Questions for SPAQA GLP Monitoring Authority Roundtable 2019

Study Reporting:

1. If a study has been completed, the study report has been finalized and wet tissues were retained. Are any of the following acceptable or allowed?

a) Can additional tests or exploratory analysis be conducted by using tissue samples outside of the original study plan? Does the original study report need to be amended or can this be a new study?

Answer to question a1: No. Within the archiving period, tissues cannot be used for additional tests unless an amendment to the study report is written.

Answer to question a2: An amendment to the final study report is required. In the amendment should be stated that the tissues will be used for additional examinations. Furthermore, the archiving of the tissues/tissue samples should be explained in the report amendment. Remainder of tissues (unused) should be archived after the samples for the additional examinations have been taken.

The additional examinations can run either as an amendment to the original study, i.e. under the same study number, or in a separate study. In the latter case, the number of the separate study should be stated in the report amendment (traceability). It is recommended to conduct additional tests as part of the original study.

See also GLP Interpretations 9.2 and 9.7.

b) Does the final study report of the original study need to be amended to include the additional tests?

See answer to question 1a). An amendment to the final study report is required.

c) Are the tissue samples allowed to be used for a new study or should they be destroyed?

See answer to question 1a). Tissue samples may be used in a new study; samples then should be archived with this study according to OGLP. Remainder of tissues (not used for the additional work) should be archived with the original study and must not be destroyed. See OGLP Annex 2, section 10 para 1 and 2.
Note: If additional work was done under the original study, the archiving period should be re-started from the date of finalization of the amendment to the final report (see GLP Interpretation 10.12).

Study conduct:

2. Is an Amendment to the Study Plan required for changes to the Sponsor contact person or their details (e.g., email address)?

a) Is it acceptable to record the changes in the study folder and include the correct information in the Study Report?

b) Would it make a difference if the change occurs when all experimental work has been completed but the Study Report has not been finalized?

According to the OGLP and OECD Doc. No. 11, the name and address of the sponsor should be provided in the study plan and study report. Consequently, if changes occur, an amendment to study plan is required independent of when the changes occur.

3. Before the study start (i.e., before the study plan was signed), a pre-test was performed under the same study number to determine whether the test item would stick to the glass container. Must this non-GLP pre-test be excluded from the GLP Compliance Statement?

The pre-test was conducted prior to study initiation and was hence not part of the study and can therefore not be excluded from the statement of compliance in the study report.

If the information gathered in this assay will be included in the results of the study, the study director should identify it as a non GLP pre-test conducted prior to study start.
A master schedule listing two studies under the same study number, one being GLP and one being non GLP, may raise questions during an inspection. We suggest to add a suffix to the study number to identify the non-GLP pre-test as such.

Validation of Computerised Systems (CSV)

4. A bioanalytic LIMS system was validated by Company X. Test Facility Management (TFM) released the system for productive use (also for use in GLP studies), once the validation testing was successfully completed, but prior to the generation and signature of the final Validation Report.

a) Is this system considered validated if there is no approved final Validation Report?

According to the OECD Advisory Document No. 17, the workflow for the validation of a computerized system involves the following steps: conduct of tests following a pre-defined plan and retention of documented evidence of all testing procedures, test data, test results, a formal summary of testing (which corresponds to the validation report) and a record of formal acceptance.
In the AGIT guideline «Validation of Computerised Systems» it is recommended to document the validation in a validation report which summarizes all test results and contains a conclusion, whether the system is fit for purpose and is signed by the

validation director (chapter 8). System release by TFM is then based on the conclusion of the validation report (chapter 9).
For a system release by TFM, the essential elements of a validation report need to be available in any case, i.e. documentation of all test results and the conclusion (usually by the validation director) that the system is fit for purpose. This does not necessarily have to be in the form of a validation report (although recommended). We do not understand the procedure to issue a validation report (basis for system release) after system release. We assume that it is a deviation from the usual procedure in the test facility (i.e. from the corresponding SOP).

b) TFM did not make a risk assessment to document the rationale for their actions. Had the risk assessment been done would that be sufficient?

The purpose of a risk assessment is to determine the approach and extent of validation, not to justify deviations from the usual procedure. The deviation needs to be explained (both in the system release statement and in the validation report) and evaluated with regard to the impact on the GLP compliance of the studies concerned.

c) Does the use of this system in GLP studies need to be mentioned or excluded in the studies with respect to the GLP compliance statements?

If it can be demonstrated that the system was fit for purpose and operated correctly at the time of conduct of the study, the data/study results do not have to be excluded from the GLP statement. If this is not possible, the corresponding study results need to be excluded from the GLP compliance statement.

Archiving

Questions to the Swiss interpretations of GLP 2018 (page 32, number 10.9)

5. In the updated GLP Interpretation document (chapter number 10.9), it is defined that after moving of study material to a different archive location the "original" summary amendment must be archived in the new external archive. However, we have the opinion that since the TFM is responsible for the archived material at this external archive and from that perspective we believe that the original summary amendment can stay at our facility. Is it acceptable and sufficient to define this process in our archive SOP accordingly?

   Any change in the archive location requires an amendment of the report. This amendment is then part of the study documentation. That's why it must be archived within the archive. When the TFM wants to ensure a tracking, a copy has to be done to be kept by the TFM. This could be part of an archive SOP.

6. In the same chapter (10.9), it is also mentioned that a copy of the document needs to be sent to the notification authority. During the year, we transfer several studies

to the external archive. Is it acceptable to send a summary of these archive transfers to the authorities by the end of the year or should a copy of each summary amendment be sent separately to the notification authority?

The answer can be divided into 2 cases:

- *They are a few archive transfer but each transfer is documented with a summary amendment. It that case, and after information and discussion with monitoring authorities, it could be acceptable to collect all amendments once a year.*

- *If they are a lot of transfers at the same time, all transfer may be summarized in one single document, avoiding then to make amendments to each studies. This summary has to be sent to the notification authorities. This option has to be discussed with the monitoring authorities and adequately justified.*

7. It is also stated that an agreement with the notification authority is required. What is the rationale for obtaining this agreement with the notification authorities in case study data should be transferred to a different archive location? How should this be documented?

   In case of a multiple transfer, the possibility not to do an amendment for each study transfer but to summarize all transfers within a single document must be justified to the authorities. Then the notification authority can give the green light. This process ensure that discussion took place and that both sides agree on the process.
   There is no formal procedure to reach an agreement with the notification authority, however we recommend a written request.
   In order to keep track of the process, it is proposed to summarized the request for this multiple transfer without amendment of all studies within a signed document addressed to the notification authority.

Test Facility Organisation:

8. Should all job titles for each person has to be specified on an organigram (for example, a scientist may have multiple roles with different quality systems, each requiring specific definition)?

   It is not required to specify all job titles in the organigram. Only the GLP-relevant job functions need to be stated in the organigram (reference: OGLP Art. 5 para 2 letter c).

a) Is it acceptable to include only those that are GLP relevant in the organigram? All responsibilities and titles will be described in the individual Job Description and CV.

   See answer to first question. This is acceptable.

b) Can different organigrams show the same staff for the different quality systems (e.g. GLP/GCP/GMP)?

Yes, this is acceptable. With regard to the Swiss GLP Compliance Monitoring Units, only the GLP organigram counts. A test facility is free to manage and document its organisation. It might even be an advantageous approach for organisations with complex structures to define the GLP test facility organisation in a separate organigram.

Quality Assurance:

9. In a multisite study, the test facility has GLP accreditation but not the test sites involved. Is it expected for the test sites to have QA, and perform inspections on the phases of the study at the test sites, even if the test sites are not claiming GLP?

If the test sites do not claim GLP compliance, and the corresponding activities/data are excluded from the GLP statement, the activities do not need to be carried out under GLP (no QA required). However, TF can ensure adequate standards at test site by e.g. performing QA audits (TF QA) or by the presence of TF personnel during the study.