

“Why do similar audit findings continue to come up during subsequent audits?”

Follow Up on Audit Responses by QA

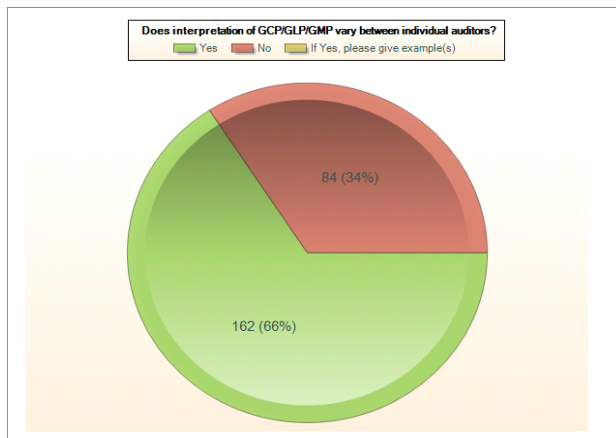
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Premier Research Group

Agenda

- Why follow up on audit reports can be an issue?
 - Conflicts in GCP/GMP/GLP
 - Importance of referencing the breached quality standard
 - Categorisation & Classification of audit findings
- Definition of Audit Findings – Critical/Major/Other/Comment
- CAPA Decision Tree – Key Elements
- Creating the Decision Tree
- Handling Client Complaints
- Steps for Developing a Decision Tree
- CAPA Event Types
- Conducting the CAPA investigation
- The 5 Whys to determine Root Cause
- Conclusions, what degree of follow up by QA is required?

Conflicts in GCP/GMP/GLP

- 62 (25%) said that they had directly experienced conflicts in the requirements of GCP/GLP/GMP.
- 162 (66%) said that the interpretation of GCP/GMP/GMP varies between auditors and 84 (34%) said not.
- GCP was perceived to be a much more open to varying interpretation by auditors
- Company auditors were sometimes raising as significant findings things that are not deemed so by regulators and vice versa.

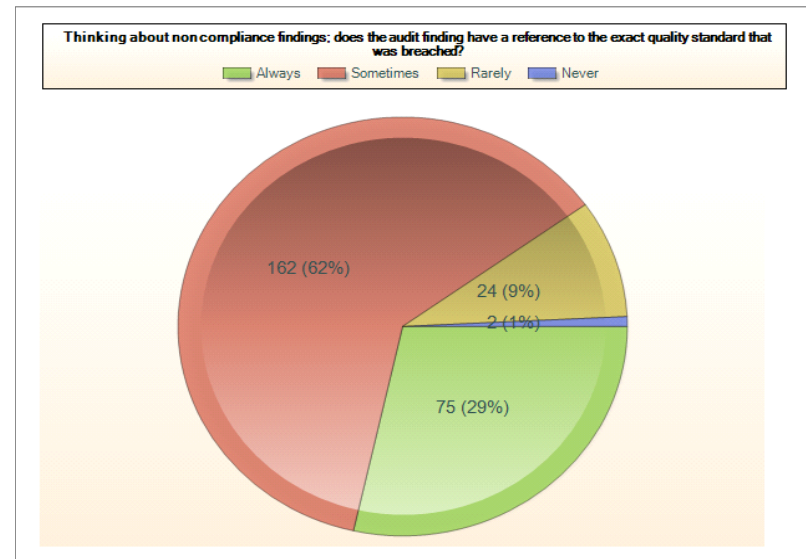


- There were problems with auditors being oriented towards their own experience in GLP, GMP and/or GCP resulting in a different emphasis in findings and what might constitute for example “relevant training” or actions conducted “in a timely manner”.

Ref: ICR
 CRfocus Vol 22
 May/June 2011:
**What’s the Real
 Value of Audit?**
 Jan Robinson

Importance of Referencing the Breached Quality Standard

- Referencing the breached quality standard was considered to be highly dependent on the auditor. In addition, only 144 (55%) said that non compliance findings were always clearly differentiated from other findings in audit reports. 117 (45%) said that they were not.



Ref: ICR CRfocus Vol 22 May/June 2011: **What's the Real Value of Audit?**
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Categorisation & Clarification of Audit Findings

- Reporting templates and categorisations are usually standardised within organisations
- Variation is seen across the industry as a whole
- 88% (229) thought that there should be standards for audit reporting, distributing and responding to audits and 30 (12%) did not.

Completely or considerably standardised	Own organisation	Across sector
Audit report format	219 (83%)	80 (31%)
Categorisation/ classification of findings	217 (83%)	97 (38%)

Ref: ICR CRfocus Vol 22
 May/June 2011: **What's the Real Value of Audit?** Jan Robinson

Definition of Audit Findings (1)

- **CRITICAL**

Conditions, practices or processes that adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.

Critical observations are considered totally unacceptable to regulatory agencies.

URGENT



Definition of Audit Findings (2)

- **MAJOR**

Conditions, practices or processes that might adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.

Major observations are serious deficiencies and are direct violations of GCP principles.



Definition of Audit Findings (3)

- **OTHER**

Conditions, practices or processes that would not be expected to adversely affect the rights, safety or well-being of the subjects and/or the quality and integrity of data.



Definition of Audit Findings (4)

- **COMMENT**

The observations might lead to suggestions on how to improve quality or reduce the potential for a deviation to occur in the future.

Note: Any of the audit findings classifications may be elevated to the next level, depending on the number of findings in a particular area

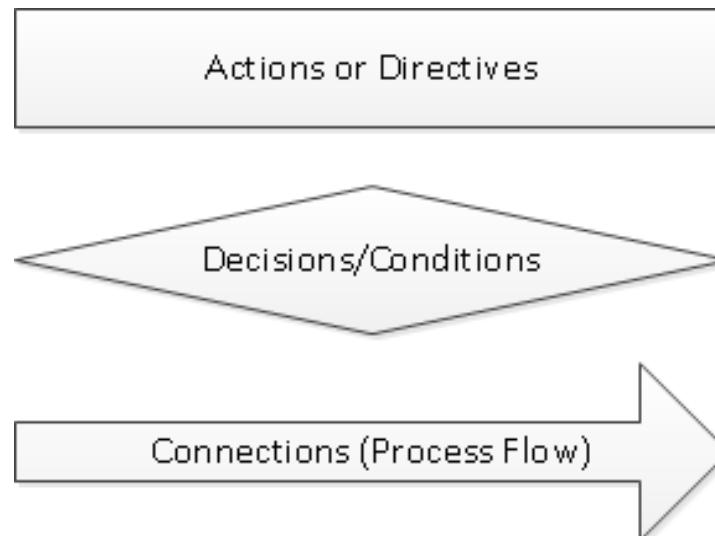


CAPA Decision Tree – Key Elements

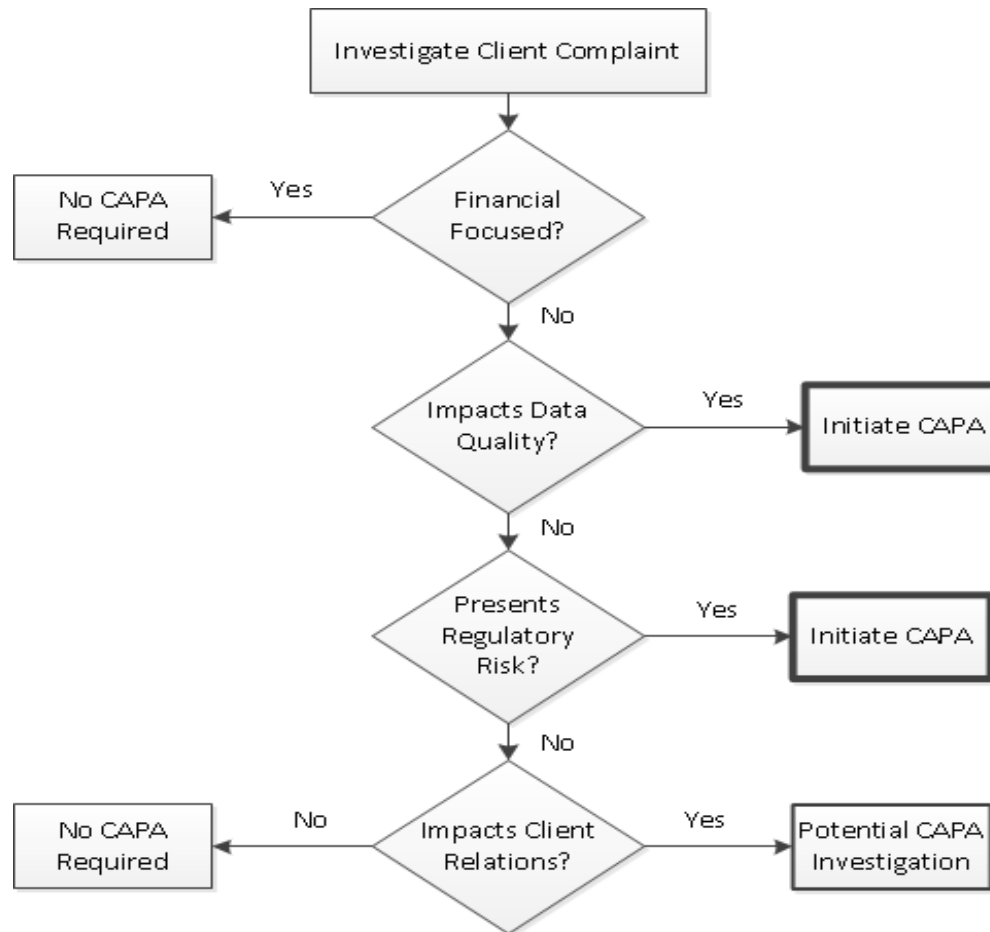
- The Depth of the Investigation must match the potential risk to the following:
 - Patient
 - Investigating Company
 - Client Company
 - Public
- Primary Goal of Investigating - to discover the cause of an undesired incident and decide what should be done to prevent it from happening again.
- For any given CAPA event, management should choose the types of events, based on the severity and likelihood for reoccurrence

Creating the Decision Tree

- Using the Decision Tree diagram allows you to document and communicate information required to make decisions efficiently and consistently.
- Constructing a Decision Tree involves the use of:



Client Complaints



Steps for Developing a Decision Tree

- Clearly state the decision
- List instructions for determining decision
- List conditions in the form of questions with “Yes”, “No” options for answers
- Place instructions individually in rectangle shapes
- Place questions individually in the diamond shapes
- Arrange shapes in logic order for making the decision
- Connect shapes with arrow to show the flow of the decision making
- Label arrows to direct users to a decision based on answers to questions

CAPA Event Types

- Process Failures (SOP)
- Client/Sponsor complaints regarding quality/non-compliance
- Audit Findings (Regulatory inspections, Audits – Internal or Client)
- System Errors (Computer/Validation, Programming)
- Employee Error (Sponsor/CRO/Site)

Conducting the CAPA Investigation

Applying the following questions will help you determine the appropriate root cause analysis for your CAPA:

- What went wrong?
- What were the consequences of the incident (event)?
- What could cause these consequences?
- What pro-active changes should be made to the process and management systems to adequately control risk in the future?

Using the 5 Whys Technique to determine the Root Cause

Example problem: Customer complaint – Monitoring Report timelines not being met

Why did customer complain?

 *50% of Monitoring Reports are not provided on time.*


Why are Monitoring Reports not turned in on time?

 *Because half of them require re-work.*

Why do monitoring reports require re-work?

 *Because key information was missing.*

Why do Monitoring Reports have missing information?

 *Because some Monitors are not entering all of the necessary information.*

Why do the Monitors not enter the required information?

 *Because template/terminology is not clear*

To Conclude – Follow up by QA What to Consider?

- Depends on your QMS and processes
- Depends on the severity of audit findings/ risk to the organisation/subject
 - Do you only follow up on Major/Critical findings?
 - What evidence do you require?
 - How do you assess risk?
- Depends on the analysis/conclusions from the organisation
 - How thorough and how timely was follow up?