



What auditors want



- RG04

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Cedric Marchand, Angelo Tinazzi
Cytel Inc.
Geneva – Switzerland
cedric.marchand@cytel.com
angelo.tinazzi@cytel.com

What is an Audit?

An audit is a Systematic and Independent examination

of trial activities and documents to determine whether the evaluated trial activities were conducted, the 'clinical' data were recorded, analyzed and accurately reported

according to the protocol, sponsor SOPs, GCP, and the applicable regulatory requirement(s)

ICH , «Guidance for Industry - E6 Good Clinical Practice: Consolidated Guidances», 1996

What is an audit

When does it happen

QC vs QA

Audits in a nutshell

What an auditor will.....

GCP and Programming

Prog Master File

QC Independency

Proof of competencies

Verification Redundancy

Conclusions

When does it happen?



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QC vs QA

- Quality Control (QC):

Documented independent verification of the accuracy of the output

- Quality Assurance (QA):

Verification Adherence to documented Processes and applicable regulations

All QC steps must be well documented: this is the responsibility of programmers

QA steps documentation are under the responsibilities of QA people

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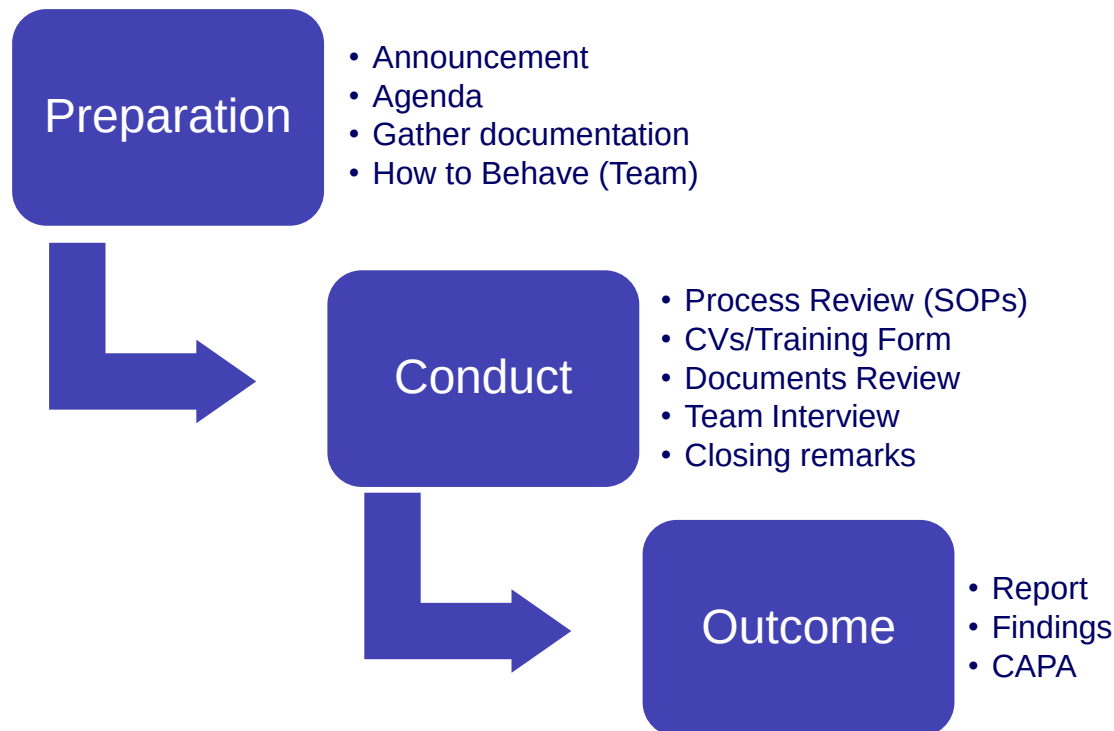
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Audits in a Nutshell

- Internal vs External (Sponsor) vs Inspections (HA)
- Qualification audit: before work is done, focus on Processes
- « Retrospective » audit: after work is done, focus on QC-QA Documentation



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What an auditor will look for?

Clear and relevant SOPs

- Are Processes « protecting » data validity and integrity?

Documented Evidence:

- What has been done, When by Who? Team List?
- Is the staff appropriately **qualified? Trained?**
- Were **SOPs** followed?
- Are key decisions documented?
- Were Contractual Obligations fulfilled?

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Staff must be qualified:

ICH E6: "Each individual involved in a clinical trial should be qualified by education, training, and experience to perform his or her task(s). "

QC must be done:

ICH E6: "Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. "

Traceability, reproducibility, and versioning:

ICH E6. "If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data."

Access-control:

ICH E6: Maintain a security system that prevents unauthorized access to the data

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Programming Master File

Documentation should be clear, complete and readily available

A PMF is a folder centralizing all the documentation that provides evidence of compliance to GCP.

To make it easier for the auditor and the audited team 😊

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The Cytel PMF

1. Training plan on input data:

all documents describing the structure and particularities of the data to use

Example: protocol, CRF, etc

2. Training plan on Output data:

all documents describing the outputs to produce

Example: SAP, mock TLF, ADaM specs, issues and decision logs

3. Training sign-off form

4. Validation Plan : Who **will do** what and how?

5. Validation Report: Who **has done** what, when and how? **Signed**

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Independency of QC

Managers train their teams on key aspects of Independency of QC for double/independent programming

- Do:
 - Question the relevance of specifications (SAP included)
 - Carefully review the output visually: is it meaningful?
 - In case of discrepancy, look for an explanation before contacting the developer.
- Don't:
 - Don't read/copy code from the developer's program
 - Don't "try to match" with the Developer's output: the objective is to find errors
 - Don't ask the Developer for the solution until 1st comparison

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Employee Training File and Proof of Competencies

Each individual involved in a clinical trial should be qualified by education, training, and experience to perform his or her task(s)

- Up-to-date curriculum vitae
- SOPs Training
- Training log of all relevant « domain-specific » training
- Programming Competencies Checklist

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Redundancy of Verifications

QC done independently

+ Lead programmer centralizing in a PMF the evidences of verifications

+ Project Managers systematically verify the availability of auditable documentation

+ Managers who regularly review PMFs

+ Internal Audit

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- A lot of programmers are resistant to « documentation »
- But an Audit without a well organized documentation is a « nightmare » for the team audited, with serious implications for your company. Follow the processes !
- Audits are useful for continuous improvement
- PhUSE Good Programming Documentation Practice Working Group?

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Cedric Marchand – Director – Head of Statistical Programming

cedric.marchand@cytel.com

Angelo Tinazzi – Director – Statistical Programming

angelo.tinazzi@cytel.com

Cytel, Shaping the Future of Drug Development



Programming Competencies Checklist

Updated Annually

Programming Competencies Checklist			
DOCUMENT REVIEW HISTORY			
Version	Section Changed	Change Made	Date
New	n/a	Initial issuance of document	1-Apr-2016
This functional checklist is meant to document the assessment of the skills required to perform the duties related to the specific function. The line manager is responsible for filling this checklist for each employee in his/her team in the 3 weeks after start of employment and then once a year. This assessment can be used as a basis for the technical development plan of each employee. It can be used to evaluate whether an employee can be given certain technical tasks and the level of oversight and mentoring needed for the good performance of a given task. Instructions: - In the attached matrix, tick the columns reflecting the past training or past experience of the employee. - Concerning the development plan, only tick the relevant competencies on which the employee should focus in the next 12 months. - Sign and file the checklist in the training log of the employee.			
Date of Assessment:			
Employee Name:		Employee signature	Date (DD-MMM-YYYY)
Manager Name		Manager signature	Date (DD-MMM-YYYY)

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Programming Competencies Checklist

Updated Annually

	Never Exposed	Occasional Use	Frequent Use	Expert	Development Plan for the next 12 months
SAS Programming					
Essential Data Manipulation Technique: - Creation of SAS variables - Sub-set of data - Combination of datasets (merge, set...) - Simple SAS macro variable - ODS Statement - ...	☐	☐	☐	☐	☐
Advanced Data Manipulation Technique - Control SAS data set input and output, - SQL technique, - Summarize, read, and write different types of data, - Perform DO loop and SAS array processing, - Advanced SAS macro programs - Customize Proc report, advanced ODS statement technique ...	☐	☐	☐	☐	☐
Tables Reporting	☐	☐	☐	☐	☐
Listing Reporting	☐	☐	☐	☐	☐
Figures Production	☐	☐	☐	☐	☐
CDISC					
SDTM	☐	☐	☐	☐	☐
ADaM	☐	☐	☐	☐	☐
Define.xml/pdf and Reviewer Guide	☐	☐	☐	☐	☐
Open CDISC Report	☐	☐	☐	☐	☐

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Statistics					
Descriptive Statistics - Categorical - counts and frequencies - Continuous - descriptive statistics (median, mean, SD, quartiles...) - Confidence Interval	☐	☐	☐	☐	☐
Inferential Statistics - Standard statistic test (chi-2, Student, t-test, Fisher, Kolmogorov-Smirnov...) - Correlation - Simple Regression Model	☐	☐	☐	☐	☐
Complex Inferential Statistics: - Survival Analysis - Cox Model - ANCOVA - Mixed Model - Complex Regression Model	☐	☐	☐	☐	☐
Clinical Trial - Regulatory Document					
ICH E3, E9	☐	☐	☐	☐	☐
Chapter 21 of the US Code of Federal Regulation - Part 11	☐	☐	☐	☐	☐
FDA PORTABLE DOCUMENT FORMAT (PDF) SPECIFICATIONS	☐	☐	☐	☐	☐
FDA STUDY DATA TECHNICAL CONFORMANCE GUIDE	☐	☐	☐	☐	☐
eCTD - TECHNICAL CONFORMANCE GUIDE	☐	☐	☐	☐	☐
Others					
PK/PD Data	☐	☐	☐	☐	☐
NONMEM Datasets	☐	☐	☐	☐	☐
e-sub services (clinical.trial.gov...)	☐	☐	☐	☐	☐
Project Management (lead programmer role, manage budget, Interaction with DM and Biostat)	☐	☐	☐	☐	☐
Additional competencies and comments					

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