Building Quality into Clinical Trials

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Cincinnati Children's Gamble Program for Clinical Studies

Objectives

- Identify strategies for developing a Quality Management Plan (QMP)
- Identify components of a QMP
- Review the implementation and evaluation process of a QMP.

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BEST CHILDREN'S HOSPITALS
U.S.News & WORLD REPORT
RANKED IN 10 SPECIALTIES
2012-13

NATIONAL INSTITUTES OF HEALTH

Infectious Diseases Clinical Research

The Gamble Program for Clinical Studies

Outpatient
Inpatient
Community
Multicenter studies

Funding:
Industry
NIH / Governmental
NIAID / DMID / VTEU

Epidemiology and Surveillance Research Program

ED / Outpatient
Inpatient
Community
Multicenter

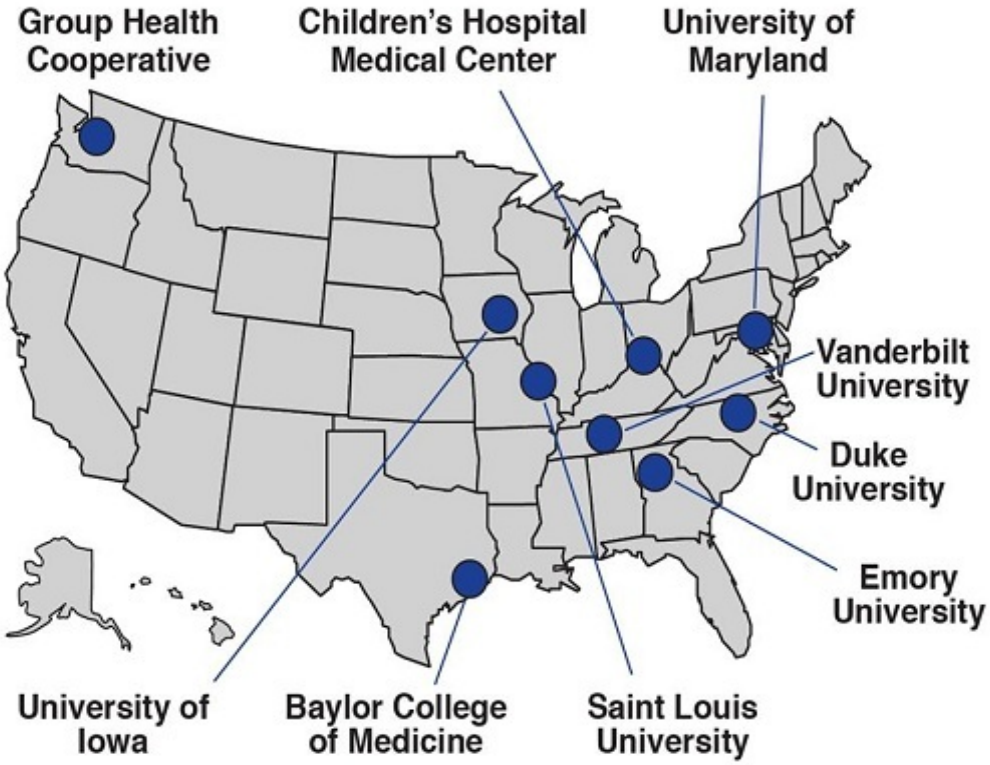
Funding Sources:
Centers for Disease Control (NVSN)
Industry

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

VACCINE & TREATMENT EVALUATION UNIT

New Vaccine Surveillance Network

National Institutes of Health
Vaccine Treatment & Evaluation Units



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Vaccine Treatment & Evaluation Units

- Established in 1962
- Resource for conducting clinical trials of vaccines and treatments for infectious diseases
- Key role to develop new and improved vaccines and therapies

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Roles of the DMID VTEU's

- Testing Novel Vaccines
- Developing Combination Vaccines
- Testing Novel Delivery Systems
  - Nasal spray vaccines
  - Edible Vaccines
  - Transdermal Vaccines

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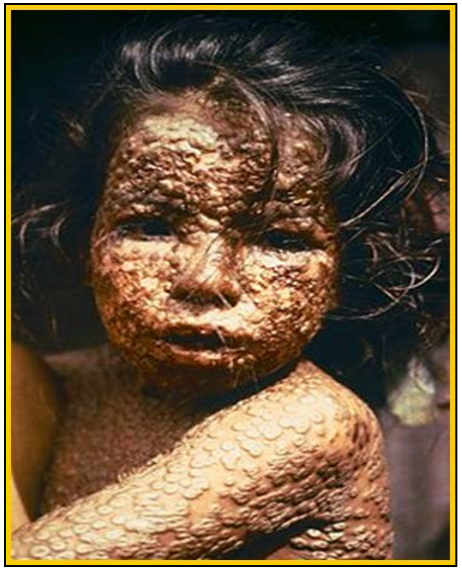
Roles of the DMID VTEU's

Strengthening the Nation's Biodefense

- Smallpox:
  explored the best way to use existing supplies of Dryvax smallpox vaccine to protect military and civilian populations



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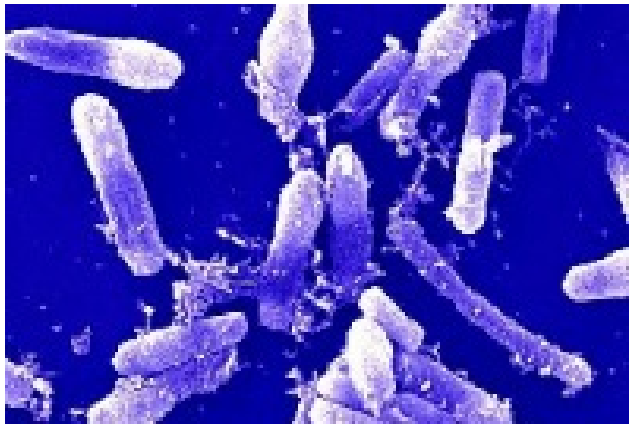
Areas of Research Interest

- Respiratory Diseases
- Diarrheal Diseases
- Bacterial Infections
- Agents of Bioterrorism
- Sexually Transmitted Infections



Bonus Question: What is the image above?

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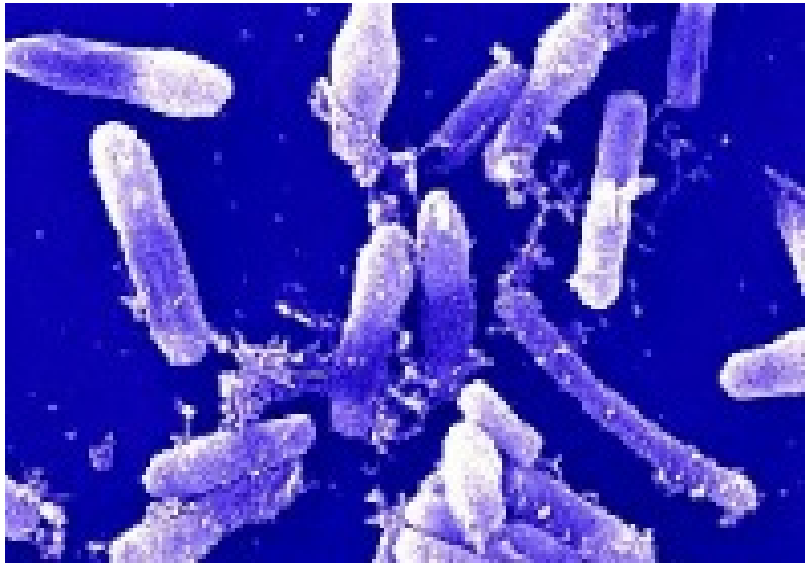
Answer: Bacillus Anthracis



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My Introduction to Quality Management

Musical Chairs

Evolution of A Comprehensive Quality Management Plan

Our Progression

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What is Quality Management?

An overall system for oversight of the conduct of clinical research

Ensures that data collected are accurate and complete.

Ensures the rights and safety of participants in clinical research are protected

Encompasses both Quality Control (QC) and Quality Assurance (QA) activities

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Purpose of Quality Management

- Facilitate planning for protocol implementation
- Assure compliance with regulations and requirements
- Identify areas in need of corrective action
- Verify the accuracy of data
- Assure readiness for external monitoring and auditing

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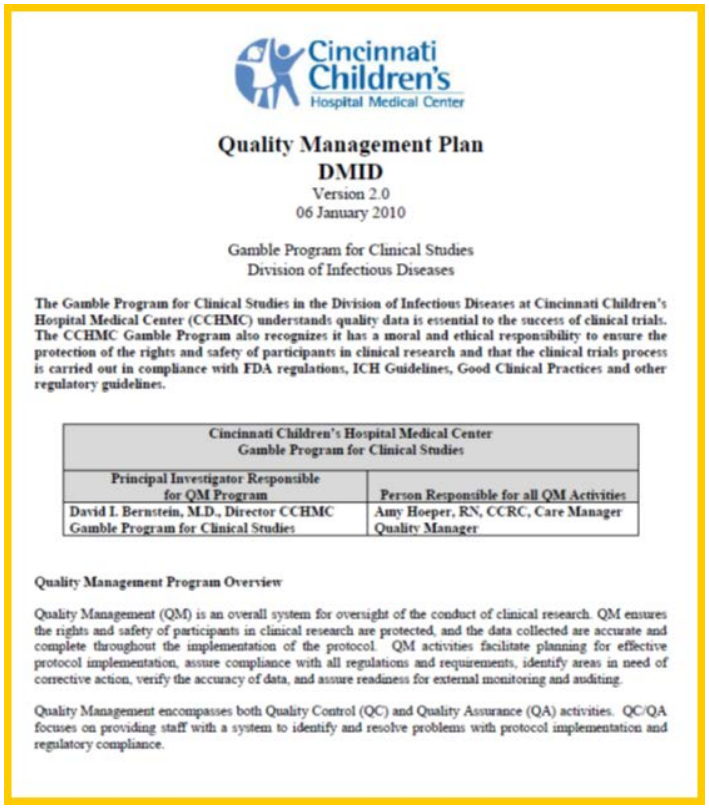
Components of a Quality Management Plan

- Formal written document detailing QMP Process
- Scope and Frequency of Activities
- Responsibility of staff and involvement
- Ongoing QM Plan Maintenance
- Documentation of Education and Training
- Process for Review and Trend Analysis



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Quality Management Plan
DMID
Version 2.0
06 January 2010

Gamble Program for Clinical Studies
Division of Infectious Diseases

The Gamble Program for Clinical Studies in the Division of Infectious Diseases at Cincinnati Children's Hospital Medical Center (CCHMC) understands quality data is essential to the success of clinical trials. The CCHMC Gamble Program also recognizes it has a moral and ethical responsibility to ensure the protection of the rights and safety of participants in clinical research and that the clinical trials process is carried out in compliance with FDA regulations, ICH Guidelines, Good Clinical Practices and other regulatory guidelines.

Cincinnati Children's Hospital Medical Center Gamble Program for Clinical Studies	
Principal Investigator Responsible for QM Program	Person Responsible for all QM Activities
David I. Bernstein, M.D., Director CCHMC Gamble Program for Clinical Studies	Amy Hoeper, RN, CCRC, Care Manager Quality Manager

Quality Management Program Overview

Quality Management (QM) is an overall system for oversight of the conduct of clinical research. QM ensures the rights and safety of participants in clinical research are protected, and the data collected are accurate and complete throughout the implementation of the protocol. QM activities facilitate planning for effective protocol implementation, assure compliance with all regulations and requirements, identify areas in need of corrective action, verify the accuracy of data, and assure readiness for external monitoring and auditing.

Quality Management encompasses both Quality Control (QC) and Quality Assurance (QA) activities. QC/QA focuses on providing staff with a system to identify and resolve problems with protocol implementation and regulatory compliance.

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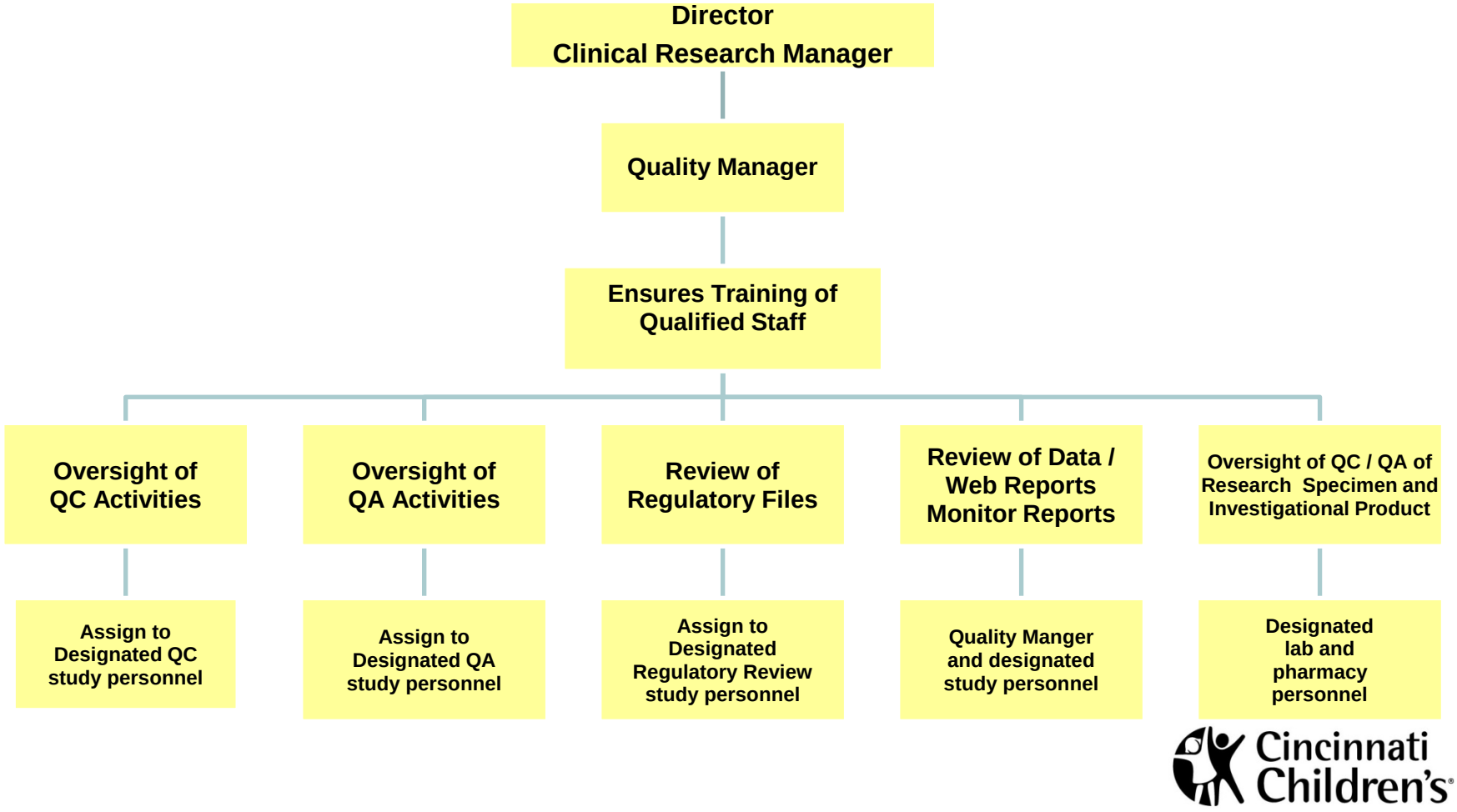
Gamble Program for Clinical Studies
Overview of Quality Management Program Structure
(Based on NIH / DMID Guidelines)



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Why Have a QM Program?

Isn’t that why we have monitors?

Isn’t that why the data center generates queries?

Isn’t that why CCHMC has ORCRA review our studies?

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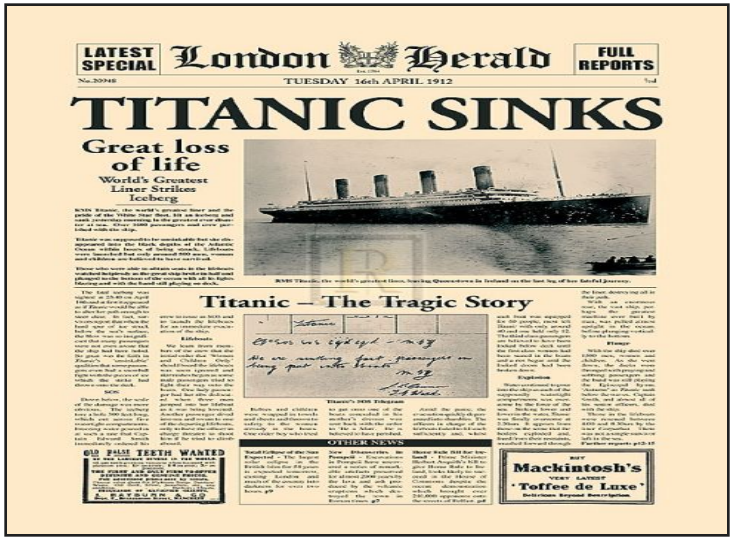
Why Have a QM Program?

- Answer: QM is a proactive method to identify and address issues before they become critical.



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TUESDAY 16th APRIL 1912

TITANIC SINKS

Great loss of life

World's Greatest Liner Strikes Iceberg

Titanic – The Tragic Story

OTHER NEWS

OLD FILM TEETH WANTED

Mackintosh's

'Toffee de Luxe'

- ***"Understanding the causes for the rapid sinking of the Titanic is necessary to prevent similar accidents in the future."*** Vicki Bassett

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Mistakes Happen

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QM is Critical During Peak Enrollment Periods

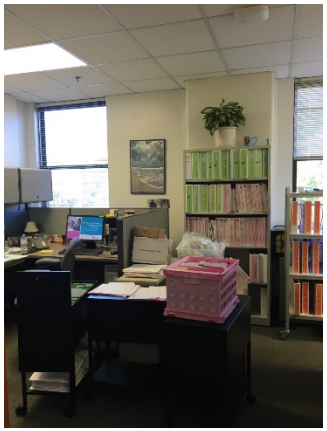
- Protocols and consents were created and IRB applications were submitted in record time for 8 H1N1 Studies

- Recruitment and study coordinators responded to approximately 10,500 calls generated by media coverage and general interest over 4 months with calls continuing in response to mass publicity regarding H1N1.

DMID Study #		Target Enrollment	Approximate # telephone Screens	Total # Screened	Number Enrolled	Visits Completed	Vaccines Randomized & Administered	Specimens Processed and Shipped
DMID 0039		200	400	260	220	1600	1041	10854 / 4658
	Adult				102			
	Elderly				118			
DMID 0047		100	250	113	108	966	322	3078 / 1539
	6-36 mo			44	41	365		
	3-9 yrs			35	33	297		
	10-17 yrs			34	34	304		
DMID 0058		60	95	79	60	169	115	2340 / 0
	Adult			49	40			
	Elderly			30	20			
DMID 0073	Adults	20	10	3	3	3	3	3 / 0

Getting Started - Important First Steps

- Communicating the need for a formal structure
- Education regarding the value of QM
- Developing your team
- Determining your Key Quality Indicators



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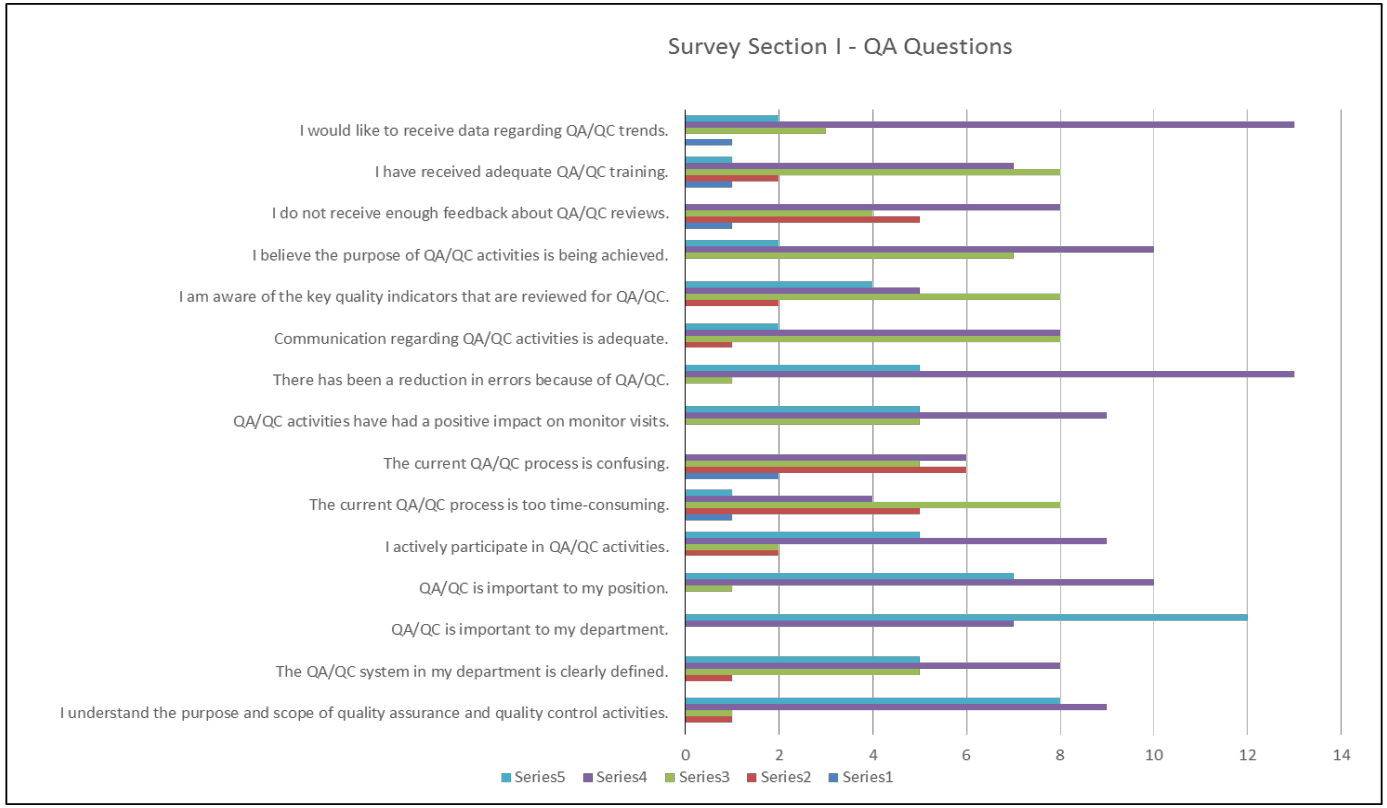
Staff Attitudes towards QA/QC



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Define Key Quality Indicators

- Scheduled Tests/Procedures
- Missed Visits, Follow-up, Tests, Procedures
- Study/Clinical Endpoints Verification
- Adverse Event Identification and Reporting
- Serious Adverse Event Identification and Reporting
- Treatment/Study Discontinuation
- Specimen Storage, Management
- Electronic Data Entry
- Data Anomalies Report
- Missing forms and Values reports

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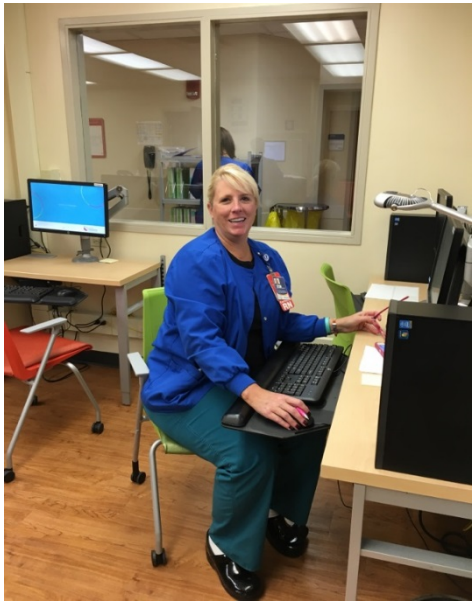
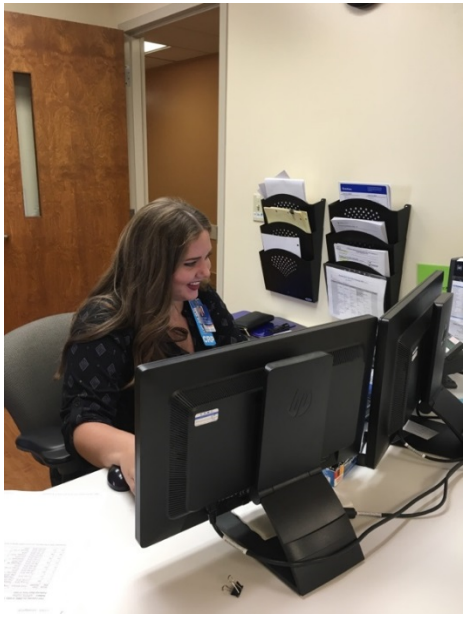
Types of QM Reviews





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Quality Control

- Ongoing, daily process of checking records for completion and logic
  - Concurrent
  - Involves 100% review of records
  - Includes documentation and observation of work processes

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Quality Control (QC) Activities

- Performed by qualified designated personnel
- Ongoing at each clinic visit
- 100% review of informed consent and eligibility criteria
- Complete QC Audit tool for each subject record
- Data entry with ongoing QC
- Return completed tools to coordinator for corrections
- Results entered onto spreadsheet
- Quality Manager reviews findings and meets with study staff to discuss trends, issues, and resolutions
- Quality Manager reports findings in monthly report to Director and Clinical Manager

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Sample QC Tool

QC Chart Audit Worksheet

CCHMC Gamble Program For Clinical Studies Cincinnati Children's Hospital	**Quality Control Notes**

Protocol #: _____ PID #: _____ Reviewer Name: _____ Date Reviewed: _____

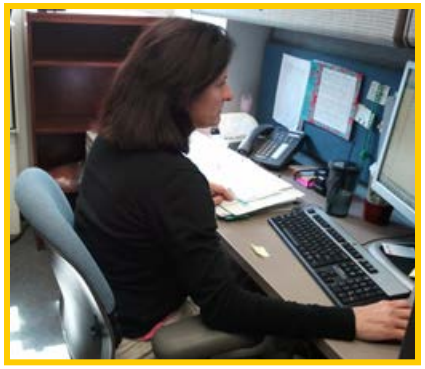
Documents requiring action (check all that apply):

☐ Inc/Exc criteria ☐ Informed consent form ☐ HIV consent form (if indicated)
☐ Visit 1 ☐ Visit 2 ☐ Visit 3 ☐ Visit 4 ☐ Visit 5 ☐ Visit 6 ☐ Visit 7 ☐ Supplemental visit
☐ Lab tests ☐ Concomitant Medications ☐ Adverse Events ☐ Serious Adverse Event
☐ Memory Aid/Diary Card 1 ☐ Memory Aid/Diary Card 2
☐ Pregnancy Test log
☐ Other

Page	**Corrective Actions Required**	**Correction completed initials:**	**Correction completed date:**	**Verified correction completed initials:**

Quality Assurance

- Retrospective sampling of “key quality indicators” to identify trends
  - Systematic, comprehensive review of all components of total work effort
    - Assess accuracy of data
    - Adherence to GCP
      - Includes clinical, sample / specimen collection and investigational product



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Quality Assurance (QA) Activities

- Performed by qualified designated personnel
- First 10 charts and minimum of 10% of total enrolled for each study
- Complete QA audit tool
- Return to study coordinators for review and corrections
- Results entered into spreadsheet
- QM meets with coordinator/pharmacy for review and to confirm resolution
- QM meets with staff to discuss trends, issues, and resolutions
- QM reports findings in monthly report to Director and Clinic Manager

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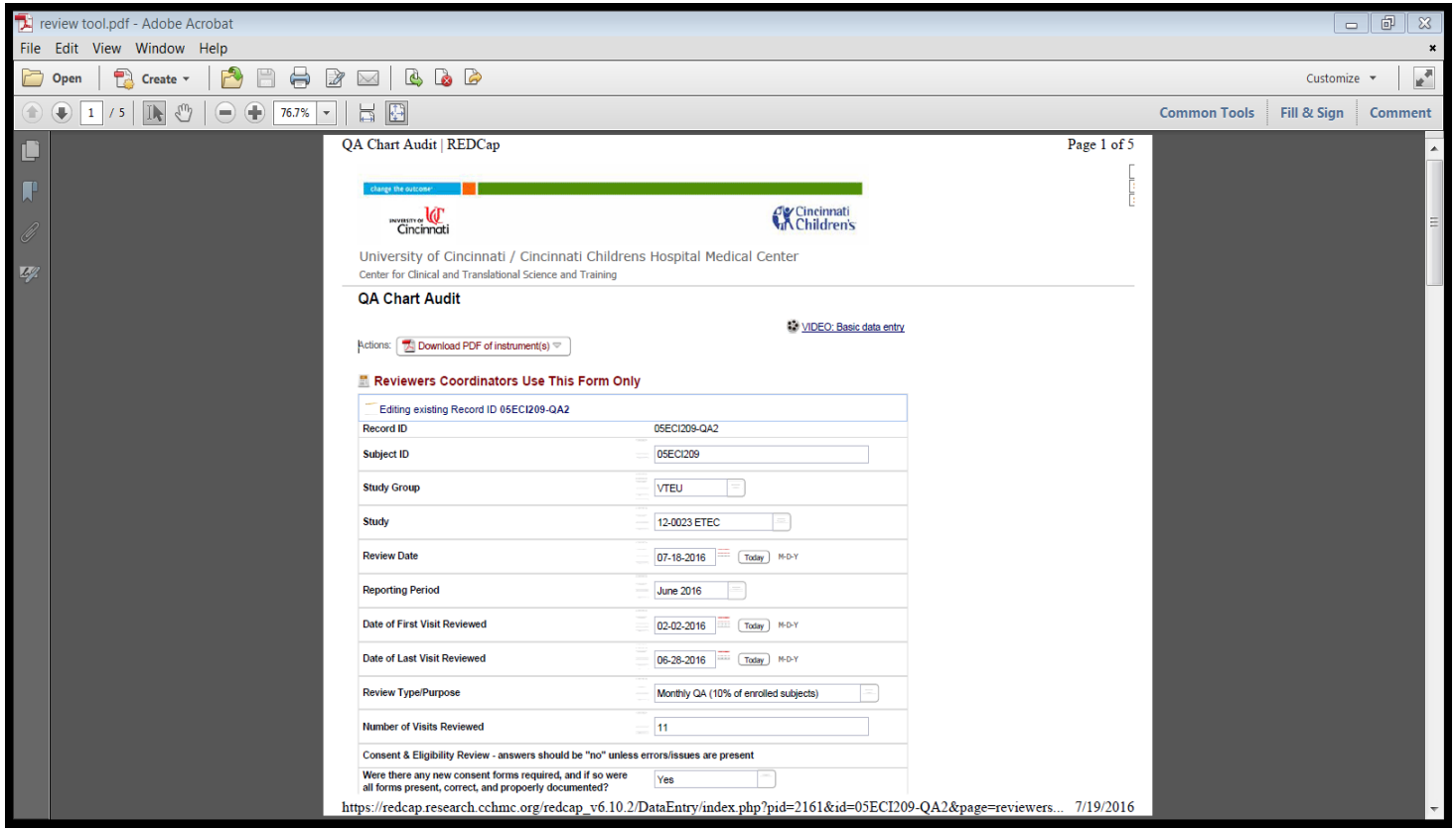
Web-based QA Audit tool



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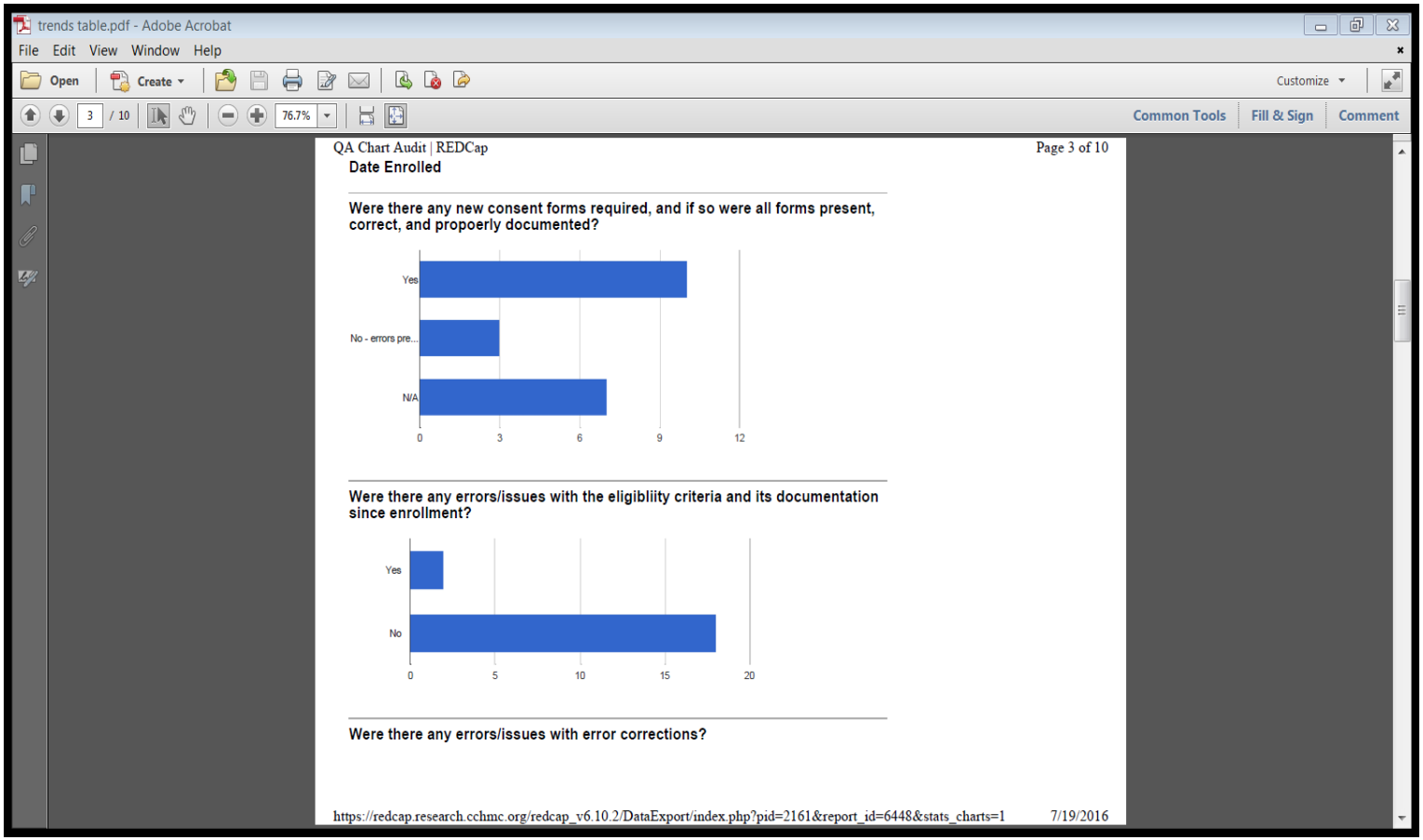
QA Trends Report Screenshot



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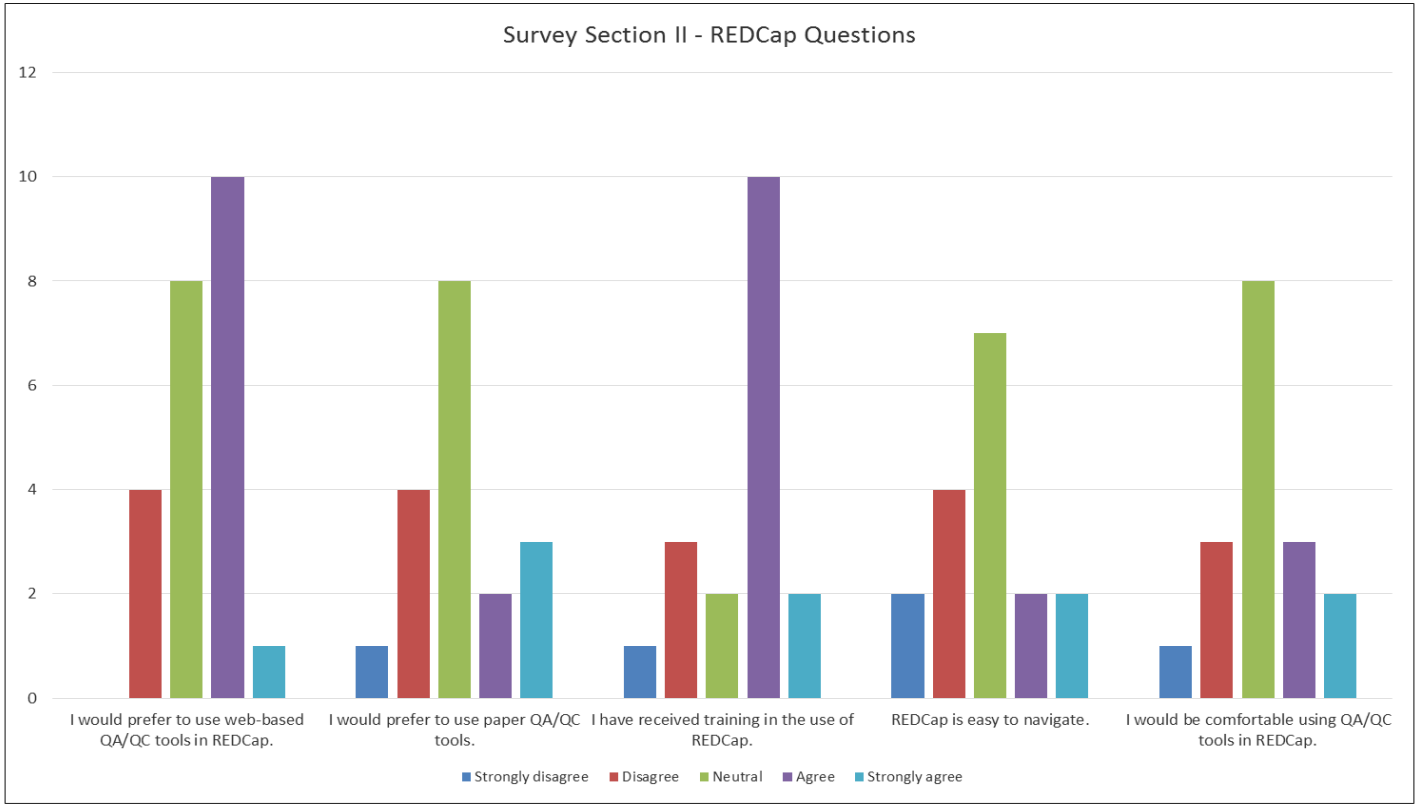
Staff Attitudes Towards Web-based QA



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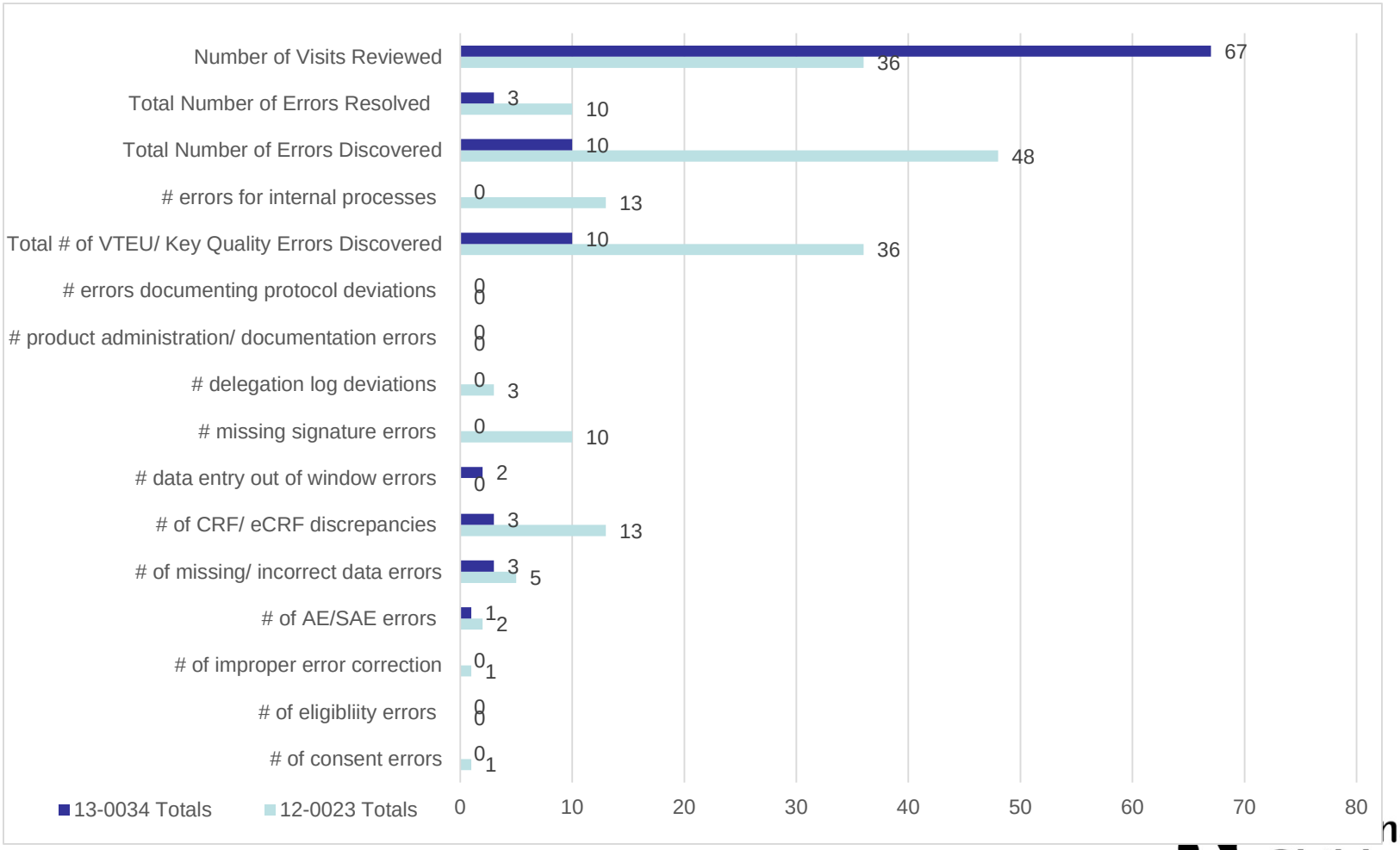
QA Trends Report Screenshot



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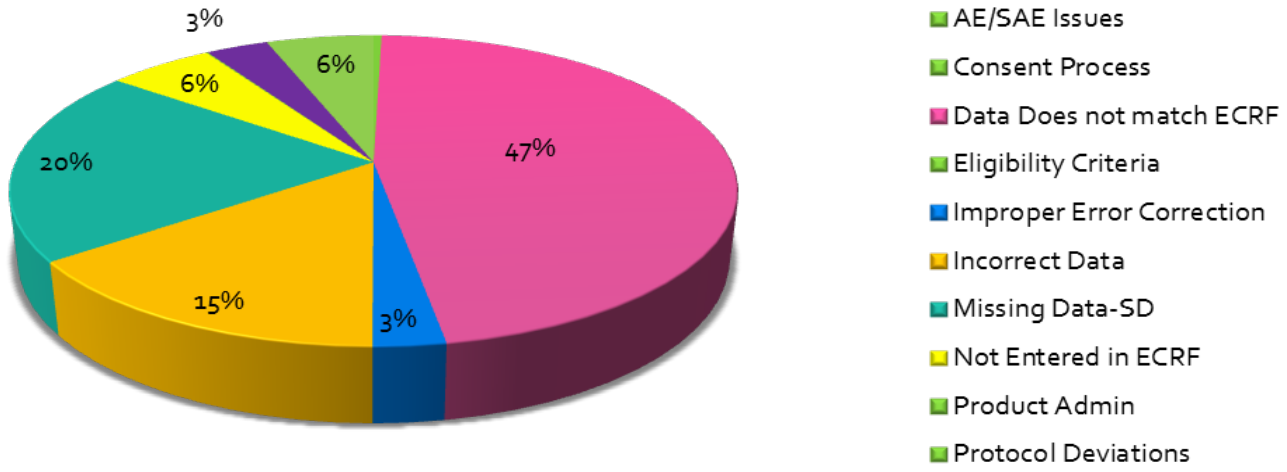
Trend Analysis

- 4 month period of time
- 10% of charts for 11 studies were reviewed
- Total 433 charts reviewed
- Assessed the following Key Quality Indicators:



- No significant trends in the following categories: Consent Process; Eligibility Criteria; AE/SAEs; Visit Schedule Compliance; Product Administration; or Specimen Collection**.**
- Trends related to data collection/electronic data entry.
- 82% of all inaccuracies occurred in the categories and were resolved during the QA process.

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QC versus QA

QUALITY CONTROL

- Done in “real” time
- Focuses on review of data collection forms

- **Does not ensure quality-** exposes lack of quality

QUALITY ASSURANCE

- Retrospective review on monthly basis
- Encompasses all aspects of study management
- Corrective Action Plans to ensure quality

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Review of Regulatory Files (Binder)

- Performed by Quality Manager (or designee) at study start-up, annually, and as needed
  - Complete regulatory review tool
  - Review Tool returned to coordinator for corrections
  - Quality Manager meets with staff to discuss trends, issues, and resolutions
  - Quality manager reports findings & actions in monthly report to Director and Clinic Manager

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Monthly Review of Data and Monitor Reports

- Performed by Quality Manager or Designee
- Web Reports
  - Data Queries
  - Manual Queries
  - SAE report
  - Missing forms
  - GT Collection & Future Use Data Discrepancies
  - Visit Schedule Compliance
  - Protocol Deviations
- Monitor Reports
  - Coordinators submit electronic copies of all reports to Quality Manager for review

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Research Laboratory and Pharmacy Activities

Performed by designated lab and pharmacy personnel

- QC: Complete QC checks
- QA Review
- Submit monthly reports to Quality Manager
- Monthly meetings with Quality Manager

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Education and Training

Departmental education and training records are maintained by individuals and the departmental Education Coordinator

- Required Education and Training:
  - Hospital Orientation
  - CCHMC Clinical Research Professionals Training
  - CITI / GCP Training
  - NIH / DMID and Other Regulatory Training

- Continuing Education and Training
  - NIH / DMID Training (per NIH requirements)
  - Departmental competencies
  - Monthly research professionals meetings
  - Annual CCHMC research symposiums
  - Protocol-specific training

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QM Oversight of Multi-Center Studies

- Quality Manager provides oversight of sub-contractor's quality management activities
  - Reviews and approves sites QMP prior to submission to sponsor
  - Reviews sites monthly QM reports
  - Participates in monitor de-briefing and QM reviews
  - Resource for site quality management activities

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Corrective and Preventive Action Plan Template

Study Title:

Protocol Number:

From:

Description of Event: *Brief description of what occurred*

Problem Identification: *Provide description of all areas affected and how the problem was discovered*

Reason for Noncompliance: *Provide summary of weaknesses/failures in systems*

Corrective Plan: *Describe details regarding the plan to resolve issue and prevent future occurrences, include references to any SOPs, institutional or departmental policies, etc.*

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Corrective Actions

STAFF RE-EDUCATION IS CRITICAL

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Maintenance of the QM Plan

- Quality Manager is responsible for:
  - Reviewing sponsor websites for QM updates and making revisions to plan as needed
  - Reviewing QM plan annually and updating as needed
  - Reviewing sub-contractor plan annually or more frequently as needed
  - Maintaining copies of all QM review records electronically
  - Submitting plan updates to sponsors for approval
  - Communication and Oversight of all QMP Activities

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BENEFITS OF QUALITY MANAGEMENT

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Benefits of Quality Management

- Involvement of all study personnel leads to increased compliance to protocols
- Creates an environment of teamwork
- Decreases number of monitor findings
- Decreases number of electronic data queries
- Enhances identification and resolution of data errors prior to data entry

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Prepares for unexpected FDA Audit

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QMP = Peace of Mind

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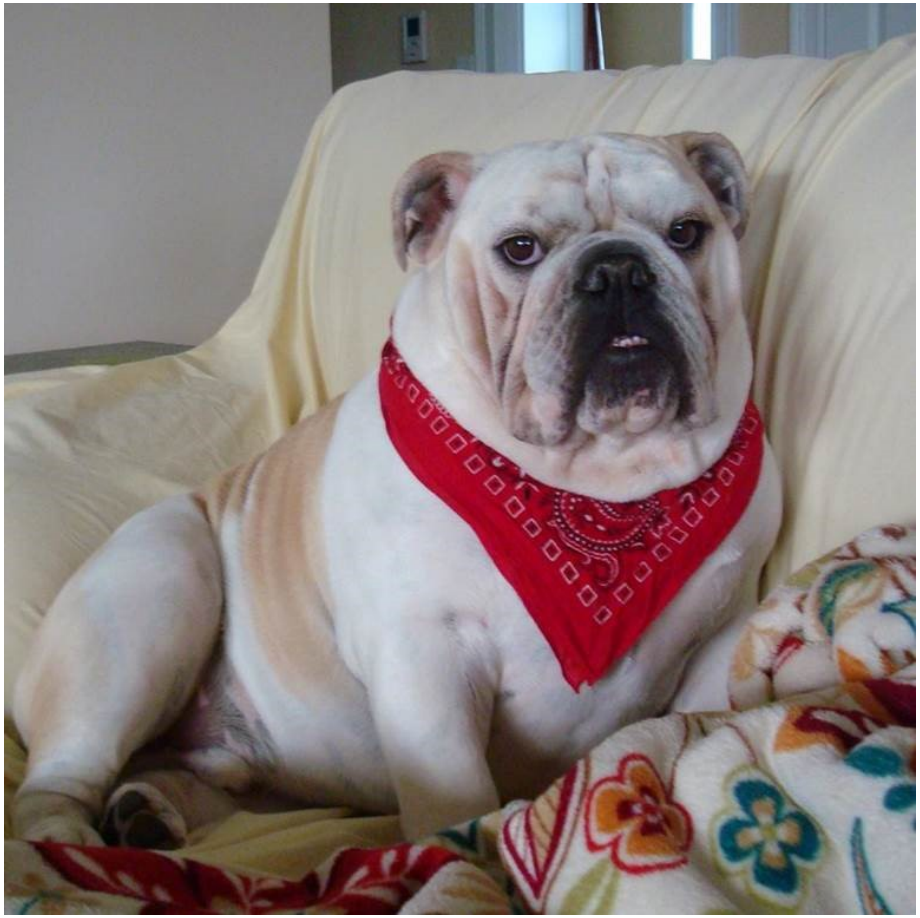
Questions



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