



**SPAQA Behörden Diskussionsrunde / SPAQA Regulatory Round Table
13. November 2007, Basel, CH**

Fragen & Antworten / Questions & Answers

Organisation und Personal / Organization and Personnel

Q 1. Ist eine Erfolgskontrolle nach einer GLP-Schulung notwendig?

A The GLP principles do not require any control after a GLP training. The training should be documented in the personal file and information on the date, the duration, the content of the training and the identity of the 'trainer' should be available.

According to GLP principle 1.1.d, test facility management should ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for these functions. Therefore, some form of control is required in this context (e.g. during QA inspection).

For some tasks, training courses should be followed by practical experience. This should be defined into the 'training criteria' for collaborators.

Q 2. Training Records:

When a complete change is made to the system used to record training (either new paper system or a move from paper to electronic) would it be acceptable to provide an assessment of current competence and then archive the old records? This would avoid the difficult and often confusing task of cross-referencing the old and new records. (MDS)

A For a better overview, the training records should be available in a chronological way. In the case of changing the recording system, a link between the previous and the new system should be available.

According to GLP ordinance 10.1(c) the training records should be archived. Maintaining the training records at the working place is not considered as archiving. The training records should be transferred to the GLP archive at regular intervals, and at least at a change of the documentation system or when the collaborator leaves the test facility.



Qualitätssicherung / Quality Assurance

Q 1. Bei einer Inspektion notiert der QA-Inspektor seine Beobachtungen auf Notizpapier. Später erstellt er in seinem Büro den Inspektionsbericht. Sind die Handnotizen 'Rohdaten' oder ist der Inspektionsbericht alleine massgebend? Was muss mit den Handnotizen geschehen (vernichten oder archivieren)?

A QA Inspection notes should be considered as raw data (= original records). According to GLP ordinance 2.2(c) the records of [QAU] inspections should be retained. As a consequence the inspection notes should be archived.

In many cases the inspection report contains only a summary of inspection results (findings), this is not enough to demonstrate the completeness of the QA inspection. It is expected that the inspection notes will allow reconstructing the activities/documents inspected.

Q 2. According to the GLP ordinance 2.2(a), QA should maintain copies of all approved study plans and Standard Operating Procedures in use in the test facility.

- a) What is QA's responsibility in regard to electronic SOPs?
- b) How are technical instructions (e.g. instructions for the operation and maintenance of computerized systems) to be handled? *(Roche)*

A Ad a) In an electronic documentation system, access to the information is not done through distribution of copies but through remote access to the electronic document.

In the case of electronic SOPs, the QA unit should ensure that they have full access to actual and previous versions of SOPs in an electronic system.

Ad b) Technical instructions (operating procedures established by the supplier of the equipment or test methods) should be available to the QA inspector during facility or study-based inspections. It is not necessary to maintain a copy of such documents in the QA Unit; however, the QA Unit should have the possibility to ask a copy in advance, to prepare the inspection.

It is acceptable to maintain the technical instruction at the working place, as part of the equipment logbook.



Prüfsysteme / Test Systems

Q 1. Ist zur Bestimmung verschiedener Parameters (Charakterisierung) eines Prüfgegenstandes die Verwendung mehrerer physikalischer oder chemischer Prüfsysteme wie z. B. HPLC, Schmelzpunktgerät, IR, pH-Meter, Octanol-Wasser (Verteilungskoeffizient) Viskosimeter, Densitometer etc, innerhalb einer Prüfung erlaubt, oder muss für jedes einzelne verwendete Prüfsystem eine separate Prüfung durchgeführt werden?

A It is acceptable to determine several parameters of a specific test item, in one study.

According to 8.2(a) and 9.2(a), the title of the study should be descriptive. 'Physical-chemical characterization' may not be enough to understand which tests are included.

Prüfungsablauf / Study Conduct

Q 1. Bei einer Multi-Site Prüfung erhält der Principal Investigator eine Kopie des Prüfplans. Darin ist vereinbart, dass alle Rohdaten, die am Prüfstandort erarbeitet werden, im GLP-Archiv des Prüfstandortes aufbewahrt werden. Muss die Kopie des erhaltenen Prüfplans auch im Archiv des Prüfstandortes aufbewahrt werden?

A In accordance with the OECD Consensus Document No. 13 on Multisite Studies, it is basically not required that the study plan is archived at the test site. In case raw data are archived at the test site, it is, however, advisable to archive a copy of the study plan at the same location to ensure that the archiving of the raw data is done in accordance with the study plan.

Q 2. Auf Wunsch des Prüfleiters muss der PI im Rahmen einer Multi-Site Prüfung den Prüfplan mitunterschreiben. Erfolgt diese Unterschrift bevor oder nachdem der Prüfleiter den Prüfplan unterschrieben hat?

A The principal investigator should sign the study plan first, as the study director is responsible for the overall conduct of the study.



Prüfungsablauf / Study Conduct

Q 3. Kann der Begriff PI auch intern innerhalb einer Prüfeinrichtung verwendet werden oder müsste diese Person besser als e.g. "Internal Scientist" bezeichnet werden?

A In accordance with the OECD Consensus Document No. 13 on Multisite Studies, a principal investigator should be responsible for a specific part of the study, for which a particular know-how is needed, and which is separated from the main study. Generally, a test site should geographically or organization-wise be located at a different site to carry an own denomination.

Terms such as 'internal scientist' should be omitted, as they are not used in general GLP terminology. Rather, the indication of the function and organization should be provided (e.g. Head of Pathology).

Q 4. Einer Prüfeinrichtung wird rückwirkend das Zertifikat abgesprochen. Welchen Status haben die abgeschlossenen Prüfungen welche während dieser Zeit durchgeführt wurden?

A In case the re-certification cannot be provided all studies are questionable and would have to be audited individually regarding GLP-compliance.

Q 5. Study Schedule:

In the study plan, an estimated completion date is provided for both the analysis and for the final report with actual dates to be included within the final report.

What is an acceptable difference in the estimate and actual dates before a study plan amendment should be written to explain them? (MDS)

A An acceptable difference for the dates in the study plan strongly depends on the type of study conducted, the justification for the delay, as well as on the schedule details provided in the study plan; in general, delays should not be more than one month.

It should be reminded in this context, that the communicated dates are an important source of information for the QA, to be able to control the relevant individual phases at the appropriate time sequences.



Prüf- und Referenzgegenstände / Test and Reference/Control Items

Q 1. What are the recommendations of the GLP monitoring authorities with regard to the maintenance of retention samples from each batch of test item:

- a) Is it permissible that each test facility defines what they mean by a short-term study?
- b) What are industry trends?
- c) What do the international monitoring authorities expect? (*Roche*)

A Ad a) In the OECD Consensus Document No. 7 on the application of the GLP principles to short-term studies, such studies are defined:

‘Short-term biological studies include acute toxicity studies, some mutagenicity studies, and acute ecotoxicological studies.

Physical-chemical studies are those studies, tests or measurements which are of a short duration (typically not more than one working week), employ widely-used techniques (e.g. OECD Test Guidelines) and yield easily repeatable results, often expressed by simple numerical values or verbal expressions.

Typical physical-chemical studies include but are not limited to chemical characterisation studies, melting point, vapour pressure, partition coefficient, explosive properties and other similar studies for which test guidelines exist.’

In particular cases, where the definition of a ‘short-term study’ is not clearly attributable, the GLP Compliance Monitoring Authorities will decide on a case-by-case basis (see also question c).

Ad b) The information cannot be provided here.

Ad c) The OECD GLP-Working Group discussed point 1a) and c) at the last meeting, and it was general consensus that the definition of ‘short-term study’, where not clearly attributable, should be left to the national GLP Compliance Monitoring Authorities.

Q 2. Ist ein Rückstellmuster bei käuflich erwerbbaaren Reference Items nötig?

A It is stated in the OGLP principles under chapter 10 a. that ‘the following should be retained in the archives for at least ten years after study completion:

The study plan, raw data, samples of test and reference items, specimens, and the final report of each study’.

Hence, a commercially obtained reference item will therefore also require a sample to be retained.



Prüf- und Referenzgegenstände / Test and Reference/Control Items

Q 3. Expiry dates:

What advice can you give for a GLP compliant procedure when no expiry or retest date is provided from a supplier of a reference/control item?

For antibodies it is quite normal that suppliers do not include this information. The OECD advisory document number 14 (The application of the Principles of GLP to in vitro studies) gives some guidance but, for example, it is not clear when the lack of this data should (if at all) result in an exclusion in the study director GLP compliance statement. (MDS)

A As indicated in the OGLP principles, in Chapter 6.1 'Records including test item and reference item characterisation, date of receipt, expiry date, quantities received and used in studies should be maintained'.

Hence, the information should be made available by the supplier. Alternatively a test on the activity of the reference item may be conducted at the test facility or site, or rules should be established providing (in an SOP) expiry dates for certain classes of compounds (e.g. such as antibodies).

SOPs

Q 1. It is clear that current SOPs must be immediately available to those involved in a study. What expectation is there for SOPs to be immediately available to management? (MDS)

A Management should be informed of the contents of SOPs as they have to sign SOPs to enforce them. It should be possible for Management to have ready access to SOPs electronically or to know where the paper copies are available.

Q 2. When a SOP is revised and the new version has both an issue date and a later effective date (to allow for training) what documentation is expected as, for that time, both versions are available to staff?

Is it acceptable to just define in the "SOP on SOPs" that users must only use the new version from the effective date (or record an deviation)? (MDS)

A Users should be instructed and trained how to use SOPs and in particular that they should use it only from the effective date. Furthermore the procedure of the revision of SOPs (distribution, training, use etc.) should be described in the SOP of SOPs.



Archivierung / Archiving

- Q** 1. Elektronische Rohdaten werden bei einer externen Firma archiviert.
- a) Welcher Status hat dieser Anbieter:
Test site, Supplier oder ist der Anbieter ein Bestandteil der Prüfeinrichtung?
 - b) Inwieweit müssen die GLP Regularien an diesem Standort umgesetzt werden?
 - c) Wird der Anbieter von der GLP Behörde inspiziert werden?

A Ad a) An external archive is part of one or more test facilities. Managements of the test facilities should ensure that all responsibilities are assigned e.g. in a service level agreement.

Ad b) All the requirements for a GLP archive have to be implemented as described in Advisory Document No. 15. A trained archivist designated by Management has to be responsible for the archive. QA has to inspect the archive routinely.

Ad c) Yes, as part of the inspection of the test facility.

GLP Behörden / GLP Monitoring Authorities

- Q** 1. Swissmedic inspections:
From your inspections this year, are there any trends in your observations? Where should we (QA in GLP facilities) be focussing our resource? (MDS)

A Inspections are tailor-made for the individual test facilities or sites, and observations therefore strongly reflect the specific needs of each facility. From our observations it is therefore not surprising that there are no clear-cut overall trends when looking at the findings at the GLP pharmaceutical test facilities inspected.

It is only when for example new guidance documents (e.g. OECD, AGIT) are published, that a certain priority is set for inspecting special topics from these documents, and QA-activities may then focus on this for the implementation of new procedures.

- Q** 2. Wann erscheint der nächste "Newsletter"?

A Probably until end of 2007.

Comment MDS:

[Please note that these questions are not all from direct experience but include the outcome of discussions with QA and study personnel from other organisations.]