External control/assessment (QA and audit)

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Day 2

Guidelines on GCP: application of principles (Part 1)

Topics summarised in this presentation are:

- method for defining quality level you want
- meaning of external controls
- quality assurance activities
- audit, audit report and CAPA

BACKGROUND

1. QUALITY must be guaranteed, so it must be planned in advance adopting a STANDARD

- the STANDARD must be established from the beginning

We always do the following controls and describe results in writing:

1…….

2……..

3……..

4…….

BACKGROUND

2. QUALITY must be certified with random risk-oriented controls

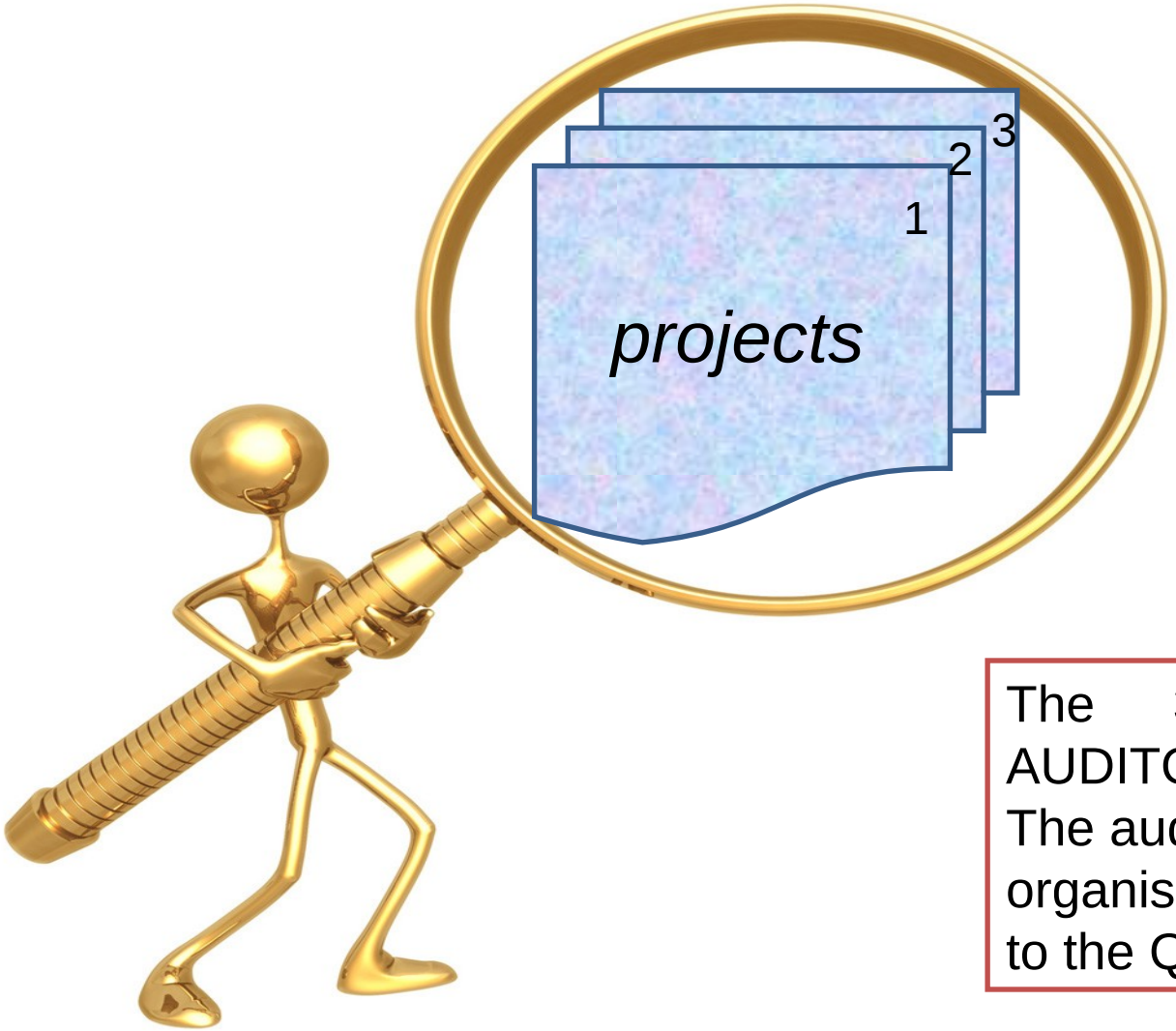
You have been selected for the following kind of verification …….

BACKGROUND

3. **The certificator (QUALITY ASSURANCE/QA) must be a 3rd party (not involved in the project implementation).**

4. **QA must be independent, that means she/he is not referring to the role responsible of the project implementation.**

"External controls" mean controls made by a 3° party



The 3rd party is the AUDITOR.
The auditor(s) in the research organisation is (are) allocated to the QA function.

The assessment made with the external controls means evaluation and classification of non-conformities.

The rating of non-conformities adopted by EMA GCP inspectorate is the following.

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 unacceptable.

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 violation of GCP principles.

MINOR: 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.

Source: Guidance for the preparation of GCP inspection reports, eudralex vol. 10 chapter IV version 28 May 2008
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm

HOW TO DEFINE A STANDARD

the standard is defined by rules to be followed by all participants to the project

European Medicines Agency

New URL: ema.europa.eu

FDA

these rules may be national and enforced by law

there are also rules expressed by each single company or organisation, in this case they are Standard Operating Procedures (SOPs)

Quality Assurance function

QA promotes and supports the expression of SOPs in whatever kind of research organisation (pharmaceutical company, public research center, hospital, etc.)

Quality Assurance function and audits planning

The auditor does the assessment of the compliance making AUDITS.
Generally, there is an audits plan made at the beginning of the year.
Projects to be audited are selected according to agreed criteria of importance, risk, or random.

The AUDIT

What can be audited:

- investigational sites
- the sponsor of the study
- the archive of the study (Trial Master File)
- one or more study documents (protocol, CRF, informed consent, other essential documents, final study report, pharmacy, laboratory, AE reporting, etc.)
- the organisation of one given structure (system audit)

The AUDIT must be prepared.

- depending on the subject of the audit, we must carefully read and understand study documents such as the protocol, CRF, SOPs followed and applicable to the study, reports of monitoring visits, etc.
- these documents are not available in an unique place and we must ask for them
- we must detect gaps (missing instructions, missing references or attachments, timelines not defined, etc.) and inconsistencies
- also specific tools may be prepared as support (check-lists, forms, memo, etc.)

During the investigational site audit:

- the study archive is verified for completeness and consistency among different documents.
- signed informed consents are always 100% verified
- facilities are visited and controlled in respect to study examinations and procedures
- the organisation of source documents (descriptions of study visits, reports of examinations, diaries, etc.) is considered for accuracy and matching of all study procedures
- some completed CRFs are 100% compared with source documents

During the audit of documents:

the audited document is verified against:

- applicable law and requirements,
- templates (if any)
- SOP applicable for the preparation
- internal consistency of information

During the audit of the sponsor:

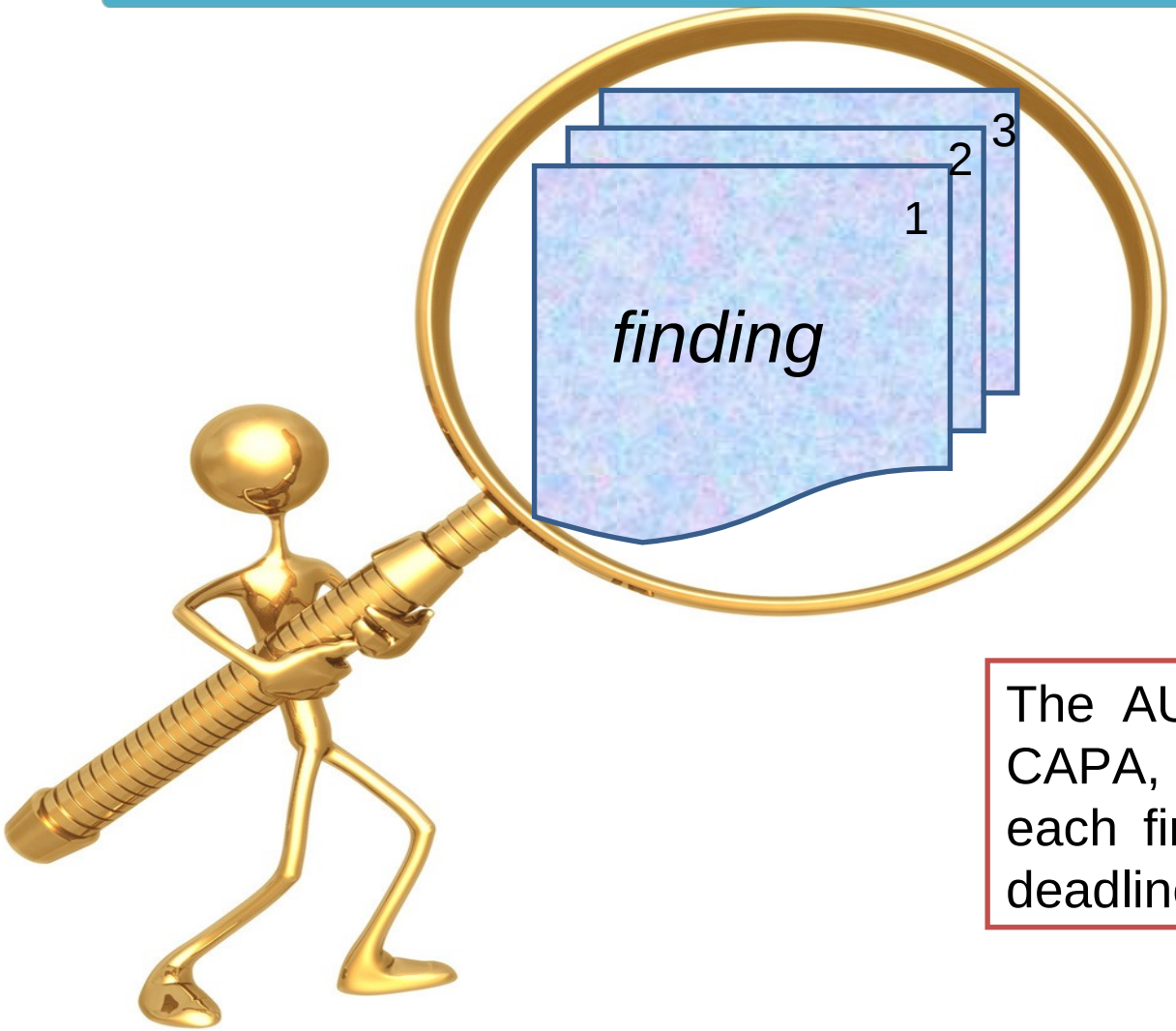
- the set of SOPs followed by the sponsor for studies implementation is considered
- the archive and IT infrastructure are controlled
- the clarity of attribution of roles and responsibilities is verified
- the training of the staff is examined
- the compliance of implemented studies is verified against regulations, SOPs, etc.

One audit report must be prepared after each audit

In the audit report the following information must be included:

- scope of the audit (name of the project/ site/ functions/ activities)
- reference documents to which is required compliance (local laws, guidelines, SOPs, etc.)
- people, documents and facilities seen during the audit on which are based the observations made during the audit
- list of the findings and their grading with reference to the document/law/SOP providing the requirement not fulfilled
- general conclusion about the results (level of GCP

The resolution of the issued observations need to be followed with a Corrective and Preventive Action Plan (CAPA)



The AUDITOR prepares the CAPA, where an answer to each finding is asked and a deadline for implementation.

You can go more in depth during the audit if you have an already started studies to verify .....

If you are auditing an organisation as system and you have practical examples to ask about running studies, the audit is more effective and you have a reliable estimate of the compliance.

In summary the function of QA is ……

To contribute to the definition of the standard

To measure the standard implementation


true
results
ETHICS
documented
evidence
QUALITY


Thank You!