ClinicalTrials.gov Updated Quality Control and Posting Procedures

October 15, 2019

U.S. National Library of Medicine
National Center for Biotechnology Information

Outline

1

Background

Current process and regulation

2

Procedures

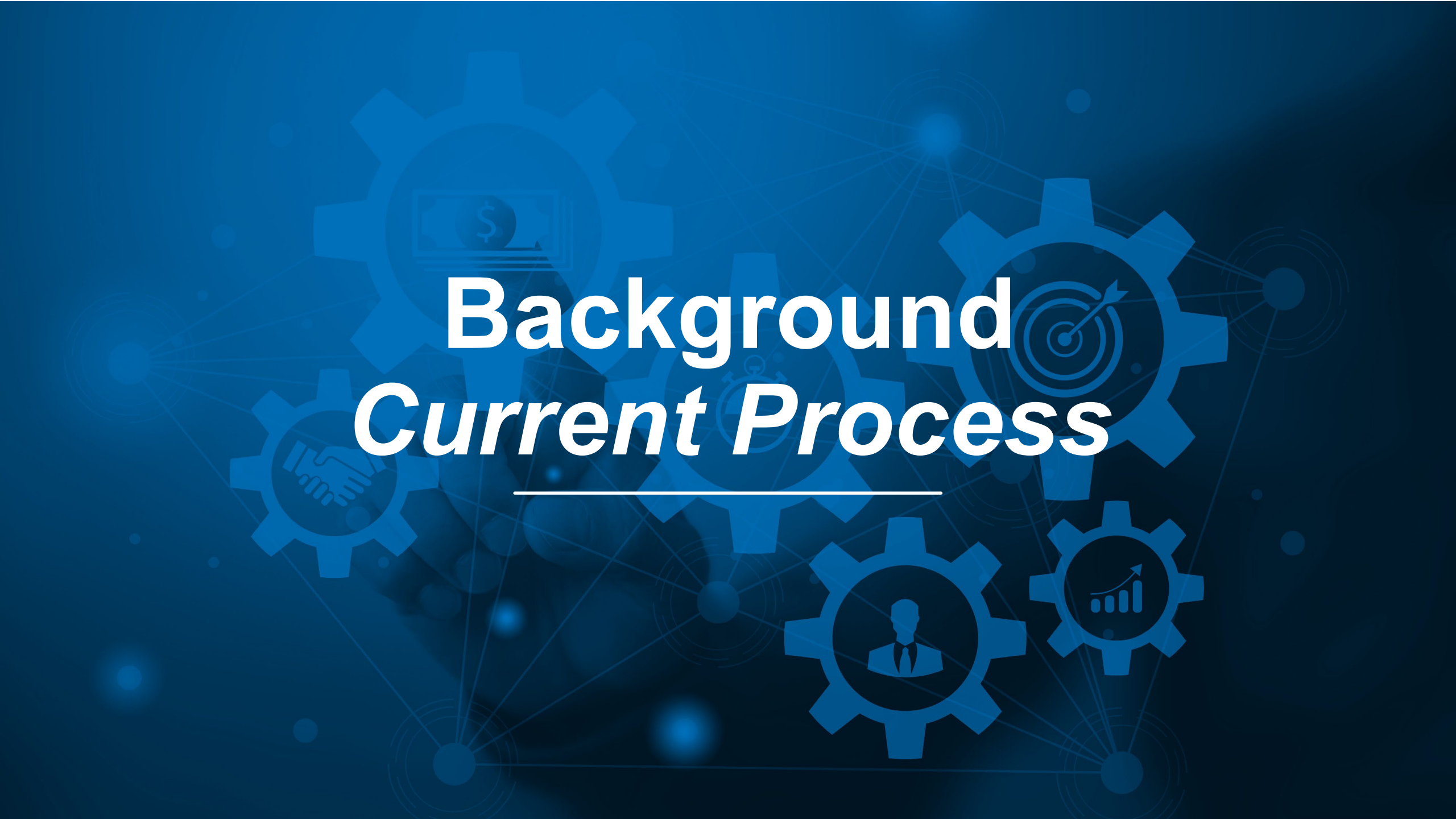
Examples

3

Implementation

Initial scope and timeline

Background
Current Process



Current: Results information submission

Update study record

Submit study record

Backend Processing

Responsible Party

QC Review Staff

1 **Sponsor Account**

2 Registration Information

Results Information

Automated Validation

3 Manual Validation Quality Control Review

No “Major” Issues

“Major” Issues

4 **Public Posting**

ClinicalTrials.gov

Address QC Review Issues

QC Review Comments

Quality Control (QC) Review Process

Two-part review process for submitted study records

- **Before submission**: Automated validation rules in the Protocol Registration and Results System (PRS)

- **After submission:** Manual review by NLM staff using established review criteria to identify apparent errors, deficiencies, and inconsistencies.
  - “Major” issues must be addressed
  - “Advisory” issues are suggestions to help improve the clarity of the record and are optional to address

PRS: Example of Automated Validation Rule

ERROR – Information is missing

Edit	Arm/Group Title	Remuverol	Placebo	Total
	▸ Arm/Group Description	Participants received Remuverol 15 ...	Participants received Remuverol pla...	
Edit	**Overall Number of Baseline Participants**	ERROR : The Overall Number of Baseline Participants has not been entered.	99	
	▸ Baseline Analysis Population Description			

CORRECTED – Missing information added

Edit	Arm/Group Title	Remuverol	Placebo	Total
	▸ Arm/Group Description	Participants received Remuverol 15 ...	Participants received Remuverol pla...	
Edit	**Overall Number of Baseline Participants**	101	99	**200**
	▸ Baseline Analysis Population Description			

Public View: Example of Submitted Results

Study Details | Tabular View | **Results Submitted** | Disclaimer | How to Read a Study Record

Results Submitted – Not Posted on ClinicalTrials.gov

Results information has been submitted to ClinicalTrials.gov by the sponsor or investigator, but is not yet publicly available (or "posted") on ClinicalTrials.gov. The submitted information may not be available if it is pending Quality Control (QC) Review by the National Library of Medicine (NLM) or if issues identified during QC review are being addressed or corrected by the sponsor or investigator. NLM's limited QC review assesses for apparent errors, deficiencies, or inconsistencies. NLM staff do not verify the scientific validity or relevance of the submitted information.

Recruitment Status :	Completed
Actual Primary Completion Date :	January 25, 2019
Actual Study Completion Date :	January 25, 2019

Information about submission and QC Review

Submission Cycle	Results Submitted to ClinicalTrials.gov	Results Returned after Quality Control Review
1	January 18, 2020	

NCBI

QC Review Criteria

Review Identifies Apparent:

- ✓ Errors
- ✓ Deficiencies
- ✓ Inconsistencies

Protocol Registration and Results Review Criteria:
https://prsinfo.clinicaltrials.gov/ProtocolDetailedReviewItems.pdf
https://prsinfo.clinicaltrials.gov/ResultsDetailedReviewItems.pdf

ClinicalTrials.gov Results Quality Control Review Criteria: Baseline Characteristics Module

Baseline Characteristics Overview

The Baseline Characteristics module is a tabular summary of each baseline or demographic characteristic for the entire study population and for each arm or comparison group (similar to Table 1 in a journal article). At a minimum, Baseline Measure Information includes Age, Sex/Gender, Race and Ethnicity (if collected under the study protocol), and any other measures that were assessed at baseline and used in the analysis of the Primary Outcome Measures. The Baseline Characteristics module allows for the submission of information describing an unlimited number of Baseline Measures, which are added by selecting prestructured measures (Age, Sex/Gender, Race and Ethnicity, and Region of Enrollment) and/or by specifying one or more Study-Specific Measures.

Baseline Characteristics Review Criteria

I. **General**
1. Written results or conclusions are not presented in any free-text field as the only means of reporting data.
2. Information provided is consistent with relevant data element definitions. Information is also consistent between data elements.
3. Baseline Measures include only baseline data (i.e., do not include Outcome Measure data).
4. Each Baseline Measure is unique and does not duplicate another Baseline Measure.
5. Each Baseline Measure contains sufficient information to be understood on its own, independent of other Baseline Measures or information in other parts of the study record.

II. **Arm/Group Information, Baseline Analysis Population Information, Number of Baseline Participants, and Number of Units Analyzed**
1. Results are presented separately for each arm of the study (i.e., "per arm"), or a valid explanation is provided for why results for each arm cannot be presented separately, as consistent with the study design and the numbers of participants in the Participant Flow module.
2. The Arms/Groups include only participants enrolled in the registered study.
3. No participants appear for first time in the study record in the Baseline Characteristics module.
4. The Overall Number of Baseline Participants, the Number of Baseline Participants in Baseline Measures, and any free-text descriptions of the analysis population are consistent.

PRS: Example of QC Review Comment

Baseline Measure

	Arm/Group Title	Remuverol
Performance Status Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants
0		5
1		23
2		1

Quality Control Review Comment provided by the National Library of Medicine [1]:

Standard QC Review Comment

Major Issues: 1) Information about the scale used in this measure appears to be missing. Additional information about the scale is typically needed to interpret measure data.

Additional Details

The Measure includes a scale. Please briefly describe the criteria for each indicated Category AND/OR please complete the scale information:
- Specify Full Scale Name and Construct (i.e., indicate what the scale measures if not clear from name)
- Specify minimum and maximum possible values and specify which values are considered better or worse outcome
- If a series of subscales are combined for a TOTAL overall score, specify TOTAL possible minimum and maximum values.
- Use "Units on a scale" or "Scores on a scale" if no other units apply.

For additional information about entering results, see Helpful Hints and Common Errors.

NCBI

Example of QC Review Comment Addressed

Baseline Measure

	Arm/Group Title	Remuverol
Performance Status Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants
0 – Fully active		5
1 – Restricted strenuous activity, ambulatory		23
2 – Ambulatory, difficulty walking		1
3 – Limited self-care, partly confined to bed		0
4 – Completely disabled, no self-care		0

[1] 5-point, ordinal scale specifying patient's ability to perform activities from 0 (fully active) to 4 (completely disabled, no self-care)

Background
Regulation

Regulation

- **42 CFR 11.44 When must clinical trial results information be submitted for applicable clinical trials …?**
  - Standard submission deadline - results information must be submitted no later than 1 year after the Primary Completion Date
    - Delayed submission of results information permitted in specific circumstances

- **42 CFR 11.52 By when will the NIH Director post submitted clinical trial results information?**
  - "… will post publicly clinical trial results information on ClinicalTrials.gov not later than 30 calendar days after the date of submission."

Final Rule: Posting and Quality Control

- Intend to continue a form of quality control (QC) review at time of submission that is similar to procedures we have been using
  - (1) automated validation rules; (2) manual review (81 FR 65064)
- Interpret the statutory posting deadline to be a clearly delineated timeline between submission and posting (81 FR 65101)
  - Information will be posted even if QC review process has not concluded
  - Posted record will contain information to make clear process has not concluded
  - Will evaluate ways posted record could specify data elements that may contain errors, deficiencies, and/or inconsistencies

Regulation (continued)

- **42 CFR 11.64(b) When must clinical trial information submitted to ClinicalTrials.gov be updated or corrected?**
  - Director may provide electronic notification to the responsible party of apparent errors, deficiencies, and/or inconsistencies that are identified by established quality control review procedures
  - The responsible party must correct or address all apparent errors, deficiencies, and/or inconsistencies in clinical trial results information not later than 25 calendar days after the date of electronic notification

Summary

NIH is required to post clinical trial information for applicable clinical trials on ClinicalTrials.gov within 30 days of submission, regardless of whether the quality control review process is complete.

Procedures

Note: Examples are intended for explanatory purposes. Specific wording and appearance may not reflect actual implementation.

Posting Results Within 30 Days

- Will post study record with results information following each QC review
- If QC review process has not concluded, include two types of information:
  1. General notice that QC review process has not concluded
  2. Brief, standard QC review comment (“major” issue) identifying relevant section and data element
- Responsible party will continue to receive in the PRS the QC review comments with additional details about the “major” issue and any “advisory” issues
- Will post all versions of QC reviewed record until process concludes (no “major” issues)
- Archive site will provide access to all posted versions (History of Changes), including those with QC review issues, consistent with current practices

Results Information Submission

Update study record

Submit study record

Backend Processing

Responsible Party

QC Review Staff

1 **Sponsor Account**

2 Registration Information

Results Information

Automated Validation

Address QC Review Issues

QC Review Comments

3 Manual Validation Quality Control Review

No “Major” Issues

“Major” Issues

ClinicalTrials.gov

4 **Public Posting**

General Notice and Standard QC Review Comments

Scope: Posting Results Within 30 Days

- Will apply to the following applicable clinical trials (ACTs) submitted with results information
  - Study Start Date on or after January 18, 2017 (Final Rule Effective Date); AND
  - Results information first submitted after implementation date (estimate January 2020)

PRS View (Not Public)

PRS Review Comments with Additional Details

NLM ID: 16908 | Example Study Record to Show 30-Day Posting Procedures | NCT11110000

PRS Review Comments – 02/17/2020 15:18

Number of Comments: 1 (see below)

Results Baseline Characteristics

	Arm/Group Title	Remuverol
Performance Status Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants
0		5
1		23
2		1

Quality Control Review Comment provided by the National Library of Medicine [1]:

Major Issues: 1) Information about the scale used in this measure appears to be missing. Additional information about the scale is typically needed to interpret measure data.

The Measure includes a scale. Please briefly describe the criteria for each indicated Category AND/OR please complete the scale information:
- Specify Full Scale Name and Construct (i.e., indicate what the scale measures if not clear from name)
- Specify minimum and maximum possible values and specify which values are considered better or worse outcome
- If a series of subscales are combined for a TOTAL overall score, specify TOTAL possible minimum and maximum values.
- Use "Units on a scale" or "Scores on a scale" if no other units apply.

For additional information about entering results, see Helpful Hints and Common Errors.

Standard QC Review Comment (Public)

Additional Details (Not Public)

Public View: Example of Results for Which QC Review Process Not Complete

Study Details | Tabular View | **Results Submitted** | Disclaimer | How to Read a Study Record

Results Submitted – Quality Control Review Process Has Not Concluded

General Description

Results information for an applicable clinical trial (ACT) is posted within 30 days of submission even if the submission has not completed the ClinicalTrials.gov quality control (QC) review process. Results information is submitted to ClinicalTrials.gov by the sponsor or investigator, and NLM staff assess for apparent errors, deficiencies, or inconsistencies. NLM staff do not verify the scientific validity or relevance of the submitted information.

All versions of ACT results information submissions, that have not completed the QC review process are posted on ClinicalTrials.gov (since January 2020). After the QC review process is completed, the results information is posted without QC review comments and previous versions are archived.

Recruitment Status :	Completed
Actual Primary Completion Date :	January 25, 2019
Actual Study Completion Date :	January 25, 2019

Submission Cycle	Results Submitted to ClinicalTrials.gov	Results Returned after Quality Control Review
1	January 18, 2020	February 17, 2020 Submission with QC Comments
2	March 10, 2020	

Links to Posted Study Record with QC Review Comments

NCBI

Public View

Posted Results for Which QC Review Process Has Not Concluded

Scroll up to access the controls

Study NCT11110000
on Date: January 18, 2020 (v6)

Quality Control Review Has Not Concluded

Note: The results information displayed below has not completed the quality control (QC) review process. ClinicalTrials.gov must post results information for applicable clinical trials (ACTs) within 30 days of submission, even if the submission has not completed the QC review process. The study sponsor or investigator is responsible for ensuring the results information meets the QC review criteria.

This submission includes brief standardized QC review comments added by the National Library of Medicine. These comments indicate the location of apparent errors, deficiencies, or inconsistencies.

For more information, see the Final Rule (42 CFR Part 11) Information page.

General Notice

Results Baseline Characteristics

	Arm/Group Title	Remuverol
Performance Status Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	29 participants
0		5
1		23
2		1

Quality Control Review Comment provided by the National Library of Medicine [1]:

Major Issues: 1) Information about the scale used in this measure appears to be missing. Additional information about the scale is typically needed to interpret measure data.

Standard QC Review Comment (Public)

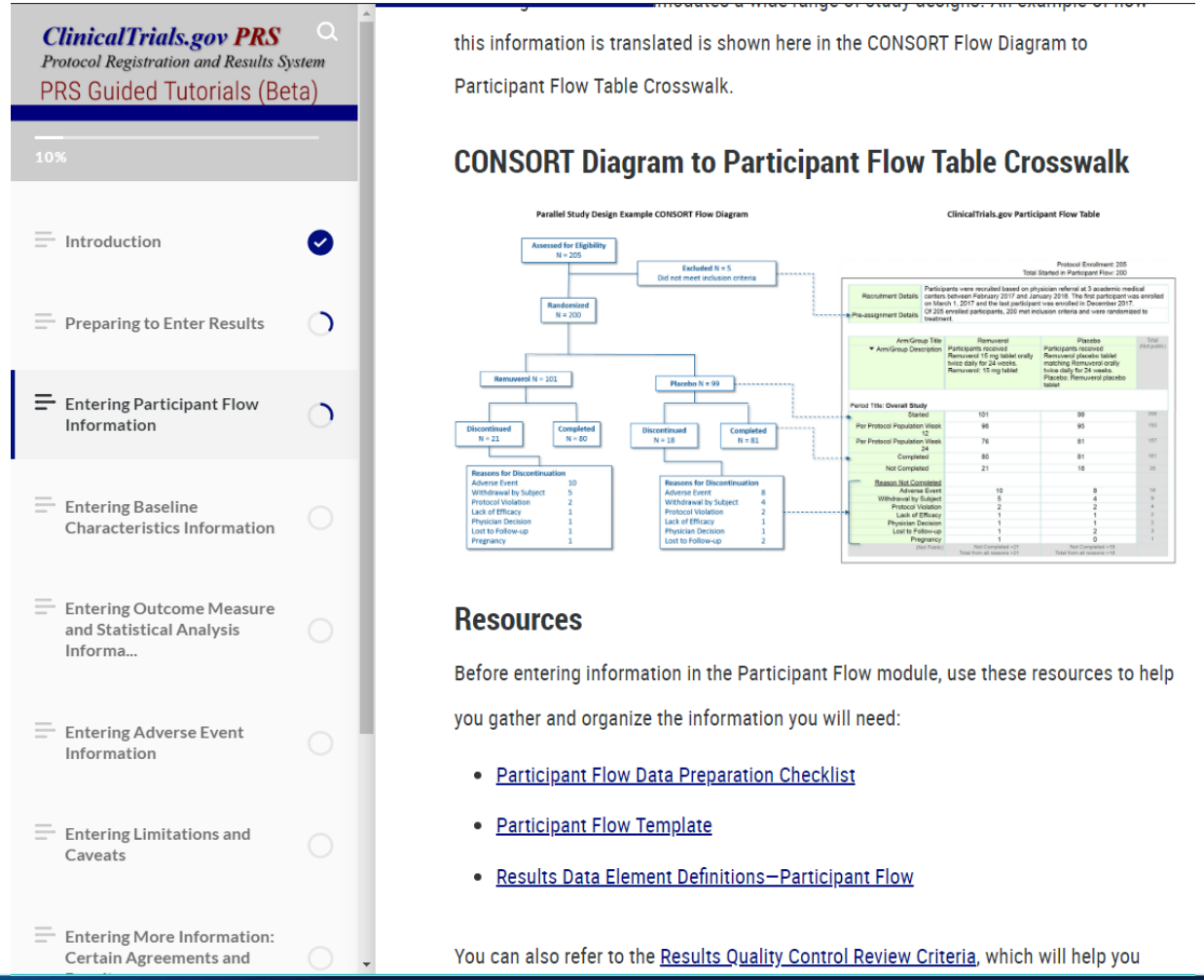
Implementation

Other Supporting Steps

- Revised QC review commenting approach to distinguish “major” and “advisory” issues
- Updated QC Review Criteria documents
- Shared data on QC review cycles and common “major” issues
- Reached staffing goals and eliminated results backlog
- Launched additional training resources
- **Pending** – Make available list of brief, standard QC review comments used to identify “major” issues

PRS Guided Tutorials (Beta)

- Launched August 13th
- Access on ClinicalTrials.gov or PRS
- Results submission content
- Registration content expected in late 2019 or early 2020
- Feedback needed *via* survey: https://bit.ly/2N1mMHV
- Further evaluation planned



Communication

We will inform you of further updates using:

- "What's New"
  - PRSTest, PRS, and ClinicalTrials.gov
- *Hot Off the PRS!* email bulletin
  - Provides timely updates for submitters
  - Sign up: https://bit.ly/33qcZBb

Having trouble viewing this email? View it as a Web page.

SHARE

Meetings + Conferences

Registration is Now Open for the ClinicalTrials.gov Webinar: Updated Quality Control and Posting Procedures. Tuesday, October 15, 2019 2 PM ET

Intended for Protocol Registration and Results System (PRS) users and presented by Rebecca Williams, PharmD, MPH, Acting Director, ClinicalTrials.gov.

Beginning in January 2020, ClinicalTrials.gov is expecting to update posting procedures for submitted results information for applicable clinical trials. Consistent with 42 CFR Part 11, the National Library of Medicine (NLM) will publicly post submitted results information within 30 days of submission, regardless of whether the Quality Control (QC) review process is complete.

For more information on the webinar and how to register, see the Training Materials page.

Results Information Submission

Update study record

Submit study record

Backend Processing

Responsible Party

QC Review Staff

1 **Sponsor Account**

2 Registration Information

Results Information

Automated Validation

Address QC Review Issues

QC Review Comments

3 Manual Validation Quality Control Review

No “Major” Issues

“Major” Issues

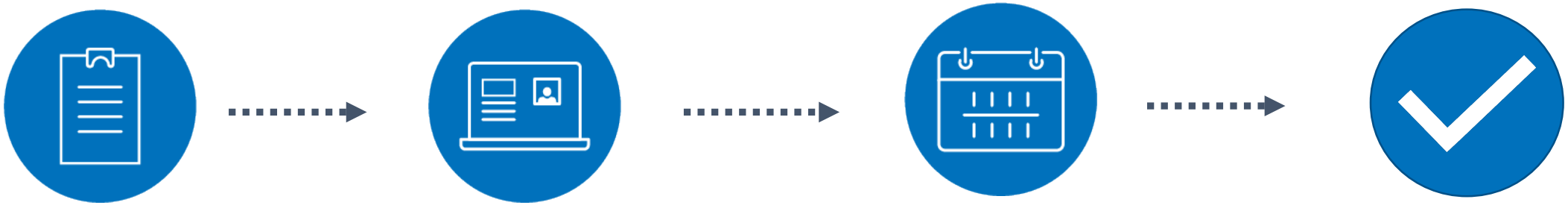
ClinicalTrials.gov

4 **Public Posting**

General Notice and Standard QC Review Comments

Implementation Plan

This procedure applies as follows:



Applicable Clinical Trial (ACT)

Study Start Date on or after January 18, 2017

Results information first submitted after January 2020 (specific day TBD)

Posted within 30 days (with or without QC Review Comments)

Questions?

Contact

register@clinicaltrials.gov

For more information see: https://prsinfo.clinicaltrials.gov

Sign up for the email bulletin *Hot off the PRS!*

https://bit.ly/33qcZBb