Internal Quality Control: A Guide to Checking your Work

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Disclosures

- I have no financial relationships to disclose
- All of the opinions expressed are my own

Objectives

Understand	Understand the Importance of Checking and Verifying Research Documentation
Learn	Learn Best Practices for Reviewing and Verifying Research Documentation
Identify	Identify Strategies for Quality Control Checks Throughout a Study's Lifecycle

Quality is Free… What costs money are the unquality things-all the actions that involve not doing jobs right the first time.

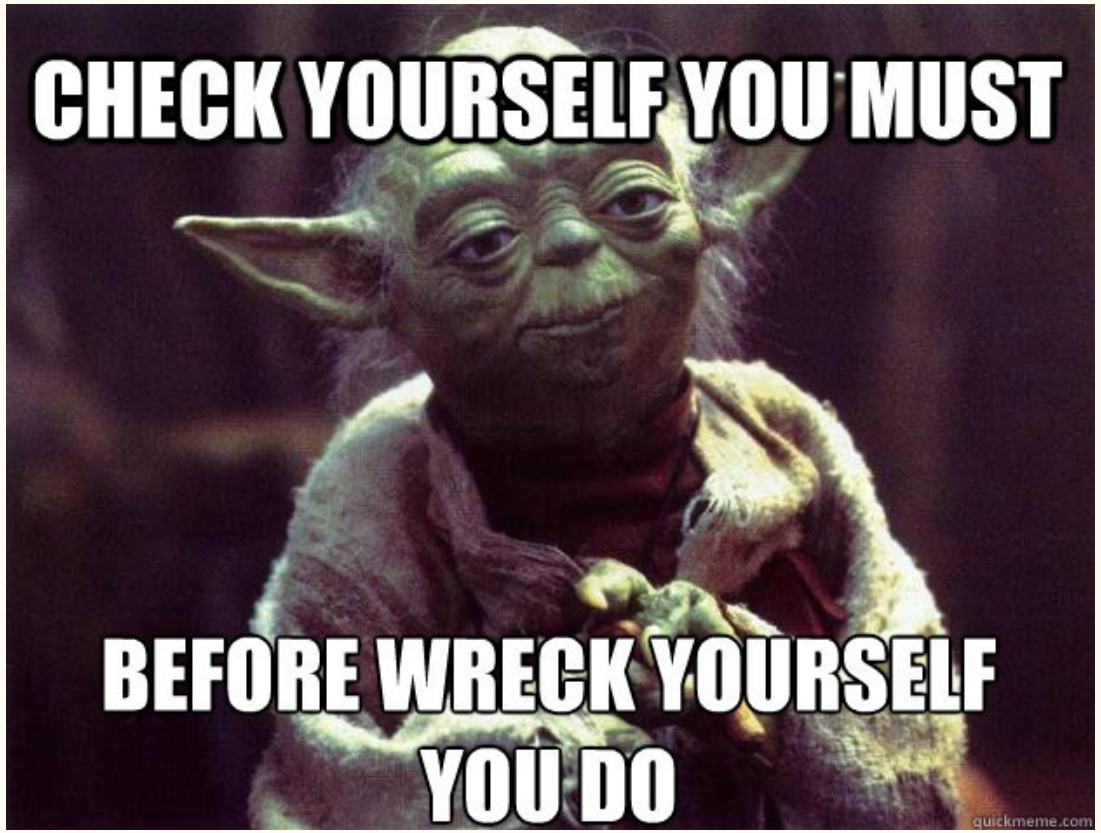
- *Philip B. Crosby*

Quality is Free: The Art of Making Quality Certain

Definitions

- **Quality Control**: Reviewing information to confirm standards are met
- **Quality Assurance**: Processes that demonstrate compliance
- **Quality Improvement:** Adjusting processes to improve compliance

Why QC?



- ✓ Helps you learn
- ✓ Helps prevent future mistakes
- ✓ Avoids over-reliance on others identifying noncompliance
- ✓ Better for you to recognize and correct than an external party

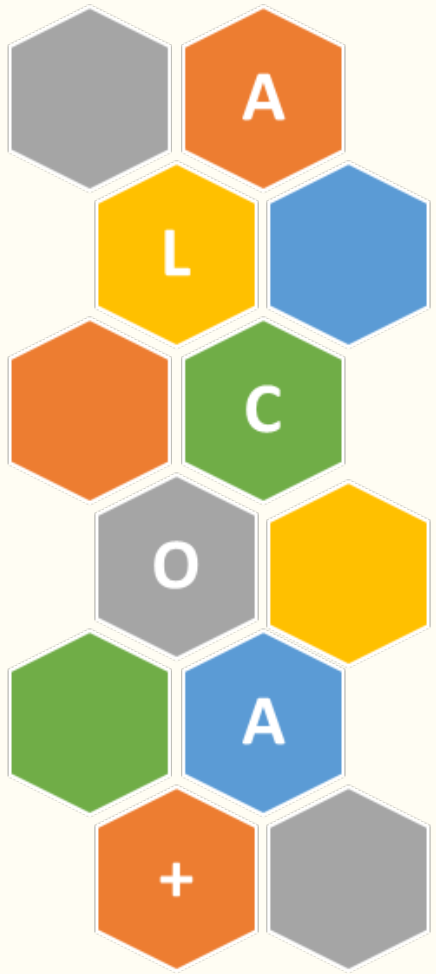
When To QC

- Before the first participant is enrolled
- After first participant is enrolled
- After each participant visit
- At IRB submission
- *Before each monitoring visit*
- *Before an audit or inspection*
- Onboarding yourself to a new study
- When training others
- *Develop QA systems to QC in real time

How to QC

Good Documentation Practices

- **Attributable**
- **Legible**
- **Contemporaneous**
- **Original**
- **Accurate**
- **Complete**
- **Consistent**
- **Enduring**
- **Available**
- **Credible**
- **Corroborated**



Checklists

- Regulatory Submissions
- Required Training/Certificates
- Essential Documents
- ICF Process
- Eligibility
- Study Visits

How Checklists Help Your Brain With Complex Tasks : NPR

What to QC

Regulatory

AKA the most important part!

Regulatory Preparation

Why do we do all this first?

Regulatory is the framework for all research conduct

It makes the QC process easier!

Regulatory Binder/Investigator Site File Review

- Review Sections for all documents
  - All versions and/or events are filed
  - If events are numbered, reconcile missing numbers
- IRB Approvals: all approved materials filed
- Implementation: documentation of implementation
- Logs:
  - During study: logs up to date
  - End of study: logs paginated and blanks lined through, initialed, and dated
- Paper: Post-It Tabs for subsections

Delegation and Training

- Delegation:
  - Accurate Active Dates
  - Appropriate/Accurate Tasks
- Training:
  - Initial and Amendment
  - Prior to/Concurrent with Implementation
- Supporting Materials:
  - CV
  - GCP
  - IATA
  - System Certificates

Role	Last Name	First Name	start date	end date	Original Protocol	PA1	PA2

a. You delegated certain tasks to individuals not qualified to perform such tasks.

> Our investigation indicates that you delegated substantial responsibilities in the conduct of this study to your study coordinator, Ms. **[redacted]** including the task of screening and enrolling subjects. Ms. **[redacted]** lacked the necessary medical training to perform the functions which she was assigned by you to carry out. Prior to joining the Urology Associates of North Texas as a study coordinator, Ms. **[redacted]** was employed as a phlebotomist, a laboratory technician, a medical instrumentation specialist, and a laboratory quality control officer. We believe that this background provided Ms. **[redacted]** with insufficient medical training to properly obtain medical histories or evaluate subjects to determine whether they met inclusion or exclusion criteria.

Monitoring Visit Follow-Up Letters

Review for any required action items

Confirm items were resolved

Identify if there were common or persistent findings

Regulatory

Compile the following information in a spreadsheet or document

- Protocol
  - Versions and release dates (IRB, Clinical Trial Management System, Email, other)
  - SOA for each relevant protocol (& important changes)
  - Labs, central vs. local collection
  - Eligibility Criteria
  - (S)AE criteria and reporting windows

Regulatory Preparation

- Confirm IRB of record for deviation reporting criteria
- Confirm if sponsor forms exist, how they are completed, and for what purpose
  - i.e. eligibility, diaries, PROs, SAE reporting, etc.
- Informed Consent and Related Documents
  - Versions and release dates
  - Confirm reconsent timepoints and parameters (all subjects, subjects in Long-Term Folow-Up)

Informed Consent

AKA also the most important part!

Informed Consent Packet

- Initial Consent Form (ICF)
- Documentation of the consent process
- HIPAA: embedded or separate document
- Optional and/or conditional consents

ICF QC

- Available
  - All pages present
- Original
  - Wet-ink signature
- Accurate
  - Patient identifiers correct
  - Dates correct
  - Formatting correct
- Enduring
  - In black or blue pen
- Complete
  - Selections (checkboxes, yes/no correct)
  - Initials present if indicated
- Contemporaneous
  - Signed before procedures
  - Right version used
- Credible
  - Consenter trained and delegated
  - Consentee is the patient or approved to consent on their behalf*

  *IRB approved method of LAR

Reconsents

- Was reconsent indicated? *Check for **all** amendments and revised IBs*
- Full Consent vs. Consent Addendum
- Was it done in a **timely** manner? (release date, medical record for timeline)
  - Was the patient seen at our site between release and reconsent?
  - Method of reconsent? (advanced verbal notification)
  - Is reconsent *actually needed* (based on patient's status on study)*?*
- Does completion (i.e. checked boxes, initials, optional samples) match on original and reconsent(s)?
- Same process (& QC) as initial consent

Strategies for Review: Spreadsheet

- Patients
- Date consented
- Date new consent implemented
- Date(s) of study or SOC visits between implementation and reconsent
- Date reconsented

	ICF version date	1/1/2025		4/6/2025	
	Implementation date	1/5/2025		4/10/2025	
	Reconsent Reqs				
Subject Number		Due Date	Date Signed	Due Date	Date Signed
#001		N/A	2/1/2025	4/15/2025	5/20/2025
#002					
#003					
#004					

Eligibility

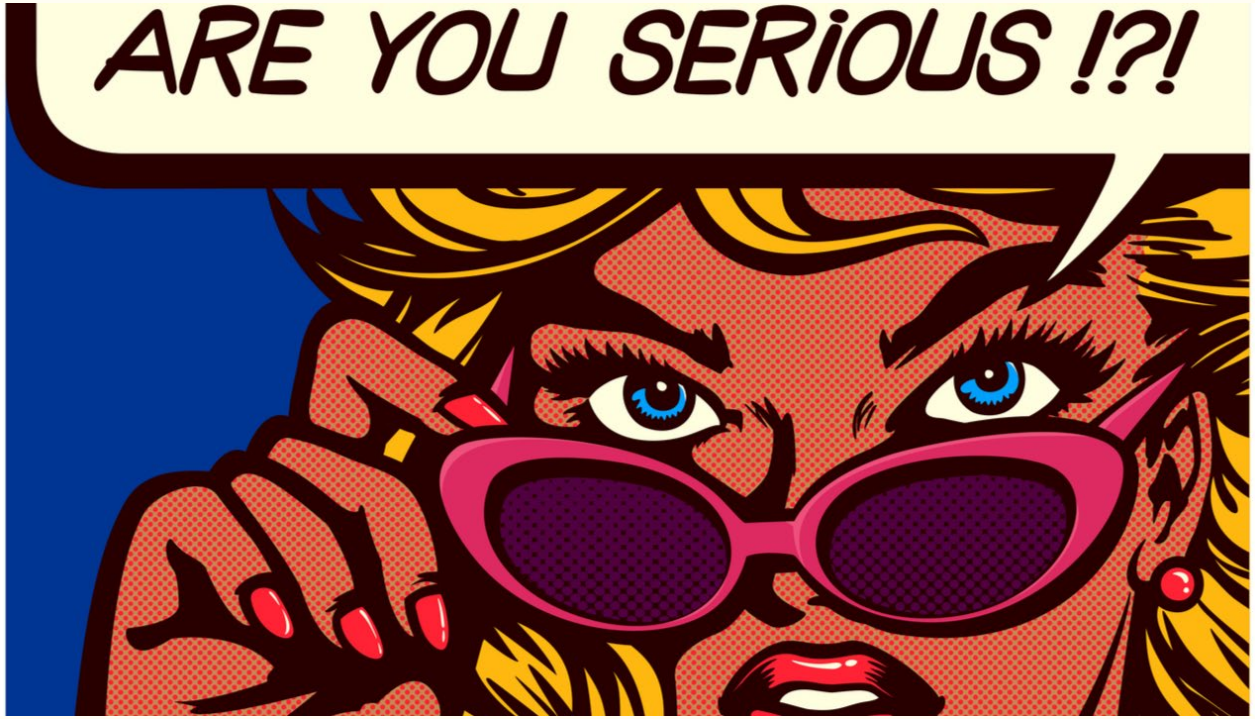
Also arguably the most important part!

Eligibility

- Does the eligibility checklist match the protocol version?
- Are all copies of supporting source documents available?
  - Relevant attestations/reviews/sign-offs available?
- *Was the patient actually eligible?*
- Are all sections checked off accurately?

Eligibility Cont.

- Was the approval ***before*** treatment start?
- Signed by appropriate personnel?
- How many timepoints does eligibility need to be reviewed? Is documentation available for all timepoints?
- Was the document approved by the sponsor? Did it need to be?
- Any eligibility-related communications present?



SAEs

Also arguably the most important part!!

Serious Adverse Events

- Method of reporting SAEs ➔ *electronic vs paper*
- Were SAEs reported within 24 hours of awareness?*
- Did the PI sign off within 24 hours?
- Source documents for attribution! (Email, paper form, log, etc.)
- Does the source match the EDC?
- Did it need to be submitted to the IRB?

Wrong. It’s time to get to work!

Now, we need to look at:

- Visit requirements
- Adverse events
- Con meds
- Medical history
- Response assessments
- Deviations
- And more!
- (all also arguably the most important part!)

*What is “Important”?

- Endpoint Evaluation
  - Safety: Changes from baseline
  - Efficacy: Treatment Response
  - Other Endpoints as identified
- Participant Protections
  - Rights: Consent
  - Safety: Assessing patients appropriately
  - Well-Being: Appropriateness for the Trial
- Regulatory Requirements
  - Investigational Plan
  - IRB requirements
  - Applicable regulations

Visit Requirements

- Compare source contents to SOA in protocol
- Check medical records, look for windows, documentation of something missing, etc.
- Lab value definitions
- Coordinator notes, provider notes, vitals
- Ask “do I need source for this?”

Documentation

- Adheres to Good Documentation Practices
- Demonstrates protocol compliance
- Addresses non-compliance
  - Education/Re-education
  - Justification if available

Notes to File

- Commensurate with finding
- Document clarifications not otherwise readily understandable

We note that generation of numerous memos to file after all subjects have completed the study does not adequately secure compliance of an investigator.

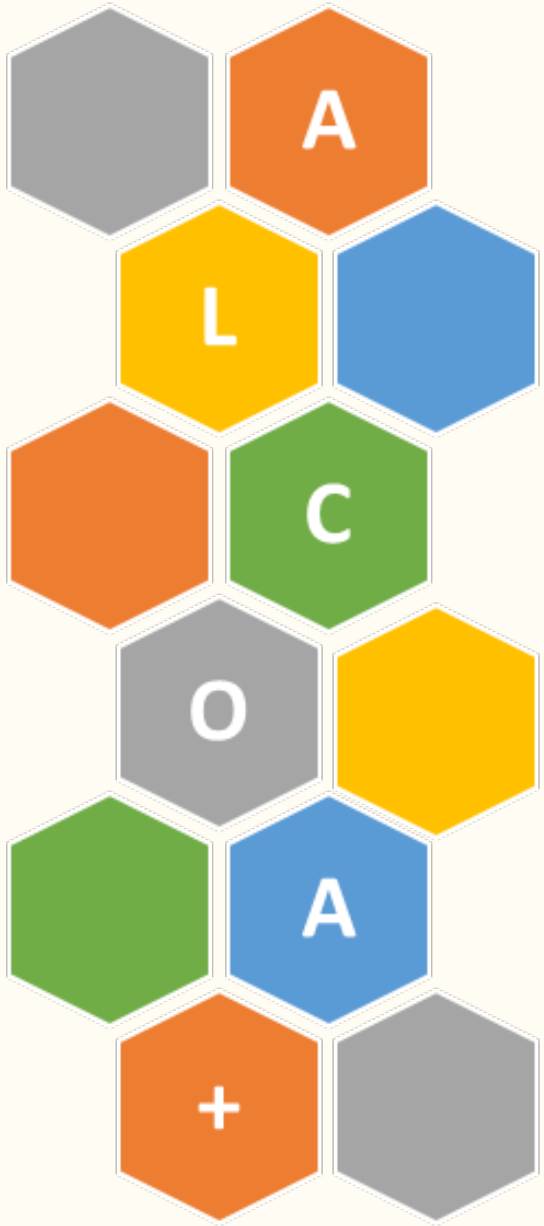
As noted previously, memos to file are inadequate to address the falsification (backdating) of study documents.

Adverse Events & Concomitant Medications

- Does the information match the EDC?
- Attribution – appropriate and up to date?
- Clinically significant lab values
- Does the Con med indication match an AE or medical history? **

Logs, Forms, and Other Source

- Accurate – missed dates, accurate dates
- Legible – can you read it; thermal paper?
- Complete – pagination, identifiers complete on each page
- Original – confirm you have the *unredacted* original
- Attributable – who did it?



Questions?

Thank you!

Special Thanks to Megan Wagner and Kristen Riley!