Questions for SPAQA – GLP Monitoring Authority Roundtable 2018

Study Plan

Why isn't it stated in the Swiss Ordinance on GLP (chapter 8.2) that the study plan must clearly state that the study will be conducted according to OGLP?

Annex 2 OGLP is a copy of the OECD GLP Principles. These principles do not require such a statement. It is also not a requirement according to the Swiss GLP program. Studies can be conducted according to OGLP only once the Test Facility is incorporated into the Swiss GLP compliance monitoring program.
A GLP compliant study plan is normally used only for GLP studies. However, if similar plans are used in a Test Facility for GLP and non-GLP studies, with a risk of confusion, then a statement in the study plan is recommended.

Test and Reference Items

Currently test/reference items are stored at room temperature in laboratories where the air temperature is controlled between 21° and 28°C but the temperatures of these rooms are not documented/recorded.

Would it be sufficient to have documentation in place showing the pre-settings of the air control in this building or would it be required to have some kind of documentation of room temperature in place?
What temperature range would you consider to be room temperature?

According to Article 6.1.2 of the GLP Principles storage procedures should be identified in order that the homogeneity and stability of test and reference items are assured to the degree possible.
In the GLP supporting documents there exists no definition of room temperature. The test facility should define the term "room temperature" as a temperature range (mean value with corresponding tolerance limits) for its purpose in an SOP or in the study plan.
The extent and frequency of monitoring required strongly depends on the nature and the temperature sensitivity of the stored test or reference items, the location of the storage premises and it may also depend on the season.
Documentation of the pre-setting of the climate control unit for monitoring purpose is sufficient only if it is verified that the preset temperature corresponds to the actual temperature in the room.

Study Conduct

Before the start of the experimental phase, it turns out that the lot number of the test item given in the study plan is incorrect. The test item is, however, unequivocally labeled with a unique test item number given in the study plan, so the change will have no consequences

for the experimental phase. Should a study plan amendment be made, or is a deviation sufficient?
After the completion of the experimental phase, it turns out that the lot number of the test item given in the study plan was incorrect. Does it make sense to make a study plan amendment after the completion of the experimental phase, or is a deviation sufficient?

Scenario "Before": A study plan amendment should be generated to ensure that the correct test item will be used in the experimental phase.

Scenario "After": A study plan amendment is not required. In this case the experimental part was completed and the study director should assess whether this deviation had an impact on the study. The deviation is to be mentioned in the final report.
The GLP authorities consider that such a scenario should not occur as long as the study personnel correctly applies the GLP principles.

Before the experimental phase, it turns out that the molecular formula or purity of the test item given in the study plan is incorrect. The error is so small that it has no consequences for the dosage of the test item during the experimental phase. Should a study plan amendment be made, or is a deviation sufficient?
After the experimental phase, it turns out that the molecular formula or purity of the test item given in the study plan is incorrect. The raw data are fine, so the experimental phase is still completed, but the subsequent calculations will have to be repeated with the corrected values. This will be done by the study director. Does it make sense to make a study plan amendment after the completion of the experimental phase, or is a deviation sufficient?

Scenario "Before": A study plan amendment should be generated to correct the wrong information in the study plan.

Scenario "After": The deviation was only identified after the experimental phase, a study plan amendment would only be required if the description regarding e.g. the calculations by the study director had to be adapted. Otherwise, a deviation in the final report is sufficient to explain the modified calculations.

Equipment Records
To keep records secure, log books are kept in the Archive with the amount of information immediately available with the equipment restricted to the following

- active logbook entry record (e.g. to record weekly cleaning)
- the equipment registration document
- if appropriate, change control documents (e.g. person responsible for the equipment; change of equipment location).

When an anomaly is identified, entry into the active logbook entry is made (for example, "software error, see Equipment Documentation. The full description is filed in the logbook in the archive. Do the inspectors expect the documented description of the anomaly to be accessible or is storage in the Archive acceptable?

Information immediately available with the equipment should be sufficient for the operator to make sure that the equipment is "under control" according to SOP.
A software error should be documented in the active logbook, with a description of the consequence (validation or not) and the date the equipment was released for use. The description of the software error may be filed in the logbook in the archive.

Study Termination
When a GLP study is to be terminated and no report will be written, a Study Plan Amendment is written. In the Amendment, does the status of the study have to be adapted to “non-GLP”?

The status of discontinued GLP studies should not be adapted to “non-GLP” because the study documentation already acquired at the time of study termination (e.g. study plan, raw data) and also the samples of test and reference items (if applicable) still have to be handled in compliance with the Principles of GLP and need to remain available, e.g. for tracing back the reasons for discontinuation of the study. The items according to Article 10.1 of the GLP Principles should be retained in the archive for at least 10 years after termination of the study (Point 10.7 of the Swiss Interpretation of the GLP Principles). Setting the state of a discontinued study to “non-GLP” would move the study out of the scope of the GLP quality system which is not acceptable.

Software
What records are expected for GLP compliance when office PC software is updated (e.g. Windows upgrade; change of Microsoft Office version used for preparation of study plans, study reports, spreadsheets etc.)?

According to the Appendix 1 of the AGIT “Guideline for the Validation of Computerized Systems” a standard office PC is a “Category A” system (Exempted Systems) for which no validation is needed, but some documentation is requested (Inventory list, system description). The AGIT Validation guideline and the OECD Advisory Document No. 17 in section 1.9 describe the documentation requirements (records).
Software upgrades in the context of maintenance should be considered as critical and the impact of all changes should be evaluated. This should be recorded. It is recommended to consider the intended change procedure as described in the AGIT Guideline for “Change Management and Risk Assessment of Validated Computerised Systems in A GLP Environment” (see point 4.4 and section 5). Regarding the preparation of study plans or study reports software upgrade might be of low impact and therefore a documentation update might be considered sufficient. For spreadsheets, the system owner should decide, based on the risk assessment, on the amount of additional testing required. This should be documented (see AGIT “Guidelines for the Development and Validation of Spreadsheets” and point 11.2 of the Swiss Interpretation of the GLP Principles).

Can the IQ/OQ of installed software for analytical equipment sample tracking system be performed remotely by the supplier or a sub-contractor? What documentation (if any) is expected to be available in addition to the IQ/OQ Plan and IQ/OQ Report?

Yes, this is possible. The supplier or sub-contractor should work according to GLP-principles and the IQ/OQ plan and IQ/OQ report is considered an adequate documentation (see also AGIT "Guidelines for Collaboration with External IT Service Providers supporting a GLP Environment").

Archive

Scenario: A document for a study has to be added after the study has been archived (for example, a Study Report (SR) Amendment, original SR signature from Sponsor).
The Study Director submits the document to the archive
The Archivist will (after the standard record of receiving into the archive is completed) add the document to the study records and add a note to the index (with date and signature).
As the study is the responsibility of Management/Archive, is this procedure adequate or would the authorities expect the Study Director to add the document? (If so, what would be the procedure if the SD for the study is no longer with the company?)

The described scenario is according to OGLP and OECD Advisory Document no. 15 and therefore adequate. It is the responsibility of the Study Director to ensure all study related records and materials are transferred to the archive. The archivist is in turn responsible for the management, operations and procedures for archiving in accordance with established Standard Operating Procedures, and the Principles of GLP.