Schweizerische Eidgenossenschaft
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Swiss Confederation

Federal Department of Home Affairs DHA
Federal Office of Public Health FOPH

Federal Department of the Environment, Transport, Energy and Communications DETEC
Federal Office for the Environment FOEN

swissmedic
Swiss Agency for Therapeutic Products

Swiss Interpretation of the GLP Principles 2019

State: Dec 04, 2019

This document contains joint guidelines for the interpretation of GLP Principles according to art. 4 OGLP established by the Swiss GLP Compliance Monitoring Units of:	Federal Office for the Environment (FOEN) Federal Office of Public Health (FOPH) Swiss Agency for therapeutic products (Swissmedic)
Sources:	Extract of SPAQA-meetings 2003 - 2016, OECD-meetings 2008 - 2014, EU-meetings 2005 – 2014 Inspectors Meetings 2005 – 2014. OECD Frequent asked Questions (FaQ) 2014-2016 http://www.oecd.org/env/ehs/testing/glp-frequently-asked-questions.htm EU GLP Working Group: Questions and Answers 2013 - 2016 http://ec.europa.eu/growth/sectors/chemicals/good-laboratory-practice/index_en.htm Working Group of Information Technology (AGIT, Arbeitsgruppe Informationstechnologie) https://www.anmeldestelle.admin.ch/chem/en/home/themen/gute-laborpraxis/agit.html

For updated answers or new questions the date of the actualisation is indicated in the right column "last update" of the table. The state of the remaining questions is May 31, 2016.

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List of abbreviations

AGIT	Working Group of Information Technology (AGIT, Arbeitsgruppe Informationstechnologie)
AOE	Areas of expertise
COTS	Commercial Off the Shelf
CRO	Contract research organization
CV	Curriculum vitæ
ECG	Electrocardiogram
ELS	Early life stage
EPA (US)	Environmental Protection Agency (of the United States of America)
FDA	Food and Drug Administration (of the United States of America)
FOEN	Federal Office for the Environment
FOPH	Federal Office of Public Health
GLP	Good Laboratory Practice
GLPMA	Good Laboratory Practice Monitoring Authority
GMP	Good Manufacturing Practice
GxP	Good (Anything...) Practice
HPLC	High Performance Liquid Chromatography
ID	Identification
IQ	Installation Qualification
IR	Infrared
ISO	International Standard Organization
IT	Information Technology
MAD	Mutual Acceptance of Data
NAChem	Notification authority for chemicals
Ö 2007 1.	Öffentliche Interpretationen 2007 mit Zuordnung zu Grundsatz
OECD	Organisation for Economic Co-operation and Development
OGLP	Ordinance of 18 May 2005 on Good Laboratory Practice (SR Number 813.112.1)
OQ	Operational Qualification
PEL	Prüfeinrichtungsleiter (Leitung der Prüfeinrichtung)
PI	Principal Investigator
PQ	Performance Qualification
QA	Quality Assurance
QAU	Quality Assurance Unit
QS	Quality system
SD	Study director
SLA	Service Level Agreement
SOP	Standard Operating Procedures
SPAQA	Swiss Professional Association of Quality Assurance
Swissmedic	Swiss Agency for Therapeutic Products
TF	Test facility
TFM	Test facility management
US	United States of America
WLA	Work level agreement

Number	Questions (*in italic*) and Answers	Last update
0	**General (OGLP and GLP Compliance Monitoring Programme)**	
0.1	*How should an already certified GLP facility proceed to include **new areas of expertise** (AOE)? Is the GLP certificate valid for the new area of expertise?* Please read section 5.2.1 of the Swiss GLP Monitoring Programm.	June 2017
0.2	*What is the status of studies performed if a test facility is not recertified (i.e. does not receive a new Statement of GLP Compliance)?* In the case a re-certification cannot be provided, the GLP compliance of all studies conducted after the last successful certification is considered questionable. The studies have to be handled on a case-by-case basis, i.e. individually audited regarding their GLP compliance.	
0.3	*Can a stamped or a preprinted date be accepted when signed by hand with initials?* *Should the date be written by hand when dating and signing with initials or would a stamped or a pre-printed date be acceptable? SPAQA Regulatory Round Table, 11 November 2003, p. 2/8* A stamped or a preprinted date is acceptable provided that the date corresponds to the actual date of signature.	
0.4	*Swiss GLP Compliance Monitoring Units' definition of short-term studies with respect to duration*: A consensus has not been reached within OECD on a precise definition of short-term studies. According to GLP consensus doc. no 7, criteria to consider a study a short-term study include "the duration of critical phases, the frequency with which such studies are conducted and the complexity of the test system as well as the routine of the personnel involved, which will increase with growing frequency of study". The Swiss GLP Compliance Monitoring Units defined the frequency, in relation to process-based inspections, as a minimum of 10 studies of the same type per year. Duration should be considered together with the complexity of the critical phases (e.g. multi-site, handling), so that a precise answer with respect to the duration cannot be given. Generally speaking the Swiss GLP Compliance Monitoring Units consider "one working week (in the same test facility)" as a reasonable limit. Consequence: - An Ames test is a short-term study - A 28 days sub-acute toxicity study is not a short-term study - A residue study is not a short-term study	
0.5	*Can test sites also be included in the GLP compliance monitoring programme?* Yes. If test sites i.e. establishments, comply to the requirements for test facilities as outlined in Art.5 OGLP and in the GLP Monitoring Programme they are included in the program and regularly inspected. The inspection can be performed independently or within the framework of	

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	the associated TF. The inspected test sites will be included in the official register and list of GLP TFs on the GLP website www.glp.admin.ch. Test sites are mentioned in the annual report to the OECD either as an independent organization or together with the associated TF. If a test site is not inspected by the Swiss Monitoring Unit the work of this test site is not recognized as GLP-compliant. Furthermore neither PI GLP Statement nor a GLP QA Statement for the phase performed can be issued by the test site.	
0.6	*Are service providers, such as e.g., contract archives, IT service providers or contract QAs included in the programme? Will a GLP certificate be issued to these providers?* Please read section 5.9 of the Swiss GLP Monitoring Programm.	Nov. 2016
0.7	*Is it a significant GLP deficiency when a study director invites the study sponsor to comment on his/her draft report before editing the final version?* It is standard practice for the sponsor to comment on the draft report. However, the study director signs the study report and carries the responsibility for compliance with GLP. The sponsor must not have any influence on the interpretation of the study data. To ensure this, correspondence between the study director and the sponsor should be retained and archived.	May 2016
1 Test Facility Organisation and Personnel		
1.1	*How should the deputization of test facility management be organized?* A suitable person must be defined to act as a deputy. This responsibility should be mentioned in his/her job description. The person has to be trained in GLP on a regular basis. *Is it possible for a test facility manager to fulfill the function of a study director?* This should be avoided if at all possible. In the case that a test facility manager must act as a study director, the deputy test facility manager must take over the role of test facility manager for those studies in which the test facility manager acts as Study Director. This procedure must be adequately described in an SOP.	
1.2	*How often have personal documents to be updated?* Job description and training records of the employees have to be kept up to date. These documents should be checked once per year and updated where required.	
1.3	*Is the test facility manager allowed to sign the study plan in the function of the sponsor?* According to the Swiss OGLP, the study plan has only to be signed by the study director and test facility manager. Many registration authorities in foreign countries also request the signature of the sponsor.	

Number	Questions (*in italic*) and Answers	Last update
	A test facility manager is allowed to sign the study plan in the function of a sponsor if he/she commissioned a study in their own test facility.	
1.4	*For certain studies, parts of the work have to be outsourced to another test facility.* *Is it possible to regard this outsourced part of the study as a stand-alone study with its own study director or should the concept of multi-site studies be applied?* In general, outsourced parts of a study should be performed as study phases (multisite study). It is not recommended to split studies in several stand-alone studies. If the sponsor *requires* the performance of the outsourced part of the work as a stand-alone study at another test facility, it should be stated in the study plan of the original study that examinations which are outsourced to the another test facility are not part of the original study and are performed as a stand-alone study to be reported separately. The concept of multi-site studies has to be applied according to OECD Consensus Document No. 13. The PI has to be mentioned in the study plan and the PI has to document that he/ she has taken note of the study plan. This acknowledgement of the PI can be a signature in the study plan or a separately signed document. The QA of the test site has to report on the results of the conducted inspections to the study director, the test facility management, the PI, the test site management and the lead QA. The PI has to ensure that all generated data are communicated to the study director and that the results of his/ her study phase are adequately reported in a phase report which includes GLP Compliance and QA statements. Alternatively, raw data including a GLP compliance and QA statement may be transferred from the Principal Investigator to the Study Director, who should ensure that the data are presented in the final report. GLP compliance and QA statements of the test site can be attached or incorporated in the final report.	
1.5	1. *Can Test Facility Management be an individual person or a team?* 2. *How is Test Facility Management involved in the approval of SOPs?* To 1.:The GLP principles permit either an individual or a team. In the latter case, the functions should be specified in the respective Job Descriptions. The organisational chart must reflect the TFM organisation. If it is a team, it should be defined how decisions are taken and how the team members are appointed. The NAChem must be informed on all changes in team members according to OGLP Art. 12. To 2.: SOPs must be approved by Test Facility Management. If TFM comprises a team of managers, then the responsibility for SOP approval can be delegated to one or more of these managers, however the delegation of these responsibilities must be in compliance with an SOP and documented in the respective manager's job description.	
1.6	*How does TFM replace a Study Director while their study is ongoing?* Test Facility Management and the newly assigned Study Director doc-	

<table>
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<tr><td></td><td>ument the replacement of the former Study Director by signing an amendment to the study plan. The amendment must include a reason for the change (i.e. a justification). The transfer of the responsibility occurs according to the OECD document 8.</td><td></td></tr>
<tr><td>1.7</td><td>Handling of multinational GLP facilities who have corporate test facility management in another country: Can the GLP test facility management be located in another country? How can test facility management's involvement in the GLP responsibilities for the different sites be ascertained?
Example: The GLP test facility management responsible for GLP sites located in Switzerland and other countries is located in US. The corporate management delegates the authority to perform duties to the site management.

Corporate test facility management has not to be located in Switzerland. The organization chart has to show the location of the TFM. TFM should be available for interviews during inspections (e.g. per videoconference). Personnel documentation should be available in the test facilities (can be copies). Procedures must be established to maintain documented evidence (e.g. training records) indicating that the TFM has received sufficient training in GLP in order to carry out their duties. Involvement of GLP activities by the corporate test facility management could be demonstrated e.g. by signing corporate (global SOPs) and minutes of meetings held with site managements and site QA's. However, since in Switzerland all study plans have to be signed by TFM, it is recommended that the TFM has an appropriate representative on site (e.g. by a manager acting as a deputy).</td><td></td></tr>
<tr><td>1.8</td><td>Which information must/should the Master Schedule contain?

The information a Master Schedule should contain are not specified in detail in the OGLP. The Swiss GLP Compliance Monitoring Units have therefore compiled the minimal information (see below). For both short- and long-term studies, the same requirements are applicable. It should, among others, serve as a planning tool, which requests a continuous alignment; however no retrospective alignment is necessary.

We recommend to mark multi-site studies on the master schedule of the test facility.

<table>
<tr><th>Information</th></tr>
<tr><td>Study identification</td></tr>
<tr><td>Phase identification[a]</td></tr>
<tr><td>Study Director</td></tr>
<tr><td>Principal Investigator</td></tr>
<tr><td>Test Item</td></tr>
<tr><td>Type of study</td></tr>
<tr><td>Study / Phase[a] initiation date</td></tr>
<tr><td>Study / Phase[a] completion date</td></tr>
<tr><td>Date of archiving[b]</td></tr>
<tr><td>GLP / non- GLP (yes/no)[a, c]</td></tr>
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	[a]) for multi-site studies: these information should be specified on the master schedule of the test site. With multi-site studies attention should be paid that a master schedule is maintained at the test facility as well as at all concerned test sites. The phase initiation date should be defined by the test site according to the type of study but it should not be before the study plan has been signed. [b]) This refers to study documentation, if not defined otherwise by the test facility. [c]) As answered in previous SPAQA round tables (2004, 2006), the authorities recommend to include all studies, in order to estimate the total workload of the test facility (OGLP Appendix 1, section 1.8). However if only a low percentage (e.g., 5 %) of GLP vs. non GLP studies is performed, a master schedule only for GLP studies (or in case of multi-site studies: study phases) and validation studies performed according to GLP should be established. For discontinued studies it's advisable to put an entry "discontinued" on the master schedule.	
1.9	*What qualifications are required to be a Study Director?* The GLP principles (i.e. OGLP, Annex 2 paragraph 1.1. g) do not explicitly demand a minimal education level (e.g., Ph.D., Msc. in Natural Sciences, Toxicologist, etc). The GLP principles (and the Consensus Document 8) solely look for professional competence of the Study Director on one hand and for his personality and experience on the other hand. This should minimally include - GLP expertise, - communication skills, - problem solving, - management, and - technical /scientific expertise.	
1.10	*The Study Director of a multi-site study is situated at a contract research organization (CRO) in which the toxicological part of the study is performed. A study phase is performed at the sponsor's site by a Principal Investigator. After termination of this study phase the Principal Investigator forwards the phase report to the Study Director.* *Does the phase report need to be signed by the sponsor?* The GLP principles do not require signatures by Test Site Management or the Sponsor on Principle Investigator's phase report; the sole requirement is the signature by the Principle Investigator, their signed GLP statement and a QA statement. If the lead QA of the test facility performed all QA activities for the phase, the content of QA activities will be reflected in the QA Statement of the study report. In this case, the phase report should show evidence that appropriate quality assurance monitoring was performed at that site.	
1.11	*When conducting studies on residuals, ecotoxicology, and ecochemistry, certain phases of a study may be performed in countries that do not have an established national GLP programme and that do not conduct regulatory GLP inspections. What measures have to be undertaken for these studies to claim compliance to the GLP regulations?*	

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	Phases conducted in countries without a GLP monitoring programme still have to obey *quality requirements equivalent to GLP*. There is no difference with respect to the conduct of the study; such studies must contain a GLP compliance statement signed by the study director. Many countries permit inspections to be conducted by foreign authorities from countries belonging to the *MAD* system. If there was no inspection by a GLP monitoring authority from a MAD full-adherent country, the phase performed by this test site has to be excluded from the GLP compliance statement.	
1.12	*Do you allow deputy study directors to be appointed, and if so, what are his/her rights and responsibilities?* *What should be done in the absence of the study director? The Principles do not refer to a "deputy study director", however Cons. Doc 8 describes the replacement of study directors.* The concept of a deputy study director is not supported in many countries since it is not sufficiently clear on who is the responsible study director for a specific study at a given time. In case of a planned absence of a study director, a new study director can be nominated for a defined period. This can be done in the study plan if it is already known. In this case, the study plan needs to be signed by the initial and the new study director. The Statement of Compliance of the final study report is only signed by the initial study director who also takes responsibility for the activities during his or her absence. Alternatively, the study director can be replaced via amendment to study plan in accordance with OECD Document No. 8 (OECD 8). Analogous procedures are applicable for multi-site studies in case of the absence of the nominated PI.	
1.13	*What is the process, when a completed and finalized study that has changed its owner or sponsor, has to be amended? Is there an obligation to nominate a new study director that signs the amendment to report?* Yes, a new study director will be nominated in a first report amendment. Then, the new study director writes the amendment to the report. If the study was conducted in conformity to the GLP regulations and archived, then all data are available in order to reconstruct the conduct of the study.	
1.14	*If the PI needs to propose a change (amendment) to the description of his phase in the study plan but the study director is on vacation and there is no deputy study director nominated, is it acceptable for the study director to sign the amendment on his return i.e. after the work has commenced?* Yes. The principal investigator should document the proposed amendment to study plan before the work starts. The study director has to be informed promptly after his return. Without delay, the study director writes an amendment to study plan based on the information provided by the PI. In the OECD consensus document no. 13, chapter "Principal Investigator", the process is only described for study plan deviations. The princi-	

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	pal investigator has to confirm the deviation and has to inform the study director in a timely manner. Thereby, the study director can approve the deviation and decide on possible measures that have to be taken.	
1.15	*"Principal Investigator/Responsible Scientist"* *In case a test site conducts non GLP-compliant phase of a GLP-compliant study: can the GLP terminology be used for this part of the study also, meaning that a PI takes responsibility for this non-GLP compliant part of the study or does this person have to be named differently (e.g. responsible scientist)?* Although use of "PI" is not restricted to GLP-compliant phases, authorities recommend using the term PI for GLP study phases only. If other terminology is used within a GLP study, the meaning of these terms should be defined.	
1.16	*Does the PI have to send study raw data to the study director?* Either raw data or a phase report have to be submitted to the study director. If a phase report is submitted, raw data can either be sent with the report or archived at the test site. Raw data must be accessible to GLP Compliance Monitoring Units in any case (originals or verified copies).	
1.17	*When laboratories or equipment of a GLP Test Facility are also used by non GLP personnel, what is necessary to demonstrate that compliance of the Test Facility is not compromised? Is it sufficient to have documentation (e.g. Job description, CV) and a training record to demonstrate relevant training (GLP awareness and use of GLP equipment)?* When laboratories of a GLP Test Facility are also used by personnel from a different, non-GLP compliant company or laboratory, their training records should be available, as documentation that they have the knowledge of the applicable requirements of GLP. Furthermore any measurement on a GLP apparatus should be documented with date/time and visa. The operation and documentation should be performed according to the SOP used for GLP work. Any problem or maintenance operation with the apparatus should be recorded. Obviously, the results of the measurements by non-GLP personnel may not be used for GLP studies.	
1.18a	*Must the personnel conducting service roles and infrastructure support be members of the GLP test facility (including GLP personnel documentation, GLP training courses)?* Concerned personnel do not mandatorily have to be members of the TF, however an adequate and continuous GLP training is required. Depending on the activity, job descriptions as well as training records should be available within the TF. The personnel should be aware of the SOPs that are relevant to their activities.	
1.18b	*In which cases can these activities be covered through work level agreements (WLA)?* *a. an administration worker whose job is to copy GLP documentation (i.e. neither generates nor modifies raw data). Can anyone produce*	

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	verified copies of GLP documents? *b. an employee whose job is to clean cages (i.e. does not come in contact with GLP animals and is not actively involved in GLP studies)* *c. an employee who is responsible for maintenance of the physical plant (e.g. cleaning of floors, heating, ventilation etc).* *d. informatics personnel responsible for on-going maintenance of servers used to store GLP data (performance of back-up, restore)* *e. informatics personnel responsible for activities not directly involved in GLP activities (e.g. Help desk representatives)* To a.: copying: In case of verified copies of e.g., raw data, a member of the TF has to verify, sign and date the documents; the copying can be performed by an administrative person. To b.: cleaning of cages: the procedure has to be performed according to an associated SOP. External staff can perform these activities based on a WLA. The TFM should insure that these co-workers receive adequate GLP training and comply with the SOP. This should be documented. To c.: facility maintenance: the cleaning procedure has to be performed according to an associated SOP. External staff can perform these activities based on a WLA. The TFM should insure that the concerned co-workers receive adequate GLP training and comply with the SOP. This should be documented. To d. and e.: IT personnel: TFM is responsible for the IT systems used by their Test Facility. It is recommended to delegate this responsibility to a designated person within the TF or to an external support company. This designated person is then responsible for the coordination of IT activities. Personal records of the IT personnel in the TF should be maintained and archived. In case of a collaboration with external co-workers, a Service Level Agreement (SLA) should be available reflecting the processes and responsibilities. The TFM should insure that the co-workers receive adequate GLP training and comply with their SOPs. This should be documented.	
1.19	*Are there restrictions on the Test Facility Manager (Prüfeinrichtungsleiter (PEL)) with respect to his/her position within the management of a company (e.g., analog to GMP guidelines)?* The test facility manager should ensure that the test facility operates in compliance with GLP. He should ensure that a sufficient number of qualified personnel, appropriate equipment and materials are available. This requirement does not define a specific position within the management of the company; however the test facility manager should have enough competence to discuss the budget of the test facility and to assume his responsibilities (nomination of study director, etc.).	
1.20	*Head of test facility management as QA? Can the head of test facility management be responsible for quality assurance?* There would be a conflict of interest, and therefore the facility would not be in compliance. An external QA could be used (in particular in the	

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	case of very small test facilities).	
1.21	*If a phase of a field trial is conducted in another Member State under the supervision of a principal investigator and a GLP compliance claim is made, should the principal investigator's test site be a member of the national compliance monitoring programme of that Member State?* The study director (or the principal investigator at the local test site) should inform the compliance monitoring authority in the country where the site is located before the start of the study phase. The compliance monitoring authority of the country where the site is located will then take a decision on a case by case basis. In case the test site is a member of the national programme where the test site is located, this GLP compliance monitoring authority should be contacted to clarify if each study with the test site should be notified.	May 2016
2 Quality Assurance Programme		
2.1	*Can the QS manual ISO 17025 substitute for a QA programme?* The QS manual ISO 17025 cannot substitute a QA programme since it is divergent in substance.	
2.2	*How often should a short-time study be conducted until it can be inspected using process-based inspections?* There are no absolute numbers. The type of inspection (study-based or process-based) does not only depend on the number of studies per week / month / year but also from complexity and duration of individual studies. Once complexity of a study (even lasting for a few hours only) is high and frequency for this type of studies is low (but not justifying routine activity), study-based inspections should be applied. In order to harmonise inspection procedure, the GLP Compliance Monitoring Units consider the following frequencies as a minimal requirement: - 01 -10 studies / year = 100% study-based inspections - 11 – 50 studies / year = minimum 20% study-based inspections - >50 studies / year = minimum 10% study-based inspections The criteria for use of a process-based inspection programme should be reflected in the QA programme. *<u>If not a part of specific GLP studies, recurrent activities such as preparation of media or solutions should be inspected in test facility inspections.</u>* Peer Review Pathology (i.e. Pathologist's review of slides) is not considered to be a short term study. Process based inspection procedures refer only to short term studies, whereas Peer Review pathology could be considered as critical study phase. Therefore the frequency of inspections for Peer Review pathology should be defined in the QA programm	
2.3	*Could you please clarify whether one and the same activity has to be inspected and documented as a process-based inspection and a study-based inspection or whether these are two independent inspections?*	

Number	Questions (*in italic*) and Answers	Last update
	In case a process-based inspection programme will be based on the above mentioned GLP interpretation, it is ambiguous why process-based inspections have to be additionally documented as study-based inspections. *If it is not the case (but rather, in addition to the process-based inspections the study-based inspections have to be performed) shouldn't the critical phases for study-based inspections be planned in advance based on the content of the reviewed study plan?* According to the frequency, short-term studies have to be inspected during their experimental phase (study-based inspection). The studies conducted in-between will not be inspected, they are considered to have been *process-based inspected*, as a consequence of the study-based inspection. The QA statement of the (study-based) inspected study will mention "study-based inspection" with the indication of the inspected phase. This inspection date will be used for the QA statement of the next X studies (of the same study type) with the indication "process-based inspection" and the indication of the inspected phase. For this purpose, the critical phases of the different short-term studies should be defined in advance and the QA should make sure that all critical phases are inspected on a regular interval. QA should also maintain documentation showing that the frequency of inspection is respected. Refer to Consensus Document No 7 II.2.2.1. [NOTE]: Because of the high frequency and routine nature of some standard short-term studies, it is recognised in the OECD Consensus Document on Quality Assurance and GLP that each study need not be inspected individually by Quality Assurance during the experimental phase of the study. In these circumstances, a process-based inspection programme may cover each study type. The frequency of such inspections should be specified in approved Quality Assurance Standard Operating Procedures, taking into account the numbers, frequency and/or complexity of the studies being conducted in the facility. The frequency of inspections should be specified in the relevant QA Standard Operating Procedures, and there should be SOPs to ensure that all such processes are inspected on regular basis.	
2.4	*During an inspection the QA inspector notes his observations on a notepad. The inspection report is compiled in his/her office later on. Are these notes considered raw data or is the inspection report alone decisive? How should theses notes be handled (discarded or archived)?* QA Inspection notes are not considered to be raw data but they are original records. According to the OGLP Annex 2, article 10 b, the records of QA inspections should be retained. As a consequence, both the inspection notes and the inspection report should be archived.	
2.5	*Do results from an inspection at a test site have to be reported to all other test sites as well as test facility management?*	

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	No, this information should be provided to the concerned PI and test site management as well as to the SD, TFM and lead QA. The study director decides whether it is necessary to forward the results to other test sites which might be affected (see OECD 13).	
2.6	*Are all QA staff allowed to sign off a QA statement, even if the study was inspected by somebody else? Which responsibilities are taken by the signee?* All QA staff can sign off the QA statement, if not defined otherwise in the QA programme. The signature on the QA statement confirms that the content of the QA Statement is complete and accurately reflects QA's inspection records.	
2.7	*How should process-based inspections in the QA statement be documented? Should they be listed with reference to the study-based inspection or is it sufficient to document them only in the QA internal records?* The QA statement has to show explicitly, that a study was inspected process-based. Furthermore, the associated study-based inspection needs to be mentioned (date and inspected critical phase).	
2.8	*Is it necessary to list **facility-based inspections** in the QA statement?* It is not necessary to list facility-based inspection in the QA statement.	
2.9	*In a GLP certified facility, is it acceptable to have consultant QA inspectors conduct all the facility and study audits?* Yes, test facility management has to ensure that there is a QA Programme with designated personnel in place. There is no requirement that these QA personnel must be internal employees (Appendix 2, Section 1.1.f). • In this case should the Head of Test Facility QA (i.e. the person doing the outsourcing) be the person named or registered with the regulatory agency as responsible for the implementation of the QA programme or should it be the Consultant? The responsibilities for QA need to be defined in the QA programme and reflected in the contract between the Test Facility and the Consultant. The situation has to be shown in the organization chart and in their job descriptions.	
2.10	*Should checks of equipment records be mentioned in the QA statement?* The content of the QA Statement is defined in the GLP Ordinance Appendix 2, sections 2.2.f and 9.2.d. Study-based inspections are scheduled according to the chronology of a given study, usually by first identifying the critical phases of the study. This includes the inspection of equipment settings/records only if they are study specific. Facility-based inspections are not based upon specific studies, but cover the general facilities and activities within a laboratory (e.g. maintenance and calibration of instruments).	
2.11	*In a test site, the original of the QA inspection report is provided to the*	

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	PI. A summary of the report findings is given simultaneously to the SD, Lead QA, Test Site Management and Test Facility Management. The PI commented report is then forwarded to Test Site Management for approval. Is this procedure acceptable? This procedure is compliant if the summary contains all findings and if it is reported promptly to all parties	
2.12	*Is there a prescribed text to be used in a QA statement?* *If yes, Where is this text published?* According to the OGLP Appendix 2, sections 2.2.f and 9.2.d. as well as in the OECD Consensus Document No 4, the "QA statement would also serve to confirm that the final report reflects raw data…." Therefore, the QA Statement should include a sentence like: "This statement also confirms that this final report reflects the raw data."	
2.13	*Must the QA inspection of draft Phase reports be communicated to the SD, Lead QA, and TFM or just to the PI/TSM?* According to OGLP "Appendix 2, sections 2.2.e" all inspection results need promptly to be reported to the Study Director, and to the Principal Investigator(s) and the respective management, when applicable. This corresponds to OECD document No. 13 section "responsibilities of test site QA". However, the principles of GLP require only one inspection of study reports, e.g. the inspection of the draft and final draft report can be summarized in one QA report.	
2.14	Is it possible to consolidate process-based inspections by grouping similar study types together in the inspection programme? (e.g Test Item Formulation for Fish Tox and Fish ELS study types). Process-based inspections refer to a given study type and should not be further combined with other type of studies. However, experiences from inspection of other study types may influence the selection of critical phases that have to be inspected.	
2.15	*How does QA review a „draft Pathology" report against raw data if the data themselves are not finalized? (Many companies use e-data capture systems to record histopathology findings. These findings are not audit trailed until the report has been finalized).* A pathology report should be based on raw data, allowing a QA check. Electronic systems should always allow an audit trail, if they are used for raw data.	
3 Facilities		
3.1	*Should GLP premises be labeled as such on site?* A sufficient separation or appropriate label to distinguish between GLP and non GLP should be ensured, to eliminate the risk of mistaken identity or cross contamination. The type and use of individual rooms within	

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	the GLP Test Facility should be documented in the site building plans.	
4	**Apparatus, Materials, and Reagents**	
4.1	*Is it required that all instruments used for GLP studies are calibrated or validated?* According to the GLP principles, paragraph 4.2, "Apparatus used in a study should be periodically inspected, cleaned, maintained, and calibrated according to Standard Operating Procedures. Records of these activities should be maintained. Calibration should, where appropriate, be traceable to national or international standards of measurement." Therefore, it is required that the instruments are calibrated in regular intervals. Computerized systems have to be validated.	
4.2	*Is a qualification (IQ, OQ, PQ) according GMP acceptable as validation according GLP requirements?* Yes, if it is sufficiently documented. The recommended procedure for validations under GLP is described in the "Guidelines for the Validation of Computerised Systems" of the Working Group Information Technology (AGIT). According to this document, the validation can be carried out in a manner analogous to a GLP study, with a validation plan, raw data and a final report. A GMP validation is acceptable, if the validation is carried out according to standard GMP procedures with IQ, OQ and PQ and if the responsibilities are clearly assigned. IQ and OQ can be carried out by the vendor on site, but must be confirmed with a written report. PQ should be done by the user on site, if necessary together with a representative of the vendor. The acceptance criteria have to be defined in order to cover possible critical conditions of the studies that will be performed in the test facility. Templates and forms of the vendor can be used if they fulfill the needs of the test facility. Even if the practical work is done together with a vendor's representative, a validation director within the GLP test facility should be responsible for the validation plan, the performance of the validation and the validation report. Test facility management is responsible for the validation of the com-puterized systems.	
4.3	*What are the verification and calibration requirements for anemometers in field studies?* According to the principles, a test facility should have established clear SOPs for the periodic inspection, maintenance, cleaning and calibration of the equipment. Anemometers are expected to be calibrated to show that they are fit for purpose. High wind speed might result in reduced amounts of test item applied to the crop and, as a result, in an underestimation of residue levels in crop samples. For that reason study plan and/or SOPs on spraying should define the conditions during spraying including the maximum allowed wind velocity during application.	May 2016
5	**Test Systems**	
5.1	*Is it possible to perform a single GLP study for the characterization of the test item if several physical or chemical test systems such as HPLC, melting point system, IR spectrometer, pH-meter, viscosimeter,*	

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	and other instruments are used, or is it necessary to perform an individual study for every test system? It is acceptable to determine several parameters of a specific test item in one study. According to paragraphs 8.2(a) and 9.2(a) of the GLP ordinance, the title of the study should be descriptive. The tests should be mentioned in the title. "Physical-chemical characterisation" is not sufficient to understand which tests are included.	
6	**Test and Reference Items**	
6.1	*Is it required that the characterisation of the test item be performed under GLP?* See (OECD19)	
6.2	*Should the determination of homogeneity, concentration and stability of the test item in the vehicle always be performed in a GLP compliant test facility?* See (OECD19)	
6.3	*Should, from a commercially available reference item, a sample be archived?* Yes, a commercially obtained reference item will also require a sample to be retained.	
6.4	*What has to be done in case the sponsor does not specify an expiry date for a test or reference item?* The test or reference item can be analyzed on site, or rules regarding the expiry date for certain classes of substances can be defined in an SOP. In the case that no expiry date is available this must be stated, justified in the final report and excluded from the GLP Compliance Statement.	
6.5	*How should a test item delivered from the sponsor be checked?* See (OECD19)	
6.6	*Should a solution of test item be used for GLP purposes if the test item expiry date (of the powder) has already been reached?* See (OECD19)	
6.7	*If the test item is sent back to the sponsor after the study, is it acceptable that it is stored in the freezer of the sponsor and not in a GLP compliant test facility?* See (OECD19)	
7	**Standard Operating Procedures**	
7.1	*When does an SOP become effective?* In case no specific effective date is indicated, the date when test facility management signs the SOP is the date that the SOP is effective.	

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7.2	*Can QA management approve SOPs?* No, all SOPs have to be approved by test facility management.	
7.3	*What are the GLP requirements regarding the creation of multilingual SOPs?* A test facility can have multilingual SOPs if the following requirements are fulfilled: 1. The original language for an SOP has to be defined. 2 .The test facility management must assure that the content of the SOP version written in different languages is similar. 3. The test facility management must approve all SOP versions written in different languages. 4. In any translated SOP reference should be made to the original. 5. In case the original SOP will be revised, also all existing SOP versions written in another language have to be revised at the same time and must be labeled with the same revision number as the original SOP.	
7.4	*Is it necessary to describe in-house test methods in SOPs?* Such test methods can be handled in a different way than SOPs and do not need formal approval from TF management. However "internal" test methods should be approved by a designated person, have a date of validity and a version number and be archived. Test methods obtained from sponsors should be handled in the same way. Deviations to the test methods during a study should be documented and treated in a manner analogous to SOP deviations (assessment by study director for their impact on the study)	
7.5	*What are the authorities expectations regarding attachments to SOPs used for documentation, e.g. forms, regarding the traceability to the "source" SOP, versioning and content of information?* Expectations are that the respective version number of the "source SOP" can be readily traced back from the attachments. Hence, the attachment must be • Identified with the SOP name and version number • Archived with the respective version of the "source" SOP The modification of attachments must be described in an SOP. Alternatively, it may be decided that changes in attachments are directly combined with a change of the SOP.	
7.6	*Who must assess the impact of facility SOP deviations? Who must be informed? (e.g. The master schedule sheet is not appropriately maintained as per internal SOP).* Ultimate responsibility lies with the Test Facility Management, who has to sign and enforce the SOP. Deviations not associated with a specific study should be provided to Test Facility Management for their assessment. Assessments should be conducted by TFM or a designated person.	

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8	**Performance of the Study**	
8.1	*How should different language versions of a study plan be handled?* According to GLP there is only one study plan, which contains all the relevant information. Abstracts or complete translations thereof are considered work instructions. They become effective by the study director's signature and should be archived upon finalization of the study.	
8.2	*When is the experimental starting and completion date of a study?* The experimental start/completion of the study is according to Annex 1 OGLP the date on which the first/last study specific data are collected. In case there is a so called pre-test prior to this date, e.g. for the collection of base-line values specific for a study, this should be considered as the experimental starting date. Since this is a rather general definition further clarification can be provided. 1. An SOP describing the conduct of a study should list specific activities to determine the experimental starting date for a specific type of study. 2. The study plan must include the proposed experimental start and completion dates, with reference to the first/last activity to be performed. (e.g. The experimental start of the study is on XX.XX.XXXX by ……..). With regard to cell culture studies, the day of seeding the cells for the first experiment can be considered as experimental starting date if the prior activities (e.g., preparation of culture medium, thawing of cells) are covered by general facility SOPs.	Dec 2019
8.3	*Are signatures on faxes or print out of e-mails acceptable as approval of acceptance of study plan or study report by PI or sponsor?* It is acceptable to sign the faxed copies and to send the originals later, but the GLPMA inspector needs to have access to the originals. *How should the approval of the PI to the description of his/her phase in the study plan be documented?* The approval can be done in written form (e.g. E-mail with electronic signature), as PI Acknowledgement or by signature of the study plan before signature by the SD. The test site management has to nominate the PI. *Are signatures on faxes, scans or print out of e-mails acceptable for PI Acknowledgments or for the approval of the study plan by TFM?* Signatures on scans or faxes are accepted. The original signed paper version has to be archived with the study documentation.	
8.4	*In the case that a PI prepares a separate phase plan (e.g., a bioanalytical plan) describing the method in more detail, is it acceptable that this separate phase plan is not attached to the study plan or to its amendments?*	May 2016

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	According to OGLP 8.2.e.5 the study plan must contain "Detailed information on the experimental design, including a description of the chronological procedure of the study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed, and statistical methods to be used (if any). Therefore the study plan must include descriptions of the individual phases. If some of the requested information is missing at the time of experimental start, the information can be added to the study plan as study plan amendment. In case the test facility or test site is located abroad and the respective national GLP monitoring unit requires a separate "phase plan" then it can be accepted under the condition that the phase plan is referenced in the study plan.	
8.5	*Does an amendment have to be distributed to all PIs, even if they are not concerned by it?* Yes, the amendments have to be distributed to the same persons to whom the study plan was distributed.	
8.6	*What is the procedure in case a GLP study is definitively terminated?* A written confirmation of the study's termination must be generated as a Study Plan amendment. The reason for the termination must be given therein. The study plan, amendment and all study documentation/materials should be archived.	
8.7	*In GLP studies, the study plan requires signatures from the Study Director to initiate the study. There is nothing in the OECD GLP guideline that QA has to sign the study plan but only to verify that the plan is in compliance with the GLP principles which should be documented (and this is done by means of an audit and an audit report) and to have a copy of the study plan.* *Is it mandatory to have QA signature in the study plan? If so, does the signature have to be the same date as the SD signature?* No, it is not mandatory to have QA signature in the study plan. QA signature in the study plan can be used as documentation of the verification in replacement of an audit report. This process should be defined in the QA programme. In the case that QA signs the study plan, this should be done before, or on the same day as that of the Study Director's signature, as with the SD signature the study is initiated.	
8.8	*As per OECD GLP, the PI acts on behalf of the SD for a multi-site study and has defined responsibility for the delegated phase of the study, and a scientist is someone who contributed to the Final report (i.e. who is usually the (Bio)Statistician).* • *Why is it that a Statistician is named as a PI and the Statistician location is considered a test site when the statistician does not participate in the study conduct or experimental phase of the study, generate or collect study raw data but only analyzes the data after the conduct of the study or experimental phase of the study has been completed?* • *In addition, if the statistician is considered as a PI and his location is a test site, then a test site QA is required and a GLP compliance statement from the statistician is required. There is no distinct descrip-*	

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	tion of the role of the statistician in OECD GLP. The statistician generates results and this should be done with a validated system as required by GLP. Therefore he is involved in the study performance. The statistician could be nominated as a member of the test facility organisation. In this case he would be considered “study personnel”. If the statistician is not a member of the test facility, he should be a member of a GLP test site. In this case, he can be designated as a PI and has to sign a GLP compliance statement for his part of the study. Finally, it the statistician is not working in a GLP structure, his contribution to the study has to be excluded from the GLP compliance statement of the study director.	
8.9	*Can a study director schedule use time periods in the study plan in order to get some flexibility in the daily planning of specific activities (such as e.g., ECG or eye examinations, euthanasia and section, etc.), thus allowing that the date of the corresponding activity can be decided within these time periods without announcing in advance the exact date per amendment to the study plan.* Yes, but these proposed time periods should not exceed reasonable time limits. QA must be informed of the actual timelines to enable them to schedule inspections etc.	
8.10	*Temperature and relative humidity in the animal rooms, and body weights of the animals to be used are indicated in the study plan as “target ranges”.* *Can this “range” be reported in the study report or are the actually measured maximal and minimal values to be mentioned as “ranges”?* Actual values have to be reported. An exception could be accepted for environmental conditions in the animal rooms (temperature, relative humidity), which should normally fall into the “target range” but among which deviations outside the normal range could occasionally be observed. In this case, the “target range” can also be mentioned in the final report in addition to the observed “deviations” which are to be reported (either globally or individually).	
8.11	*What is to be documented if solutions of test or reference items were prepared before signature of the study plan?* If the solutions cannot be prepared again after signature of the study plan, the study director should exclude these activities from his/her GLP compliance statement and indicate the reasons for that. In case these solutions were prepared in another GLP study this should be described accordingly in the study plan and must not be excluded from the GLP compliance statement.	
8.12	*In order to calculate the concentration of test/reference item in study samples, chromatograms generated during analysis are subject to appropriate quantitation integration methods. Automated integration is used as the default method.* *Please comment from a GLP perspective on the acceptability of re-integration of chromatograms. If re-integration is permitted, presumably this should only be under certain circumstances which are clearly de-*	

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	fined by SOP and can be fully traced in the raw data. Re-integration is permitted as long as the re-integrated chromatogram can be traced back to the “source chromatogram”. The reason for the re-integration should be indicated. Re-integrated chromatograms must be clearly identified as such and the procedure for re-integration needs to be described in an SOP. The original (source chromatogram) needs to be kept with the raw data.	
8.13	*How should mistakes occurring during a study be documented?* Spelling errors, calculation errors etc. have to be corrected with date, initials and reason. They are not considered as deviations to the study plan and are not stated in the report. Mistakes occurring during the performance of the study (deviations to study plan, to SOPs or analytical methods; e.g. application of a wrong dosage) or the occurrence of unexpected events (e.g. power black-out in the temperature-controlled rooms) have to be documented in the raw data with date, initials and reason by the study director/ PI. They have to be commented as deviations to study plan in the study report and the impact of the deviation on the results of the study has to be assessed.	
8.14	*What has to be considered when in addition to the OECD GLP Principles, additional GLP guidelines are mentioned in the study plan?* *The sponsor wants to include other GLP regulations than the Swiss OGLP and OECD guidelines in the study plan (e.g. JMAFF, EU, FIFRA).* *a) Is there a change in the duties of the test facility?* *b) Would legal issues be expected?* If it is stated in the study plan that the study will be conducted according to the listed regulations/guidelines, it has to be ensured that all additional requirements of these regulations/guidelines will be followed. If however the study plan only states that the guidelines listed are compatible with the OECD GLP Principles, then no additional assurances/activities are needed. An example of such a phrase has been agreed with US EPA: "Conducted in accordance with OECD Principles of GLP, which is compatible with EPA GLP (40 CFR Part 160 and 40 CFR Part 792)", No legal issues are expected in Switzerland. Legal issues could however arise depending on the cited legislation and its implementation in the respective countries.	
8.15	*Is it possible to use General Study Plans in conjunction with Study Specific Supplements for studies that are significantly longer than 1 month in duration but that are routine in nature and frequently conducted?* *If not, what is considered reasonable as the cut-off point?* *If yes, would such procedures be accepted by other regulatory agen-*	

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	cies? A general study plan and study specific supplement can be used for the conduct of short-term studies. Short-term study is only defined as "study of short duration, with widely used routine technique", however the OECD consensus document no 7 gives some general aspects to be considered (duration of critical phase, frequency of the studies, complexity of the test system, ..). Generally speaking "one working week, in the same test facility" is a reasonable cut-off point. An OECD regulatory agency has the possibility to request that the Swiss GLP Monitoring Authorities conduct a study audit, if it has reasons to think that the GLP principles were not respected for that study or in the case that the studies' results are very important for the assessment of the test item. The use of a general study plan in conjunction with a study specific supplement - as far as both documents contain all required information to conduct the study - is certainly not a reason to raise a doubt about the studies' GLP compliance.	
8.16	*Please define „Pathology raw data". If pathology raw data includes the interpretations of the study pathologist that are found in the Pathology report, when does this „pathology raw data" become final?* (Background information: As per the FDA interpretation given in the Preamble, 58.3(k) defines raw data as laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities and are necessary for the reconstruction and evaluation of the final report. Although the notes taken by a pathologist during histopathological examination of slides are indeed the result of original observations, these notes are not necessary for the reconstruction and evaluation of the final report. The final report is evaluated by an analysis of the pathology syndrome as described in the pathologist's report, which is required under § 58.185(a)(12). Further, because § 58.190(a) requires histopathological blocks, tissues, and slides to be retained as specimens, the final report can be reconstructed by verification of the pathology findings by, e.g., a second pathologist or by a team of pathologists. The pathologist's interim notes, therefore, which are subject to frequent changes as the pathologist refines the diagnosis, are not raw data because they do not contribute to study reconstruction. Accordingly, *only the signed and dated final report of the pathologist comprises raw data with respect to the histopathological evaluation of tissue specimens.* Raw data are defined in the OGLP as all original test facility records and documentation, or verified copies thereof, which are the result of the original observations and activities in a study. Pathology raw data should be handled in the same way as other raw data. The signed report of the pathologist comprises the raw data.	
8.17	*Under which circumstances may study plan provisions take precedence over SOPs? Is QA allowed not to highlight differences between study plans and facility SOPs as deviations claiming that SOPs are superseded by study specific methods and procedures detailed in the study plan?*	

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	Such a practice can only be accepted under certain conditions. Deviations from the study plan should also be documented in the study records and, additionally, be presented as such in the study report. There should be a very detailed study plan signed by the study director and verified by QA and there should be no ambiguity between the study plan and the SOP.	
8.18	*The study plan can contain confidential items which the study director may not wish to disclose to all test sites to which experimental phases are delegated.* *Is it acceptable that in the copy of the study plan that is sent to some test sites certain parts are blackened? Would it be acceptable that test sites just receive the information they need to perform the delegated phase in a study plan amendment (with no copy of the blackened study plan)?* All personnel involved in a study need to have full access to the complete unedited study plan and its amendments. If the identification of test items or reference items systems is a concern, the GLP principles allow the use of codes to conceal the identity of the test items or reference items.	May 2016
8.19	*Should method validation be completed prior to the initiation of a GLP study?* There is no requirement to finalise the validation of all methods that will be used to conduct a GLP study before the initiation of the study. However, there is an expectation that methods are fully validated before the results of the study are considered to be valid (posted on 21 January 2016).	May 2016
8.20	*What standard should be applied to the validation of methods which are used in GLP studies and how should it be applied?* There is no requirement to perform method validation in compliance with GLP in Switzerland. Since parameters of the validated method are used in the GLP study (for example threshold, linearity, accuracy, precision, stabilities, equipment settings, etc.), data should be accurately recorded and stored in a manner that protects its integrity. Validation data may be required for study reconstruction and, consequently, it should be retained for an appropriate period of time – at least 10 years in Switzerland.	May 2016
8.21	*Re-calculation of bioanalytical data is sometimes required by registration authorities. If the bioanalytical raw data has been defined to be paper instead of the original electronically acquired data, how are these re-analyses to be performed (Manual entry to analysis software? Reversion to original e-data?)* It is possible to use original e-data, but it should be verified that these data are identical with the original raw data on paper. This check should be documented and eventually justified.	May 2016
8.22	*Currently it is accepted that for electronic data the paper printouts are defined as GLP raw data. Often companies still retain additionally the electronic data in the system or on a separate server. What are the expectations concerning the retention of electronic data in bioanalytical labs especially data derived from e.g. acquisition software like Analyst?* These additional electronic data are not considered GLP raw data according definition. Obviously, the printed data have to contain all infor-	May 2016

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	mation, not only the measured raw data, but also methods, acquisition parameters, measuring sequences and so on. Therefore, there are no requirements regarding storage of the same data in electronic form.	
8.23	*When commercial software is used that has different options for data evaluation, how detailed should the description be in the Study Plan (is software name and version sufficient or must the evaluation parameters to prevent bias be stated)? Is the advice different for software such as Excel than for scientific software (e.g. Parallel Line Analysis (PLA))?* The study plan should - in addition to software name and version – include the parameters for data evaluation or instructions how the evaluation should be done and documented. It can also refer to an SOP on data evaluation or give a set of criteria that have to be considered for chosing appropriate parameters.	May 2016
9 Reporting of Study Results		
9.1	*Can a flawed final report be declared invalid and be rewritten?* Mistakes or flaws detected after completion and signing of a final report can only be corrected via an amendment to report. A declaration of the invalidity of a final report and/or replacement of such a report through rewriting, independent of the size of the rewritten part, are not allowed according to GLP regulations.	
9.2	*Normally, additional experimental work for an otherwise finalized study is reported via an amendment to finalized study report. Can an otherwise finalized study also be reopened by an amendment to study plan?* No, if a study has been terminated by the study director through his signing of the final study report, a study can only be reopened and/or modified through an amendment to final study report (see GLP Ordinance, paragraph 9.1.4.). This is also valid in case additional experimental work is needed. *Please describe the approach that should be taken in the event that:* *a) the phase report has been finalized (signed/approved by the PI) but the sponsor requests some additional investigations. The study report has not yet been finalized by the SD.* An amendment to the study plan should be written. An amendment to the phase report should be used for the documentation of the additional investigations. *b) the phase report has been finalized (signed/approved by the PI) but the sponsor requests some additional investigations. The study report has already been finalized by the SD.* An amendment to the final report should be written by the study director with the contribution of the PI, describing the additional investigations. The results of the additional investigations should be reported in	

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	a further amendment to the final report.	
9.3	*What is the accepted time span between the dispatch of the draft report to the sponsor and archiving?* The time span for receiving the sponsor comments should not exceed six (6) months. Raw data should be stored in a safe place during this time. If the draft report is still with the sponsor after that time, the SD should contact the sponsor and ask for the commented draft report. In case of no answer within two weeks the study should be archived without finalisation. If the sponsor sends the commented draft report at a later date, the study needs to be taken out from the archive. (see also 10.2).	
9.4	*One test item has several trade names. Within a single study, the sponsor requires several final reports, one for each name. Is this possible?* No. However, it is possible to use a neutral code for the test item. The various synonyms must be documented within the study documents.	
9.5	*Can the sponsor sign the final report after its finalization?* If the Sponsor does not sign promptly, the Study Director can archive a copy of the partly signed report and add the completed signature page later (if received!). If the signature page is not returned, this may mean the archived copy has only photocopied signatures (although these can be marked as authenticated copies). According to the OECD principles, the sponsor's signature is not necessary in the final report. Therefore, the final report can be finalized without his signature. The sponsor can sign later.	
9.6	*How many "original" (signed) reports can there be?* Having only one signed original report is preferred. If several "originals" are needed, the number of copies and the distribution list should be defined in the study plan. The individual copies are numbered. The procedure has to be described in an SOP.	
9.7	*What is the procedure to introduce editorial changes in a finalized report?* An amendment to the final report must contain a justification and has to be signed by the study director. The corrections or additions can be documented in the amendment itself or may be integrated in the report by an exchange of pages. The replaced pages have to be labeled clearly as "amended pages" and the original pages must be incorporated in the amendment. The amendment must contain a QA statement that confirms an inspection of the amendment by QA personnel. *What has to be done if experimental data have to be added?* If additional experimental activities should be performed, a first amendment to report should describe the activities and is verified by	

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	QA. A second amendment to report should contain the results of these investigations. In this case, the study director has to sign a new GLP compliance statement. The amendment must contain a QA statement that confirms an inspection of the amendment by QA personnel.	
9.8	*How should the reformatting of a study report (e.g. to meet the requirements of a particular authority) be done?* Reformatting is a mere administrative rearrangement of a study report. The copy of the original study report which has been reformatted by the study director should be marked on the front page as “Reformatted Report”. A supplementary sheet containing information regarding the authenticity can be attached to the report. In addition, the Table of Contents may be adapted. After being signed by the study director the reformatted study report has to be archived together with the original report.	
9.9	*What is the correct sequence of Signatures on the Final Report?* Test Facility Management should ensure that all final reports for which GLP compliance is claimed are audited by QA personnel. This audit should be conducted at the final draft stage, when all raw data have been gathered and no more major changes are expected. After the following checks, the QA representative signs the QA statement: • all issues raised in the QA audit have been appropriately addressed in the final report, • all agreed actions have been completed, • no changes to the report have been made which would require a further audit and • the Study Director’s claim to GLP compliance can be supported. The Study Director carries the overall responsibility and confirms with his signature on the report that a signed QA statement is available in the report. It is recommended that finalisation of a study report by the Study Director should not take longer than 5 business days after the QA statement has been signed. The same principles apply for phase reports.	
9.10	*Which information pertaining to computerized systems used in the study have to be reported in the study report?* In the study report all of the computerized systems (e.g. measuring devices or analysis software) used during the study have to be listed. The version of the software relevant for the study has to be indicated as well. When a computerized system specified in the study plan is changed during the study (e.g. different software or different software version) from that which was listed in the study plan, then the modification has to be recorded in an amendment to the study plan or as a deviation. Further information concerning the system’s validation, system owner, or previous modifications have to be documented and archived in the test facility.	

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9.11	A CRO drafts a phase report with data of performed analyses. Tables show only single values but no group averages or standard deviations. After review the sponsor monitor would like to add tables with averages and standard deviations and results (e.g. bioanalytics) from other study phases in the summary. He delivers the tables to the PI for their integration into the report. The PI finalises the Phase Report with Tables he did not create. *How should the PI respond if the Study Director or Sponsor wants to have data added to the phase report that the PI had nothing to do with?* *What must the PI or the Study Director/Sponsor consider and document?* Regarding other data, e.g. the results from other phases: It should be mentioned in the report that these data were provided by the Sponsor. The PI statement of GLP compliance should reflect this fact. Simple mathematical operations such as average and standard deviation can be calculated by the PI. He can calculate them from his data and include them in his phase report.	
9.12	*If two different formulations are tested in a study, can there be two different independent study reports, reporting the results for each formulation?* No, according to the principles, the final report should contain "all information and data required by the study plan". This means that there cannot be two different final reports, each reporting only half of the data required by the study plan. A GLP study strictly has one study plan and one study report (the so-called 'rule of ones'). This also applies to multi-site studies, as outlined in OECD consensus document 13 on 'The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies'.	May 2016
9.13	*As per GLP principles, "the storage location of the study plan, samples of test and reference items, specimens, raw data and the final report are to be specified in the final report". Historically, the "location" was interpreted to be a physical location.* • *To what level of detail must this location be referenced (Company name/city/Country) or more detailed?* • *For electronic final reports and/or electronic raw data stored in a cloud or via an external storage providor, what physical location should be provided? (In a cloud environment, this could easily change and would not be transparent to the SD).* • *Do amendments to the report have to be written each time a location changes?* • *Could one state under who's responsibility the materials are stored rather than a physical location?* The description of the location should be sufficient to permit access to the study specific documents or samples and depends on the test facil-	May 2018

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	ity situation. It is e.g. acceptable to indicate "stored in the GLP archive of (or at) the test facility", since the name and address of the test facility are indicated in the final report. In the case of storage at a contracted archive, the name, city and country of the place or of the archive owner is expected. *In the case of e-archiving, the name and address of the test facility should be mentioned. In case of external storage of electronic documents, also the name and address of the e-archive service provider should be available.* *When a storage location changes there should be a documentation allowing to identify the new location. This can be an amendment to final report.* If a high number of reports is affected please see interpretation 10.9.	
9.14	*What is the position of the GLP Compliance Monitoring Units about the issuance of interim reports (e.g. a study report issued before the end of the experiments of the study) that claims GLP compliance?* Sponsors can request test facilities to generate interim reports for studies that are conducted in accordance with GLP. An interim report is a report of a non-completed study. Interim reports are requested by some receiving authorities in specific circumstances, for example, in case of public health alerts to expedite the availability of the test item for clinical purposes or to collect information on its toxicity. There is no objection to the generation of interim reports that do not contain a study director's claim of GLP compliance. However, the GLP Principles only recognise one final study report which details the conclusions of the study. The interim report that claims GLP compliance should therefore clearly indicate which phases of the study are completed and which are not. This information should be presented in a way that is transparent and avoids any confusion between an interim report and the yet to be issued final study report. Any GLP compliance statement submitted with an interim report should indicate to what extent the study is compliant with the GLP Principles at the date the interim report was written. Specific attention should be paid to the validity of the results presented in the interim report. Any limitations to the validity or associated interpretation of the results should be clearly stated as part of the interim report. The interim report should also include a QA statement detailing the portion of the study covered by QA inspections.	
10 Storage and Retention of Records and Materials		
10.1	*Can GLP and non-GLP documents be archived together?* GLP regulations do not exclude shared archiving of GLP and non-GLP documents. However, i) restricted access to GLP documents must be guaranteed, and ii) management of the GLP area must not be negatively impacted. If GLP documents are stored physically separated from non-GLP documents within the same room (i.e. in a separately secured cabinet), restricted physical access only applies to the GLP documentation.	
10.2	*Is it allowed to establish interim archives?* Interim archive is not a GLP term and thus its use should be avoided.	

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	Relevant documents of ongoing studies, which have to be stored temporarily (i.e. waiting for the Sponsor's comment) can be transferred to the archive on a temporary basis. They have to be registered by the archivist. Study directors should use lockable cabinets for short-term storage.	
10.3	*Does the loss of "documents" have to be considered as major deviation?* Yes, in case the documents are listed in Chapter 10.1 of Annex 2 GLPV. The studies impacted by the loss of these documents might be considered as non compliant depending on the nature of the documents.	
10.4	*Can study directors, QA or, laboratory personnel or Test facility management act as archivist?* Study directors may not act as archivists due to their involvement in the conduct of studies. Facility management and QAU personnel may take this role. However, in that case, inspection of the archive has then to be performed by another QA person or by an external QA. Laboratory personnel can act as archivists even if they are involved in the conduct of studies. However in the role of archivist they directly report to the TFM.	Nov. 2016
10.5	*Which requirements apply to data archived on CD-ROMs?* For all data/document archiving (paper, magnetic tapes, optical disk, etc.), the same requirements apply concerning access controls, orderly storage and retrieval, and stability under archiving conditions. In case of archival on CD-ROMs the following aspects need special attention: • If data from several studies are archived on the same CD, a detailed index is necessary. • CD must be readable at all times during the archive period. This needs special consideration in the case that the computerized system or the CD player are replaced. • All original test facility records and documentation, or verified copies thereof are defined as raw data. When original raw data are scanned and saved on CD the process should be validated and documented. The CD is considered as a "verified copy" of the original raw data. • Methods should be in place to avoid or at least clearly document erroneous or intended changes of the data on the CD. Related documents: - OECD advisory document No. 15 "Establishment and Control of Archives that Operate in Compliance with the Principles of GLP". - Working Group for Information Technology (AGIT) document "Guidelines for the archiving of electronic raw data in a GLP environment" (Link AGIT).	May 2019
10.6	*Is it possible that a Study Sponsor archives the study documentation for a finalized study?* Yes, if the documents are archived according to GLP requirements for the required retention period. However, for inspections by the GLP MA,	Dec 2019

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	the documents must be made available at the test facility's site – i.e. the Sponsor must return all documentation to the Test facility for a GLP MA inspection or a certified copy of all records must be maintained. The archive location of all original documents must be stated in the final report of the study. If the location is changed during the archival period, e.g. upon request from the sponsor, an amendment to the report would have to be written. If a high number of reports is affected please see interpretation 10.9.	
10.7	*If a study is discontinued before finalization, is it required to keep documents and samples for 10 years?* Yes. The documents listed in article 10.1 in the principles should be stored in the archive for at least 10 years after termination of the study. According to the GLP principles, article 10.2, samples of test and reference items and specimens should be retained only as long as the quality of the preparation permits evaluation.	
10.8	*Documents regarding repair and maintenance work of equipment should be kept close to the respective equipment. The same applies for manuals, logbooks etc. In case the equipment is decommissioned all documents need to be archived.* *What needs to be done with the documents in case* *a) the equipment will be transferred to another department (e.g. non GLP)?* *b) the equipment is temporarily put out of use/deactivated ?* *c) the equipment will be sold?* According to section 10.1.d of the OECD Principles on GLP and the actual version of the Swiss Ordinance on GLP, documentations and reports from maintenance and calibration work of equipment should be archived. a) In case the equipment will be transferred to persons not working under GLP, the equipment documents and reports or verified copies of thereof should be archived. All activities performed as a consequence of the transfer need to be documented and archived. b) Documents can be left for a short time together with the Out of Use or deactivated equipment, however it is recommended to transfer the documents in the archive to guarantee their long-term retention. In any case, one must make sure that the allocation of the documents to the respective equipment is guaranteed, eventual maintenance work is documented and any potential loss of information is obviated. The deactivation, transfer of documentation to the archive and the reactivation of the instrumentation, if applicable, must be documented. c) In case the equipment is sold, the documentation and report or verified copies of thereof have to be archived.	
10.9	How are study reports amended if study-related data for a high number of studies is moved to a different archive location during the 10-year archiving period?	Nov. 2018

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	The location of the study-related data needs to be indicated in the final report or in a respective amendment to report. If study-related data for a high number of studies is moved, for justified reasons and in agreement with the notification authority, a document can be established which is signed by the test facility management, instead of an individual amendment per report. The document has to describe the transfer as well as the location of the new archive including the date of transfer. The document has to be kept in the new archive (original) and if the test facility does no longer work under GLP, also by the contact person of the former test facility. Furthermore, a copy of the document needs to be sent to the notification authority.	
10.10	*Is it acceptable to use IT companies based in another country to perform electronic archiving and data back up? What measures should test facility management take to ensure that the facilities are fit for purpose? Is there a need for QA monitoring of these functions as part of the facility inspection? What level of training should the employees of the IT company receive? What level of access to data should individuals have?* Electronic archives are allowed also when they are located abroad. The following must be assured: Access for inspections (QA and/or GLPMA) must be guaranteed at any time. Personnel with the necessary know-how regarding the management of the electronic archive must be available during inspections. In case an inspection is requested by a Swiss GLP monitoring authority, the procedures as described in OECD Consensus Document 12 would apply in order to guarantee the mutual acceptance of this inspection. Documentation and safety measures as required in OECD Documents No 10 and 15 must be available and described in SOPs and/or a SLA. The following roles should apply for QA: QA must be able to read the electronic data independently or in special cases with the support of an IT person. Test facility management is responsible for the inspections of electronic archives. Duties and responsibilities must be described in the QA program. An archivist should be nominated who is responsible for the retrieval of the archived material as well as for the maintenance of the archive index, if needed in cooperation with an IT person. Regular GLP training is requested for IT personnel working within a GLP test facility. External IT suppliers should have an understanding of GLP and should be trained in all aspects relevant for the system and their role.	
10.11	*Sponsors are often without their own GLP compliant archive. Often the sponsors require archiving study data themselves, although they don't have a GLP compliant archive. How should a CRO behave in such a*	

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	case? In the case that the sponsor does not have a GLP compliant test facility but would like to archive a GLP study at their site, the Test Facility must inform the sponsor in writing that the study data must be available in case of an authority inspection or a study audit. Furthermore it has to be archived according to GLP principles. If this cannot be guaranteed by the sponsor, the study would lose its GLP compliance. If the sponsor's archive is not under the supervision of a GLP monitoring program (as part of a test facility or only as an archive), the archiving period in this archive should be excluded in the GLP statement of the study director. If the original study documentation is available for an inspection within a reasonable time frame, the retention of copies by the Test Facility is not necessary. Otherwise, verified copies should be made before the study records are sent to the sponsor.	
10.12	*a) What is the authorities' expectation on the archiving period, when during this period an amendment to report is requested for any reason?* A prolongation of the archiving period due to an amendment to the final report depends on the impact on the study. Therefore an addition or correction of the final report without any impact on the study does not necessarily extend the archiving period of 10 years. *b) Would it make any difference on the archiving period whether additional work was conducted for this amendment to report or only information was added or corrected?* If additional work was conducted or the study might otherwise be affected, the study should remain in the archive for 10 years from the date of the finalization of the amendment to final report. *c) Is there any QA documentation that authorities expect to find for longer than ten years in the archive?* QA documentation should be kept in the archive as long as the corresponding study is kept in the archive. Therefore situations can arise in which QA documentation should be kept in the archive for longer than 10 years after the completion of the study.	
10.13	In-house GLP studies were performed by Company A to support the non-clinical safety of Compound X. Company A sells Compound X to Company B. All studies/results become the legal property of Company B. • *What records must Company A retain to show to the GLP Monitoring Authorities if any?* Company A should retain a list of the studies and eventually other documents transferred from its GLP archive to another GLP archive (it is assumed company B has a GLP archive). The list should also contain	

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	the reason of the transfer and be signed by the archivist of the new archive, to acknowledge the receipt of the documents. Final reports of transferred studies should be amended to document the new archiving location. This can be done for each study or as a comprehensive amendment. If it is done as comprehensive amendment, a copy should be sent to the monitoring authorities to document the transfer. • *What is the retention time of the documents which must be retained by Company A?* As long as the documents are expected to be archived (10 years after the study completion date) • *Must Company A make copies of non-study documentation (e.g. personnel records and equipment/facility records) to provide to company B?* As long as the company A maintains a GLP archive, it is not mandatory to make copies of non-study related documentation for company B.	
10.14	*What is the expected time span for archiving of facility records (e.g. maintenance records, staff training documents, records of environmental monitoring)?* Facility documents need to be archived on a regular basis as defined by test facility SOP. Depending on the quantity of documentation (e.g. maintenance work for equipment) archiving should be done on a yearly basis or every two years.	
11 Information Technology		
11.1	*Computer Systems Validation: In the AGIT Guidelines, validation responsibilities are defined for System Owner, Validation Director, Personnel and Management. In a small company, there may not be enough appropriate staff to allocate separate roles.* *Can (for example) the System Owner also be Management and Validation Director? If not, which roles can be combined and which must remain as independent functions?* The roles of Management, Validation Director and Quality Assurance should be separated under all circumstances. This follows from the view of a validation as being analogous to a GLP study. Additional functions such as a system owner can help to allocate responsibilities to suited persons, but they are not mandatory. In a small test facility, it is e.g. possible that the test facility manager or the validation director act as system owner. However, if the validation director is the system owner, the release of computerized systems should be done by TFM. See AGIT Guidelines for the Validation of Computerized Systems (Link AGIT).	
11.2	*Data validation in Excel spreadsheets is not straight forward and the validation can be circumvented by pasting data into cells. Is a validation nevertheless required for GLP study related activities?* If a test facility considers Excel spreadsheets not to be secure enough	Dec 2019

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	for the intended purpose, they should not use them. Although there are ways to circumvent some security measures, it is possible to reach an acceptable level of security, dependent on the purpose of the spreadsheet and programming/ validation efforts. See Swiss OGLP and OECD Advisory Document no. 17 Application of GLP Principles to Computerised Systems and AGIT Guidelines on Validation of Spreadsheets (Link AGIT).	
11.3	*E-Forms: An e-Form (electronic raw data) is completed and approved by more than one individual. Later an editorial correction is required and performed. An editorial correction being e.g. typo or obvious mistake but nothing changing the meaning of the data. Is an additional subsequent approval (by all individuals) necessary or is the entry in the audit trail sufficient?* During the conduct of the study, the entry in the audit trail is sufficient. The situation is comparable to a correction on paper raw data, with justification, date and signature. After the completion of the study, such a change should no longer be possible. (the data must be locked in such a manner that further changes are not possible).	
11.4	*How should one deal with an Online IT-Service tool for incident management (including account management) for GLP Computerized systems (Server based, global system)?* *Does the tool need to be tested to show that it is "fit for purpose", controlled access, etc.) or are only the incident management and account management processes themselves considered to be GLP relevant?* One has to decide whether the system is GLP relevant. See AGIT Guidelines for the Validation of Computerized Systems (Link AGIT): The following questions may guide the decision process: • Will the system be used to produce, process, or maintain data that are intended to be used in regulatory submissions? • Will the system be involved in the environmental control processes (e.g. temperature, humidity, light) of test systems, test items or specimens used in GLP studies? • Is the system part of a process liable to inspections by GLP monitoring authorities (e.g. electronic document management system for SOPs or training records)? • Will the incident management system be used to identify and/or modify the validation status of other computerized systems? ➢ If the answer to any of these questions is yes, the system is GLP relevant and should be validated. In addition, it should be possible to trace all incidents requiring remedial action reported for a computerised system to the affected GLP studies and vice versa, either within the incident management software or by a separate documentation. According to the description above, incident management and account management might be part of a GLP process that might be inspected. If this is the case, the system should be validated.	Dec 2019
11.5	*The Computerized System is accessed through Internet explorer (Intranet) but running on a central Oracle server. Does an installation of security patches, active-X elements, Microsoft service patches on the server and/or the accessed workstation require change controls?*	

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	This has to be evaluated based on the nature of the computerized system and its way of interaction with the operating system and the browser software. The basic question is whether these patches and functions are a part of the computerized system or not. If the additional patches and functions are used during the operation of the computerized system, or if they may influence the operation or the data of the computerized system as specified in the user requirements, they are a part of the computerized system, and change control is required. After any new installation of such elements, the function of the system has to be tested. The automatic installation of such items should be avoided.	
11.6	*Whilst AGIT clearly defines the role of validation director there is no reference to an overall system owner as GAMP 5 does. Do the Swiss authorities recommend/recognize other guidance regarding CS such as GAMP and the DIA publications (Red Apple and Peach)?* The role of the system owner has been defined in the AGIT Guidelines for the Validation of Computerized Systems (Link AGIT): The system owner, if designated by the test facility management, is responsible for ensuring that the computerised system is operated and maintained according to the principles of GLP and maintained in a validated state. The Swiss authorities recognize other guidance as long as the implementation is compliant with the GLP requirements. The relevant documents are the Swiss Ordinance on GLP, then the OECD consensus and advisory documents, and then the AGIT guidelines.	
11.7	*Although AGIT recommends executing a validation project in the same way as a GLP study and there are numerous advantages for using this comparison, when documents require revising or amending for any reason, producing an amendment with solely the changes is not as effective as producing an updated version of the complete document especially regarding the impact of this to the traceability matrix and ease of reading by system owner and users. What would be the opinion of Swiss authorities regarding this dilemma?* The recommendation to conduct the validation in analogy to a GLP study was focused on the initial validation plan. After the system release, changes such as modifications or repairs will lead to complete or partial validation activities that have to be documented. • Changes to validation documents could be added as amendments (incremental), or • the complete validation document could be revised, or • a new validation study can be performed in case of significant changes. The chosen modification process should be described in an SOP, and allow the traceability of requirements, changes, tests, results and decisions. If new versions of documents are created, it has to be clear which versions are valid.	
11.8	*a.) What validation activities would GLP Compliance Monitoring Authorities expect to see for the introduction of a Digital Signature system for approval of SOPs, Study Plans, CVs, Training Records and other*	Dec 2019

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	GLP documents? *The package identified is a "Commercial Off the Shelf" (COTS) product that can either be installed on individual PCs or on a server (in-house or outsourced) and claims to meet e-signature regulatory requirements (e.g. FDA; Sarbanes Oxley).* *b.) What other regulatory issues should be considered (e.g. if there is no final printed document)?* *Ad a.)* The electronic signature system is part of a process liable to inspections by GLP monitoring authorities, since the documented approval of SOPs, study plans, CVs etc. is a relevant element in GLP. IQ and/or OQ can be performed and documented by the vendor using his own protocols, procedures and tests. In this case the validation plan refers to these two phases and should be issued and approved prior to starting the PQ. During PQ it should be demonstrated that a computerized system is suitable for its intended purpose in the user's environment as defined in the user requirement specifications. However, the complete validation documentation should be available. Ad b.) Section 3.9 (p. 24) of OECD Advisory Document No. 17 Application of GLP Principles to Computerised Systems and the AGIT Guidelines describe the requirements to consider when using electronic signatures. Particularly the following GLP relevant issues need to be considered: • Access to documents for the inspectors during GLP inspection must be guaranteed. • Associated documents e.g. SOPs have to be modified. • Adequate management of electronic documents should be provided. (see AGIT publications)	
11.9	*Are generic system administrator accounts appropriate in a GLP environment? i.e. an account with ID and password given to multiple individuals for the purpose of installing patches, initiating a data restore etc. Actions taken would not be traceable to a given individual.* ID and password should always be associated with one individual person. In justified cases, it is possible to use a general account for several users under the requirement that each action would be traceable to an individual person and appropriate documentation of the actions are available (date, time and reason).	
11.10	*The AGIT Paper "Change Management and Risk Assessment of validated computerized systems in a GLP environment" describes the responsibility of QA during the change management process (Link AGIT). Would you consider a scaled approach to QA involvement (risk based), with justification, based on whether the system changes are of low (validation status remains unchanged), medium or high impact?* The degree of QA involvement should be described in an SOP. A	

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	scaled approach is possible. All actions and documentation of the change management process should be covered by QA, since even changes with a low impact have an execution step, function tests and documentation. System changes with high impact will require more involvement of QA.	