ClinicalTrials.gov Results Development and Management: A Successful Approach

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History of ClinicalTrials.gov

1997
- FDA Modernization Act Mandates Registry

2000
- ClinicalTrials.gov was launched

2007
- Section 801 of FDA Amendments Act

ClinicalTrials.gov Reporting Requirements

- By regulation:
  - Applicable trial registration
  - Reporting of results within one year of primary completion
- 'Responsible Party' is required to provide trial results to ClinicalTrials.gov data base
- Required results:
  - Study disposition and baseline characteristics
  - Primary and secondary outcomes
  - Adverse events

Who was Involved

DAIT

- Division of Allergy, Immunology and Transplantation (DAIT)
  - One of three extramural divisions of the National Institute of Allergy and Infectious Diseases (NIAID) that supports research at academic and research institutions, part of the National Institutes of Health (NIH)
- Sponsor/Responsible Party for a diverse clinical trials portfolio
  - Allergy/asthma; autoimmune; transplantation

Rho

- Contract research organization
- Statistical and data coordinating center for multiple DAIT funded networks/ consortia

NIH National Institute of Allergy and Infectious Diseases

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Challenges

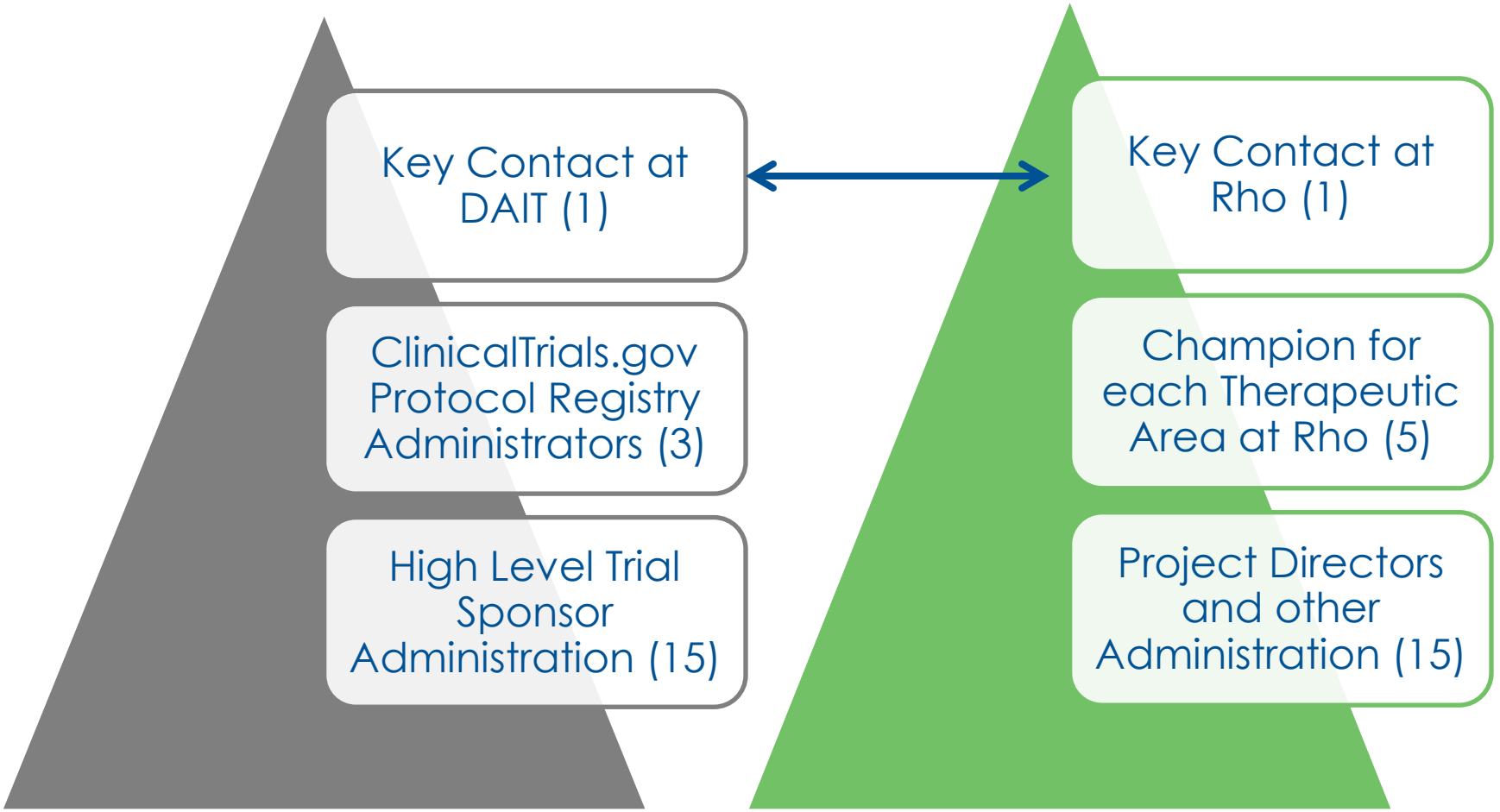
- ClinicalTrials.gov was a new system
- Professionals new to ClinicalTrials.gov process were trying to develop results for each trial that needed to be posted
- Quality of results submissions varied from trial to trial
- All key stakeholders were not getting the opportunity to review developed results prior to their release to the public

Key Strategies

Overarching Goal: Develop standards and process to guide ClinicalTrials.gov results development

1. Create core working group
2. Create and maintain study portfolio overview
3. Develop best practice standards
4. Establish iterative standard review and approval process

Working Group



Study Portfolio Overview

- Develop a management system
  - Identify which of the active trials need to begin ClinicalTrials.gov results development
  - Track results development progress
  - Identify issues as they arise
- Regular meetings between Key Contacts and Champions
  - Review status report
  - Discuss issues
  - Provide accountability and guidance

DAIT as the Responsible Party for Applicable Trials- ClinicalTrials.gov Cross Sectional Overview

Phase	N= (%) of the Applicable Trials
I/II	7 (11%)
II	48 (76%)
II/III	1 (2%)
III	3 (5%)
IV	4 (6%)
Total	**63 (100%)**
ClinicalTrials.gov Results Development Status: N=	**Status**
4	Priority
36	Not Due
2	ClinicalTrials.gov QA
21	Record results posted to public

Standardization – Results Template

Study:
<Primary Results or Final Results>

Baseline Measures Overview

Number of Participants

	<Arm/Group Title #1>	<Arm/Group Title #2>
*Overall Number of Baseline Participants		
Baseline Analysis Population Description *(350)*		

***Age**

Age Continuous (years)	<Arm/Group Title #1>		<Arm/Group Title #2>		Total	
	Mean	SD	Mean	SD	Mean	SD

Age Categorical (participants)	<Arm/Group Title #1>	<Arm/Group Title #2>
≤ 18 years		
Between 18 and 65 years		
≥ 65 years		

***Region of Enrollment**

	<Arm/Group Title #1>	<Arm/Group Title #2>
United States		

Additional Baseline Measurement

Race (NIH/OMB)	<Arm/Group Title #1>	<Arm/Group Title #2>
American Indian or Alaska Native		
Asian		
Native Hawaiian or Other Pacific Islander		
Black or African American		
White		

Study:
<Primary Results or Final Results>

Ethnicity (NIH/OMB)	<Arm/Group Title #1>	<Arm/Group Title #2>
Hispanic or Latino		
Not Hispanic or Latino		
Unknown or Not Reported		

Study-Specific Baseline Measure Title *(100)*				
Baseline Measure Description *(600)*				
Measure Type *(Limited Selection)*				
Measure of Dispersion *(Limited Selection)*				
	<Arm/Group Title #1>		<Arm/Group Title #2>	
	<Measure Type>	<Measure of Dispersion>	<Measure Type>	<Measure of Dispersion>
(Category; 50)				
Unit of Measure *(40)*				

Results: Outcome Measure Data

Outcome Measures – Endpoint #1

Overview

*Outcome Measure Type *(Limited Selection)*			
*Outcome Measure Reporting Status *(Limited Selection)*		Anticipated Posting Date	
*Outcome Measure Title *(255)*			
Outcome Measure Description *(999)*			
*Outcome Measure Time Frame *(255)*			
Safety Issue? *(Yes/No)*			

Population

Standardization – Adverse Event XML

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Serious Adverse Events

	Anti-CD3 mAb Plus Diabetes Standard of Care Treatment	Diabetes Standard of Care Treatment
Total # participants affected/at risk	**10/52 (19.23%)**	**1/25 (4%)**
Immune system disorders		
Cytokine release syndrome [†A]		
# participants affected/at risk	2/52 (3.85%)	0/25 (0%)
# events	2	0
Infections and infestations		
Cellulitis [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Diarrhoea infectious [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Infection [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Injury, poisoning and procedural complications		
Skull fracture [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Splenic rupture [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Metabolism and nutrition disorders		
Diabetic ketoacidosis [†A]		
# participants affected/at risk	1/52 (1.92%)	0/25 (0%)
# events	1	0
Hypoglycaemia [†A]		
# participants affected/at risk	2/52 (3.85%)	1/25 (4%)
# events	2	1

National Institute of Allergy and Infectious Diseases

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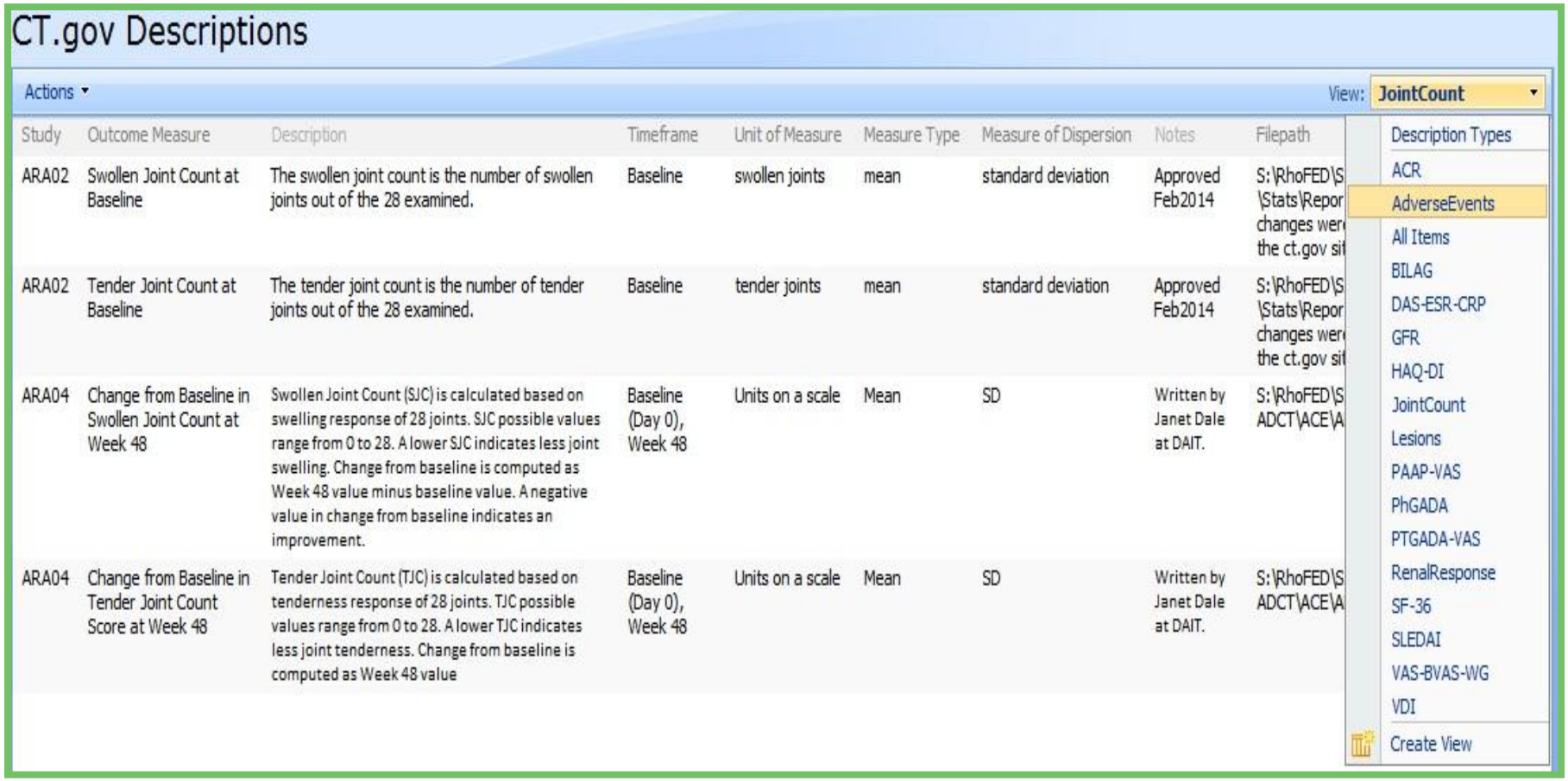
Standardization – Description Dictionary



CT.gov Descriptions

Actions ▾ View: JointCount

Study	Outcome Measure	Description	Timeframe	Unit of Measure	Measure Type	Measure of Dispersion	Notes	Filepath
ARA02	Swollen Joint Count at Baseline	The swollen joint count is the number of swollen joints out of the 28 examined.	Baseline	swollen joints	mean	standard deviation	Approved Feb2014	S:\RhoFED\S \Stats\Repor changes wer the ct.gov sit
ARA02	Tender Joint Count at Baseline	The tender joint count is the number of tender joints out of the 28 examined.	Baseline	tender joints	mean	standard deviation	Approved Feb2014	S:\RhoFED\S \Stats\Repor changes wer the ct.gov sit
ARA04	Change from Baseline in Swollen Joint Count at Week 48	Swollen Joint Count (SJC) is calculated based on swelling response of 28 joints. SJC possible values range from 0 to 28. A lower SJC indicates less joint swelling. Change from baseline is computed as Week 48 value minus baseline value. A negative value in change from baseline indicates an improvement.	Baseline (Day 0), Week 48	Units on a scale	Mean	SD	Written by Janet Dale at DAIT.	S:\RhoFED\S ADCT\ACE\A
ARA04	Change from Baseline in Tender Joint Count Score at Week 48	Tender Joint Count (TJC) is calculated based on tenderness response of 28 joints. TJC possible values range from 0 to 28. A lower TJC indicates less joint tenderness. Change from baseline is computed as Week 48 value	Baseline (Day 0), Week 48	Units on a scale	Mean	SD	Written by Janet Dale at DAIT.	S:\RhoFED\S ADCT\ACE\A

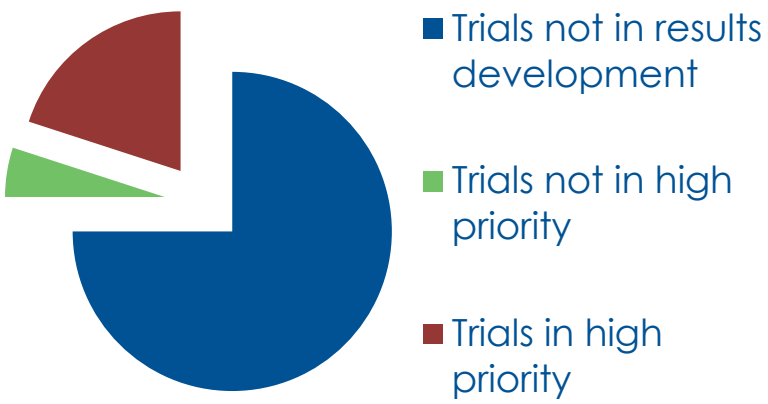
Description Types
ACR
AdverseEvents
All Items
BILAG
DAS-ESR-CRP
GFR
HAQ-DI
JointCount
Lesions
PAAP-VAS
PhGADA
PTGADA-VAS
RenalResponse
SF-36
SLEDAI
VAS-BVAS-WG
VDI
Create View

Comprehensive Review

- Identify important stakeholders who need to review/approve what will be seen by the public
- Two tiers of review
  - 1st tier involves key investigators and researchers on the trial
  - 2nd tier involves high level individuals at DAIT responsible for ClinicalTrials.gov results

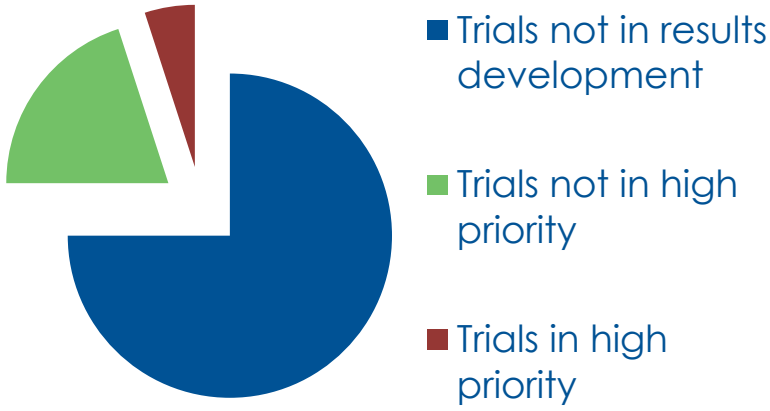
Results after 3 years

Before Strategies were Implemented



- 6+ months to develop results
- No overall management of all trials in ClinicalTrials.gov results development
- No iterative review process

After Strategies were Implemented



- 3 months to develop results
- Overall management of all trials in ClinicalTrials.gov results development
- Iterative review process

Ongoing Challenges

- Delayed response from necessary trial team results approvers
- Time to obtain ClinicalTrials.gov approval of results
- Different expectations from ClinicalTrials.gov approvals between trials

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Thank You!

For questions contact Elizabeth Paynter:
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