Information Submission Panel

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Information Submission Session Goals

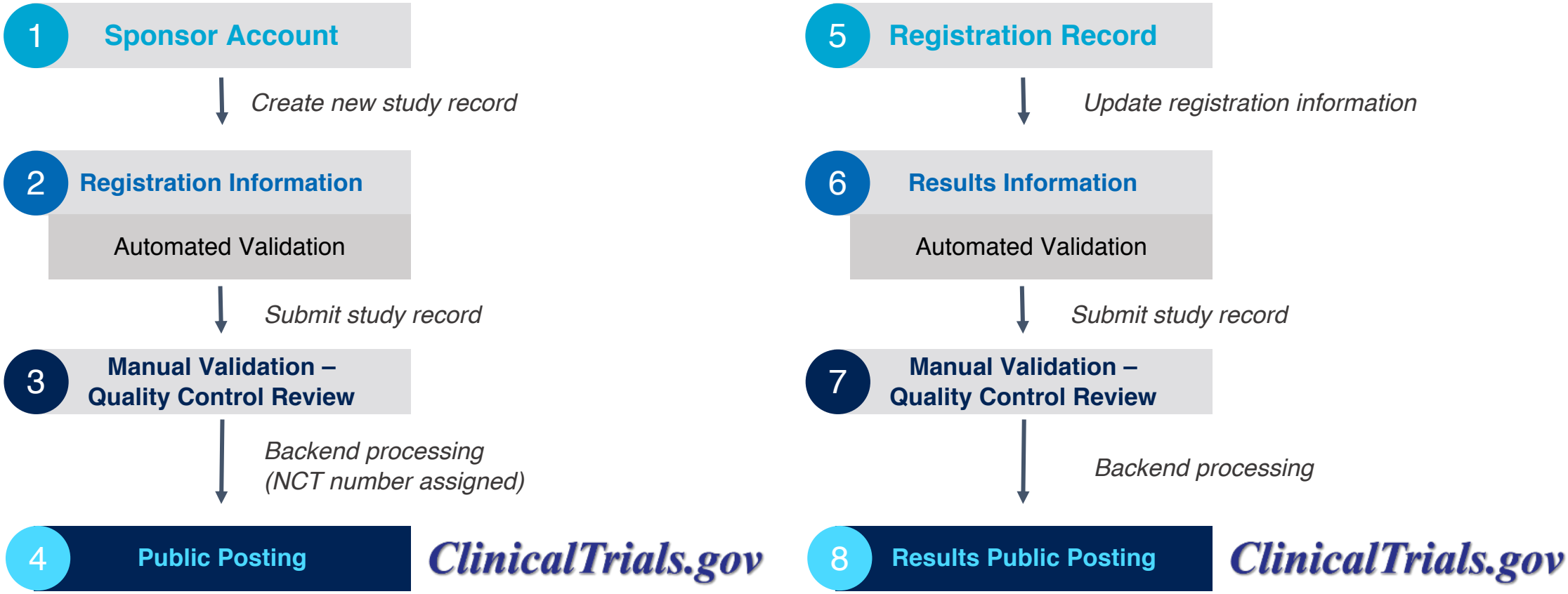
- Share the responses and key themes from the RFI
- Provide specific organizational examples of information submission workflows
- Obtain further input from meeting participants on topics related to RFI themes

Background

RFI Topic 2: Information Submission

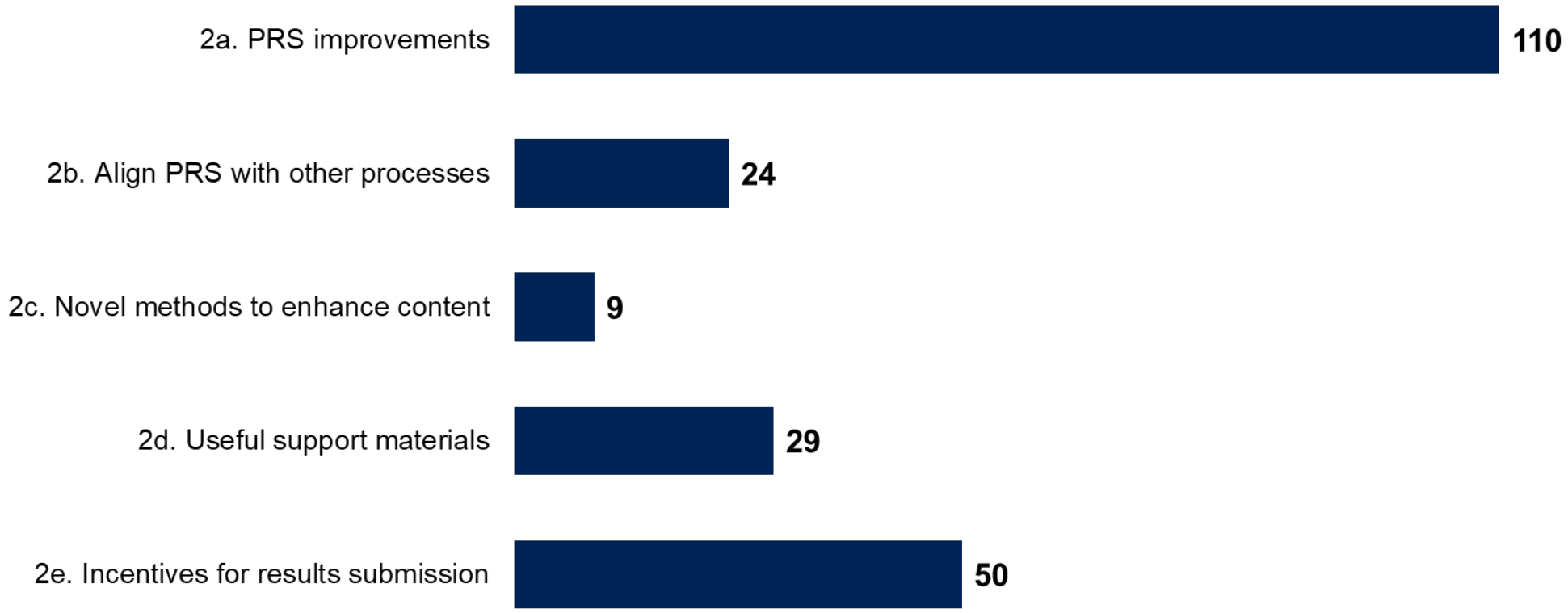
2. NLM sought broad input on initiatives, systems, or tools for supporting assessment of internal consistency and improving information submission through the Protocol Registration and Results System (PRS).
    a. Identify steps in registration and results submission that could be improved
    b. Describe opportunities to better align PRS submission with organizational processes (e.g., interoperability with IRB or CTMS applications or tools)
    c. Describe novel methods for enhancing submission quality and content
    d. Suggest informational materials that would make submission and quality control review processes easier
    e. Suggest ways to provide incentivize or recognize the efforts of individuals and organizations in submitting complete, accurate, and timely information submissions

Information Submission Overview



Information Submission RFI Response Summary

Information Submission: RFI Responses



Information Submission 2a. Improve PRS

Identify steps in the information submission process that would most benefit from improvements

Top Comments

Website Function	Percent	Comments
Data Entry	32.7%	140
Data Element Definitions	12.9%	55
Administration	12.1%	52
QC Review	8.9%	38
Notification	6.3%	27
User Support	5.8%	25
Results Reporting	5.4%	23
Validation Rule	4.2%	18
Updates	2.1%	9
Others	9.6%	41

Information Submission 2b–2e Examples

2b. Systems for interoperability with PRS
- Most frequent: Clinical Trial Management System (CTMS)
- Other: IRB reporting

2c. Emerging methods for enhancing PRS
- Most frequent: Natural Language Processing
- Other: API, machine learning/AI

2d. Requested submission-related information materials
- Most frequent: Clearer Data Element Definitions
- Other: More templates, review criteria

2e. Incentives for quality trial reporting
- Most frequent: Public recognition
- Other: Organizational statistics for PRS users, enforcement

2a. Improve PRS - Key Response Themes

Data Structure and Format

Additional standardization for some data elements

More flexibility for data elements and record structure

Structural support for a variety of study designs

Data Entry, Submission, and QC Review

More tools to simplify data entry

Additional streamlining of QC review process

Workflow Management

More customizable features to manage workload

Theme: Data Structure and Format

EXAMPLES

- Additional standardization for some data elements
  - Structured Eligibility, Contacts & Locations, Conditions, IPD sharing, Arms and Interventions
  - Enhance compatibility across multiple platforms
- More flexibility for data elements and record structure
  - Ability to customize study design features for different stages of study in registration
  - Increased character limits
- Structural support for a variety of study designs
  - PRS templates structured for traditional study designs (e.g., parallel, crossover, dose escalation) and non-traditional study designs (e.g., adaptive, master protocol)

Theme: Data Entry, Submission, and QC Review

EXAMPLES

More tools to simplify data entry

- Just-in-time help to clarify requirements and information needed
- Outcome measure libraries
- A feature to upload a publication or data in Excel and extract results
- PRS user interface improvements (e.g., shortcut links, copy changes to multiple places)
- Additional help resources (e.g., common issues, plain language data element definitions)

Additional streamlining of QC review process

- Easy access to one-on-one assistance
- Process for disputing and removing QC comments
- Consistency between reviews

Theme: Workflow Management

More customizable features to manage workload

EXAMPLES

- Login dashboard with metrics and to do list with actionable links
- Customizable record tags for Sponsors to flag records (e.g., NIH, Common Rule, ICMJE, institution specific)
- Customizable email lists
- More options for Record List, Planning Report, and Problem Report (e.g., additional columns, movable columns with filtering and sorting)
- Streamlined record edits and submission workflow
- Customizable submission process to fit multiple organizational workflows

Carrie Dykes, PhD

Director of Research Services, Clinical and Translational Science Institute, University of Rochester Medical Center

Academic Administration of ClinicalTrials.gov

Unique Issues

- Competing academic, research, and clinical responsibilities among PIs
  - Multiple levels of research responsibility
  - Different rules for different studies of their research portfolio
- Faculty act as individual entities
  - Focus on individual mission/research interests
  - Collaborations require cross-college/cross-boundary communication
  - Varied levels of risk aversion
- Turnover
  - Lack of formal exit communication procedures for PIs and study team members leaving the institution
  - Data stewardship (especially when PIs leave)

Academic Mission

- Teaching institutions, often working with investigators on first study and they are learning the ropes

Role of Academic Administrators

- Create accounts for university study teams
- Help investigators determine if registration needed
- Help investigators register studies
- Help investigators enter results
- Help investigators resolve problem records
- Track institutional metrics
- Provide education

Sizes of Academic Institutions

Johns Hopkins

- 5 separate PRS accounts
- 1,800+ total records
- 2 FT, 5 PT staff
  (~2.5 total FTE)

Rochester

- 1 PRS account
- 546 total records
- 1 individual
  (0.1 total FTE)

Clinical Trials Registration and Results Taskforce (CTRRT)

Mission:
Focus on the requirements for clinical trials registration and results reporting that affect U.S. academic health centers.

- Understanding and applying the requirements
- Identifying best practices
- Developing tools
- Serving as a communication forum

220+ Institutions – 480+ Members

https://ctrrtaskforce.org

Co-Chairs: Sarah White (MRCT), Anthony Keyes (JHU)

Monthly calls featuring representatives from;

- ClinicalTrials.gov
- FDA
- OHRP

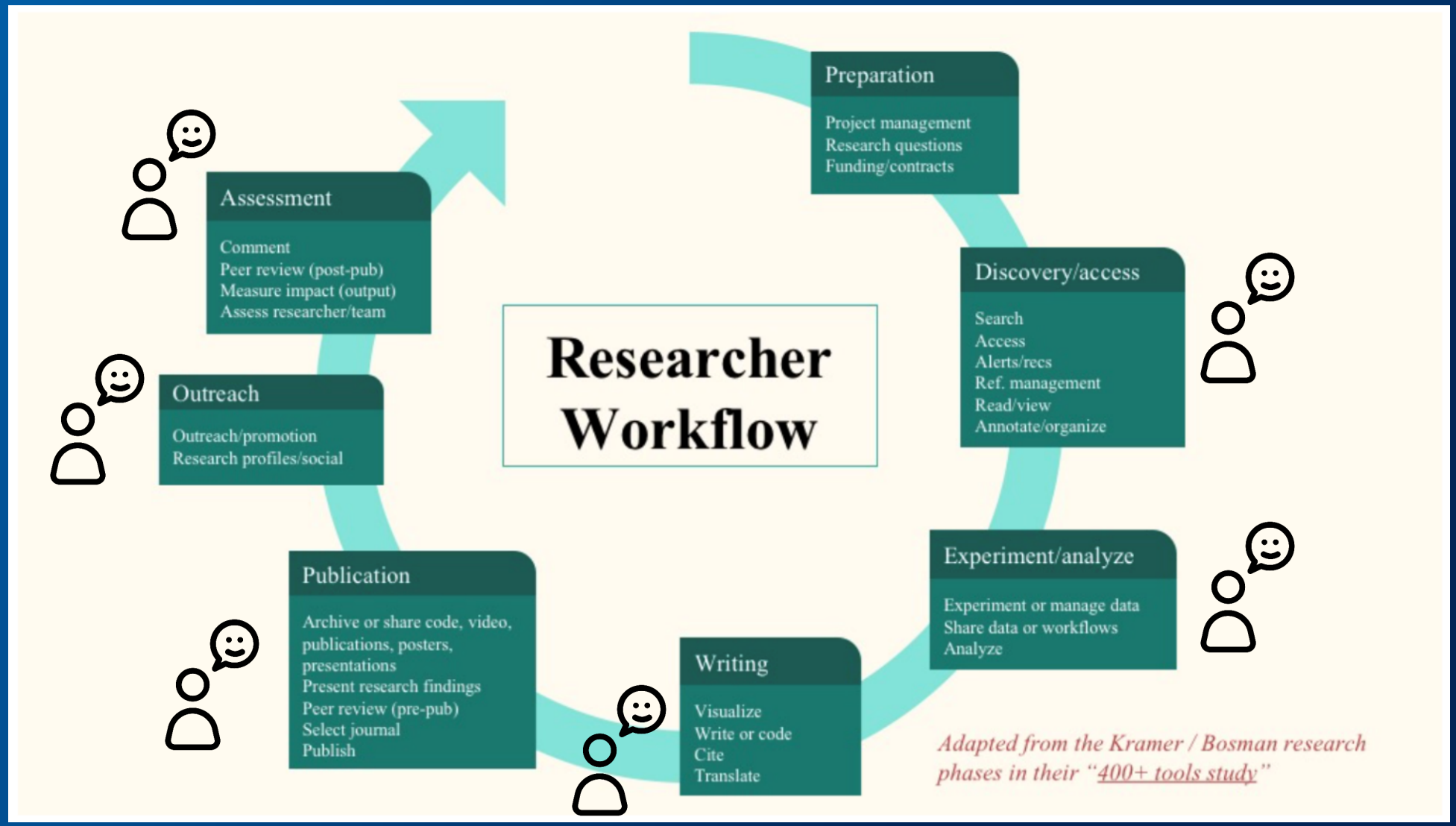
Metrics

- # of
  - Total records
  - Active records
  - Problem records
  - New registrations
  - Records with results entered within specified time frame
- Records with late results and result due within 3, 6, 9, and 12 months
  - ACTs and NIH
- % compliance
  - Registrations and results reporting
- Registration cycle time, # of registration cycles
- Results cycle time, # of results cycles

Sally A. Gore, MS, MS LIS

Manager, Research and Scholarly Communication Services, Lamar Soutter Library, University of Massachusetts Medical School

Supporting Researchers and Staff Using ClinicalTrials.gov



Credit: https://scholarlykitchen.sspnet.org/2018/08/30/mapping-open-science-tools/?informz=1

Areas of Support that Intersect with ClinicalTrials.gov

Different Audiences / Different Levels

The need(s) and the support varies.

Clinical Researchers

- Research Administrators
- Research Staff
- Clinical Staff
- Administrative Staff

Basic Researchers

- Lab Administrators
- Research Staff
- Lab Staff (students, postdocs)
- Administrative Staff

Providing Expert Support Involves:

- Clear, easy to access, up-to-date instructions
- Training opportunities
- Consistency
- Contact

Again, for different audiences.

Evaluation / Impact

- Compliance
- Grant Funding
  - Progress reporting
  - New proposals
- Faculty portfolios
- Bibliometrics / Altmetrics
  - Publications
  - Patents
  - Policy statements
  - Social networks

Barbara Kress, BSN, RN

Executive Director of Clinical Trial Data Disclosure and Transparency, Merck

Industry Experience

Organizational Structure Evolution

2007 Registration Group formed as part of Informed Consent Department

- Started with 1 Full-Time Employee (FTE) and 1 Full-Time Contractor (FTC)

2008 Results posting: Decentralized - responsibility of the Clinical Research Department

2009 'R2' Department was created. Centralizing both registration and results posting.

2010 Clinical Data Disclosure and Transparency Department created

2017 Responsible for registration, result posting, redaction operations, and data sharing

Staffing:

- 12 FTEs, 18 FTCs
- 2 Directors, 13 Medical Writers, 4 Registry/Results Leads, 2 Redaction Operations Specialists, 3 Data/Document Specialists, 5 Trial Transparency Specialists, and 1 Administrative Assistant

The Running of the Reports

Daily

Receive notifications from the document repository when protocols and CSRs are finalized

Weekly

Transparency Specialists run reports from the Clinical Trial Management System (CTMS):

- Site Change Report: information, contact changes, additions.
- Study Change Report: dates, status changes

Monthly

Registry/Results (R2) Leads run Scoping Reports

- Identify trials that require registration and results posting based on trial start date and primary completion date

Initial Registration, Results Posting, & Amendments

- Based on the Monthly Scoping Report
  - R2 Lead
    - Identifies trials for registration and results posting based on the trial start date or primary completion date
    - Receives finalized protocols, CSRs, and amendments
    - Assigns therapeutically aligned Medical Writer to author in a vendor provided transparency management system
    - Sends completed registration/results records to quality control review
    - Sends completed record for internal review and approval
    - Releases the record through the transparency management system to the NIH
    - Monitors for NIH acceptance/comments
      - If comments are received: brings comments to weekly Medical Writer meeting

Updates to Existing Registrations

- Trial Transparency Specialist (TTS)

  Runs weekly change and site reports from the Clinical Trial Management System (CTMS)

  Site Report: Updates site information automatically from the report to the transparency management system

  - TTS submits the record in the transparency management system that uploads the information to the NIH

  Change Report: TTS reviews for trial milestone date changes, study status changes

  - Updates the record in the transparency management system
  - The R2 Lead sends the record for internal review and approval
  - R2 Lead submits the record in the transparency management system to be uploaded to the NIH

Tips for Success

Dedicated Team –

Subject Matter Experts (SMEs): A team familiar with the format and requirements of NIH disclosure is able to advise on timing and data requirements. They prepare disclosures with a higher probability of acceptance after one round of QC review.

Trained Medical Writers –

- Experienced in sourcing information from documents (i.e., protocols, study reports) and presenting it in another format
- Able to identify key components of a study, such as interventions, arms, and endpoints
- Developed with mentorship and training
- Regularly asked for feedback to identify any areas for potential process improvement in the group
- Recognized for great work and appreciated in front of their peers

Tips for Success (cont.)

Guidance Documents –

- Guidance documents provide medical writers with support on how to create clinical trial records for ClinicalTrials.gov
- These documents walk writers through each section of the record, offering definitions, the location of source information, examples, and contacts for additional support
- These are ‘living’ documents that are updated as learning and the environment evolves
- SOPs: Internal audits

Quality Control Review –

- Medical writers have their work reviewed by a fellow medical writer, a QC Reviewer
- The QC Reviewer checks each record against source documents (i.e., protocol, study report) to confirm accuracy
- The QC Reviewer also uses a “QC Checklist” that contains points of consideration for ensuring a quality record. Some of these points originate from a QC checklist provided by the NIH, other points originate from within the organization. The “QC Checklist” notably helps to ensure consistency within records submitted to the NIH.

Tips for Success (cont.)

Medical Writer Meeting –

- Medical writers convene at a weekly meeting to share learning, discuss process improvement, and review feedback from the NIH
- Major Comments are discussed as a group to ensure a thorough understanding of the comments and decide on a plan forward
- These comments are added to a log that is maintained by the group for future reference as well as to help identify trends in feedback and adjust accordingly

Contacting the NIH –

- Bring questions directly to the NIH for discussion. This is to ensure that plans for presenting trial information is an appropriate use of the database.
- Feedback from the NIH is shared with the medical writers at the weekly medical writer meeting and often added to the guidance documents and/or checklist
- This approach also reduces the need for rework, as would be required following Major Comments

Operational Performance: Metrics

The only way to know a process is working is to collect and analyze metrics. With so many points to analyze, which do you choose?

- Authoring Time
- Review and Approval Time
- Quality Control Review Time
- Adherence to process and laws
  - Is this reported to someone in your institution?
- Acceptance Rate/Rejection Rate

Tools and Services

- TransCelerate Common Protocol Template
  - Protocols not written for ‘cut and paste’ to ClinicalTrials.gov
  - TransCelerate Protocol Template provides common structure and language
  - Enables endpoints that map to objectives
  - Supports CDISC TA standards
- Clinical Trial Management Systems
  - Tracks trial milestones
  - Download reports
  - Connects directly to transparency management platforms
- Vendors
  - Full or partial service transparency companies
  - Clinical Trial Disclosure Management Platforms (vendors)
    - Provide expertise with disclosure laws
    - Streamline disclosure management
    - Audit trails
    - Authoring, review, and approval
    - Metrics

Up Next…

11:30 a.m. – 12:20 p.m.

Website Functionality Panel

- Rebecca J. Williams, ClinicalTrials.gov
- Alissa Gentile, The Leukemia and Lymphoma Society
- Seth A. Morgan, National Multiple Sclerosis Society
- Steven Woloshin, The Dartmouth Institute
- Stephen J. Rosenfeld, Secretary's Advisory Committee on Human Research Protections (SACHRP)

We are currently on a break. We will resume at 11:30 a.m.