availability.

In addition, can you please answer the questions listed below and provide a response within the next week? These items typically cause the longest delay for site activation, as you probably already know, so I would like to initiate the process early if possible.

1. Will lab receive the lab kits, materials, etc. before the SIV?
    a. Can you please provide an estimated shipment/delivery date for the lab kits?
    b. Lab kits/materials can be shipped to the following address:

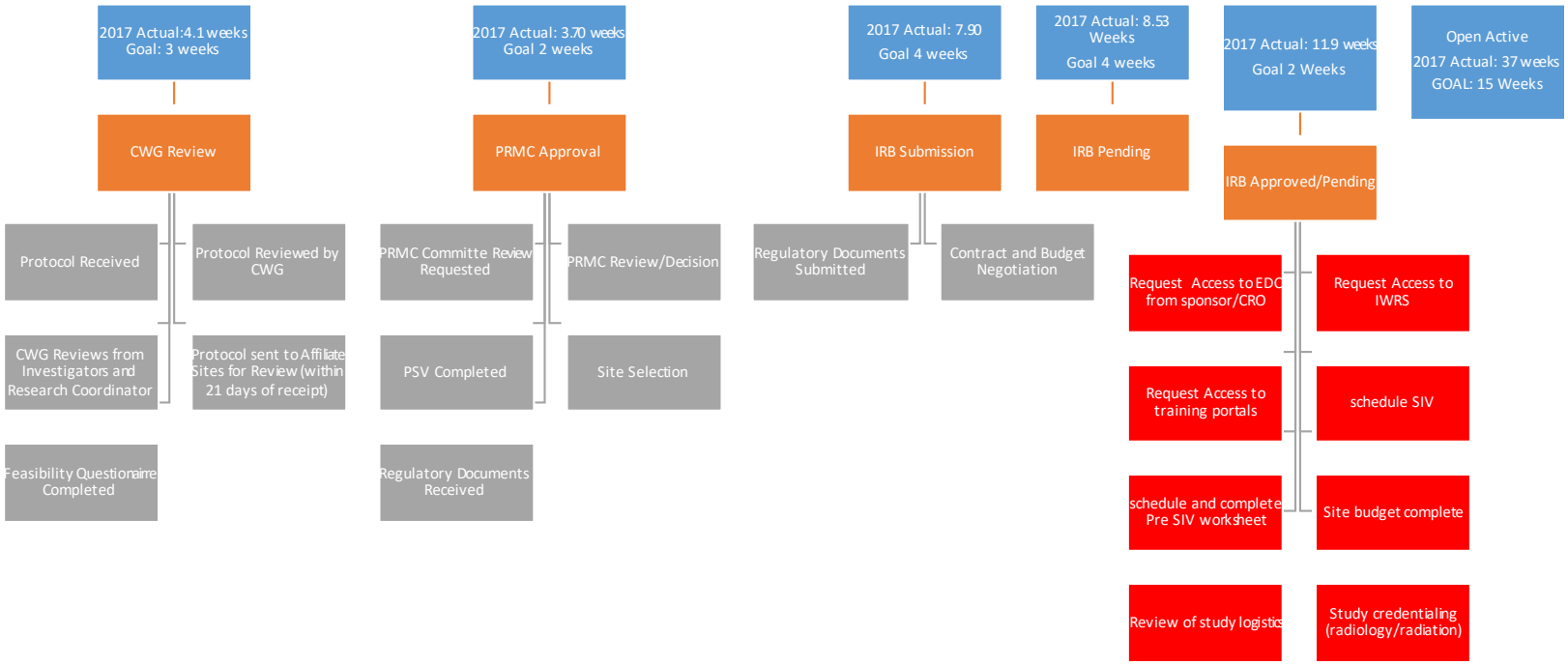
Updated 4/26/18

Study	Awaiting Protocol	CWG Review	CWG Approved	PRMC Pending	PRMC Approved	IRB Pending	Pending	Action Required
Alliance AFT-28	11/3/2017	11/13/2017	12/5/2017	1/8/2018	2/9/2018			Being submitted to HRRC d/t translation
EISAI E7080-M001-222	2/12/2018							Sent Synopsis to PI
Genentech YO40425		11/2/2017	11/7/2017	11/13/2017	12/15/2017	1/26/2018	2/1/2018	OA: 3/30/18
INST UNM1709 ECHO	10/3/2017							
INST Atlantic Health System1801	2/23/2018 LPB and PI have called sponsor with no response							4/3/18: CWG approved receipt of final protocol.
Mersana MER-XMT-1522-1-6.1	2/16/2018:	3/30/2018						PSV scheduled for 5/21/18

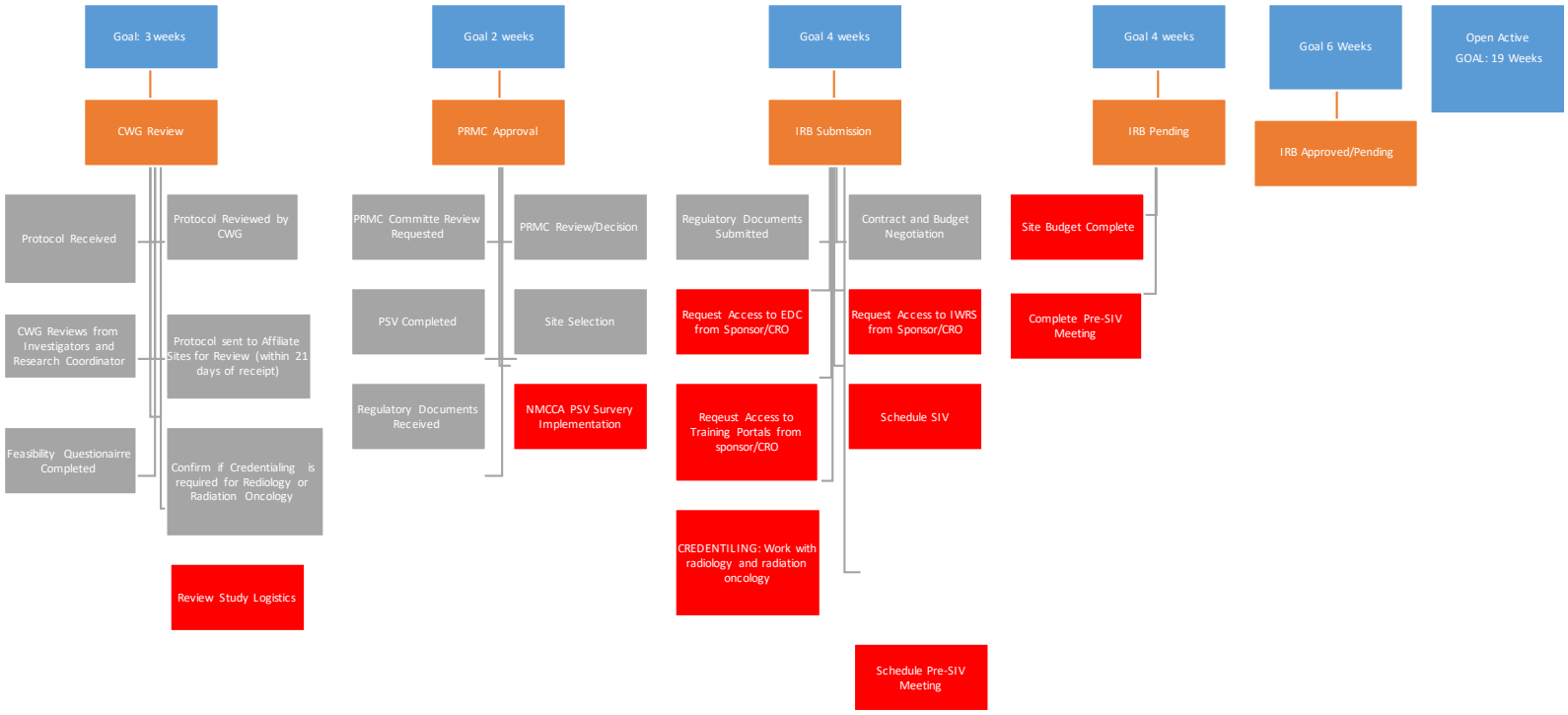
Instructions

- After following the instructions below, delete this slide so that the Title Slide becomes slide 1.
- Enter the Study Number and the Title on the title slide (Slide 1)
- Enter your name and credentials on the title slide (Slide 1)
- List key inclusion criteria
- List key exclusion criteria
- List the study drug or treatment. Briefly describe the class of drug (if applicable) and potential side effects
- Are there adverse events specific to this protocol/treatment? If yes, what are they and what should the study team be looking for regarding signs and symptoms?
- Describe the protocol specific stopping points (this could include when a patient would be taken off treatment or off study)
- List 2 or 3 informed consent talking points with potential participants

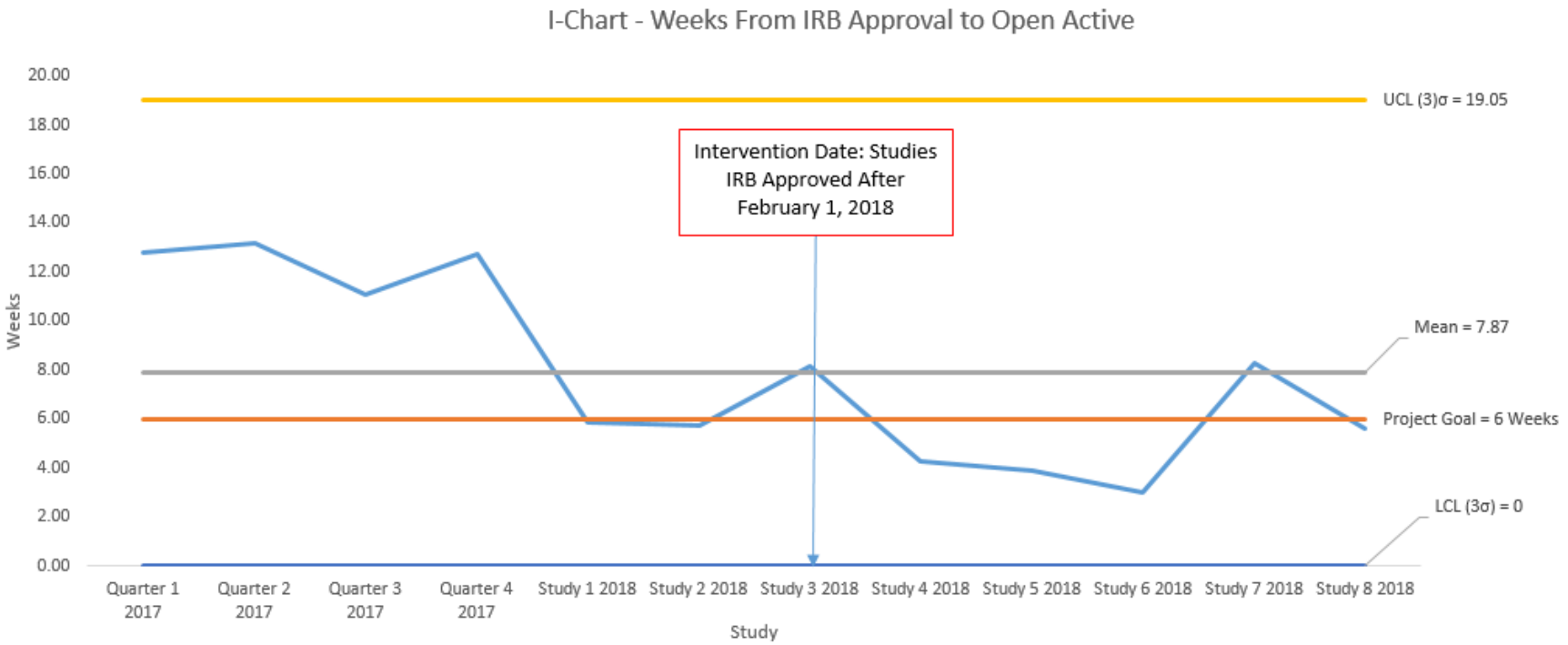
Process Map: Pre Intervention Work Flow 2017



Process Map: Post Intervention



Change Data: I – Chart



Conclusions

- Based on 2017 data, the longest timeline in clinical trial activation at UNMCCC/ NMCCA is IRB approval to open active.

- A focus group approach allowed direct participation of involved staff to identify problems and formulate realistic solutions:
  - Previously set goal of 2 weeks is unrealistic.
  - The time to complete tasks cannot be shortened.
  - The consensus was to shift the tasks to run in parallel with earlier timelines . The focus group determined that this will not increase staff workload and stress.

- This process was a constructive exercise creating a positive team experience that encouraged collaborative problem solving

Next Steps/Plan for Sustainability

1.Continue monitoring timelines through 2018

2. Schedule a follow up meeting with focus group to assess effectiveness of interventions and identify areas of improvement

3. Examine results by clinical trial type: Industry, NCTN, IIT

Improving Start-Up Times in Oncology Clinical Trials at an NCI Designated Comprehensive Cancer Center (NCORP site)
An ASCO Quality Improvement Project

Leslie Byatt, CCRC; Kaylee Deutsch, MHA, CCRP ; Zoneddy Dayao, MD

University of New Mexico Comprehensive Cancer Center and the New Mexico Cancer Care Alliance

Abstract

Delays in opening clinical trials adversely affect patient care. New Mexico Cancer Care Alliance's (NMCCA) / University of New Mexico Comprehensive Cancer Center (UNMCCC) average time from clinical working group (CWG) review to trial opening is 33 weeks. Shortening this time will expedite patient access to novel therapies.

AIM

1. To define the average time a protocol stays within each timeline for clinical trial initiation
2. To identify the timeline where an intervention will make the most impact in shortening start-up time
3. Through an ASCO driven project, create an intervention with the goal of decreasing this time by 50% by December 31, 2018

Goal: Identify where delays occur in the process and create strategies to shorten the time of trial activation without creating excessive burden to staff and financial resources.

Methods and Materials

1. Data Gathering

This study analyzed 81 clinical trials opened in 2017 which included industry, investigator initiated and NCTN trials. Data on the average time a trial spent in the following timelines were collected and a Pareto chart was generated (Figure 1):

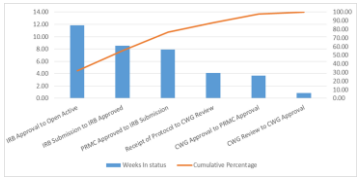
- Clinical Working Group Review
- Protocol Review and Monitoring Committee (PRMC) Approval
- IRB Submission
- IRB Pending
- IRB Approved
- Open Active

2. Focus Group Approach

After identifying the timeline accounting for the longest delay, a focus group of staff directly involved in this process was organized. Two meetings were conducted.

First meeting: Identify barriers. A blinded approach to data collection was used.

Second meeting: Interactive discussion. The top 3 barriers were identified and strategies were formulated, in the context of staff limitations.



3. Focus Group Outcome

Data from 2017 showed that the time between IRB approval and a study becoming open active was 12.67 weeks. As outlined in Figure 1, this represents 38% of the total time (33 weeks) for trial initiation. The data allowed us to identify the timeline that would be the focus of intervention.

The focus group identified the delays encountered from IRB approval to open active as represented in Figure 2.

Among these, the 3 lengthiest processes identified were:

- Scheduling and Completion of Site Initiation Visits
- Completion of Site Budgets
- Access to study portals, EDC, IWRS

There was agreement amongst all the group members that the time to complete these tasks could not be shortened due to staffing resources. However, strategically shifting these tasks by working in parallel with earlier timelines is estimated to decrease the time by at least 50% (6 weeks).

On closer analysis of the average length of these processes, it was also determined that the NMCCA's arbitrarily set goal of reducing this timeline to 2 weeks is likely not achievable and 6 weeks is a more realistic goal.

Process Interventions

To effectively implement the shift in the new workflow, beginning February 2018, strict deadlines for the 3 priority processes will be established for each new trial submitted to IRB.

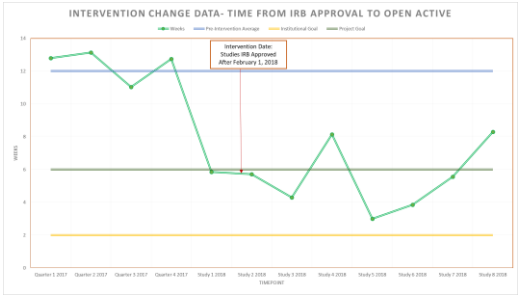
Process interventions include:

1. New study feasibility questionnaires will be given to sponsors to identify barriers earlier.
2. Template emails have been drafted for the regulatory coordinators to communicate more efficiently at the time of PRMC approval.
3. A template for timeline reporting to the clinical working groups has been created and mandatory deadlines will be established and tracked.

Pre-Intervention Work Flow

Post Intervention Work Flow

Results



Our data shows that our interventions have had a strong positive impact on our timelines. Our intervention data tracks all studies that have been submitted to the IRB after January 1, 2018. Of the 8 studies submitted and IRB approved after our intervention was put into place, 6 met our goal timeframe of 6 weeks to activation after IRB approval.

Of the two studies that did not meet our new goal of 6 weeks, one was delayed due to difficulty scheduling the site initiation visit with the sponsor. The other was delayed due to delays in scheduling the SIV and the completion of the site budget.

Conclusions

Detailed analysis of 2017 data of newly opened trials at NMCCA/ UNMCCC showed that protocols spent the longest amount of time from IRB approval to open active. The identification of this delay is the critical first step in developing strategies to shorten time to trial initiation at our institution.

The focus group identified the most significant causes of delay. It was determined that shifting the tasks to run in parallel with earlier timelines will allow for the same amount of time for task completion without increasing the stress on the clinical trials staff. It is anticipated that this strategy will reduce the amount of time from IRB approval to open active from 12 weeks to 6 weeks.

This process was a constructive exercise creating a positive team experience that encouraged collaborative problem solving.

Next Steps

1. Continue monitoring timelines through 2018
2. Schedule a follow up meeting with focus group to assess effectiveness of interventions and identify areas of improvement
3. Examine results by clinical trial type: Industry, NCTN, IIT