Good Laboratory Practice

GUIDELINES FOR THE ARCHIVING OF ELECTRONIC RAW DATA IN A GLP ENVIRONMENT

Release Date: 31.01.2018

Version: 2.0

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1 FOREWORD

The aim of the present document is to provide guidance on the GLP-compliant archiving of electronic raw data. It will aid test facilities and promote the use of a common standard, but it should not be considered as a legal document. The test facility management may use different approaches that are in compliance with the GLP Principles [1, 2]. The present guidelines may evolve according to experience over the next few years and may also depend on interpretations made by other OECD member countries.

The AGIT (**A**rbeits**G**ruppe **I**nformations**T**echnologie) is a working group consisting of representatives from Swiss GLP monitoring authorities and Swiss industry with the aim of proposing procedures, which are practical for use in test facilities fulfilling GLP regulatory requirements.

The Guidelines for the Archiving of Electronic Raw Data in the GLP Environment were issued as Version 1.0 in May 2003. This updated version (version 2.0) is in line with the OECD Advisory Document No. 17 (replacing OECD Consensus Document No. 10) [3].

2 INTRODUCTION

Computerised systems are used for the acquisition, processing, reporting, archiving and retrieval of electronic records. The benefits of computerised systems include the possibility of further processing and analysing electronic raw data.

A critical issue regarding electronic data systems is the long-term archiving and retrieval of electronic raw data.

These guidelines are based on the Swiss Ordinance on GLP [1], the OECD GLP Principles [2] and the OECD Advisory Documents No. 17 and 15 [3, 4]. The archiving of electronic raw data in conformity with GLP Principles requires a comprehensive understanding of the nature of electronic raw data. Therefore, the intention of this document is to clarify important aspects of electronic raw data.

Other relevant guidelines, e.g. FDA 21 CFR Part 11 [5, 6], are considered where appropriate.

Based on GLP requirements, raw data (including electronic raw data) have to be archived. No specific requirements regarding the data format are specified. However, in order to ensure readability throughout the retention period, it should be possible to retrieve the electronic raw data in proprietary and human readable form as required by FDA 21 CFR Part 11 [5].

3 SCOPE

This document provides guidance on:

- Regulatory (GLP) requirements for electronic archiving
- The integrity of archived electronic raw data
- The availability of electronic raw data during the required retention period

- Long-term considerations of archiving to meet GLP requirements
- Special requests from the registration authorities, such as specific data formats allowing reprocessing of data, are not considered in depth in this document.

4 RAW DATA

Raw data are defined in the Swiss Ordinance on GLP [1] as follows:

Raw data means all original test facility records and documentation, or verified copies thereof, which are the result of the original observations and activities in a study. Raw data also may include, for example, photographs, microfilm or microfiche copies, computer readable media, dictated observations, recorded data from automated instruments, or any other data storage medium that has been recognised as capable of providing secure storage… for at least 10 years.

Raw data can be paper-based or in electronic format, therefore the raw data format should be defined for each computerised system.

4.1 Definition of Electronic Raw Data

OECD Advisory Document No. 17 does not give a formal definition of electronic raw data [3]. For the purpose of the present guidelines, the following definition of the term electronic raw data and its various forms are given below.

Electronic Raw Data:	Original records generated by means of computerised systems and stored on digital media. In a broader sense this may include data processed subsequently, and stored on digital media, which are necessary for reconstruction and evaluation of the final results.
Proprietary Form:	An electronic file format, which needs a dedicated software to be read and processed
Human Readable Form:	A file format that can be interpreted by standard software to view the content in human readable form as text, figures, graphs, tables, etc.

4.2 Elements of Electronic Raw Data

Electronic raw data are considered as the data themselves and their related meta-data. The data represent the core data elements (measured values), whereas meta-data are considered as the attributes of the measured values (e.g. study number, time, sample identification) and technical properties (e.g. field properties, table relationships, keys).

Additionally, all changes to electronic raw data have to be recorded in an audit trail specifying the original and modified data, the reason for the change, the date and time, and the identity of the person changing the data.

In analogy to the requirement for handwritten signatures in paper-based systems, an electronic signature is required for electronic raw data generation [3, 9]. Further *legal* regulations for digital signatures are described in the Bundesgesetz über die elektronische Signatur [7].

4.3 Critical Issues concerning Raw Data

For each computerised system, the electronic raw data have to be defined with respect to the measured values, their meta-data, audit trail specifications and electronic signatures. The relationship between the data elements has to be kept during the whole life cycle of the electronic raw data (recording, changes, and archiving). This should also be ensured for the generation of electronic raw data in human readable form.

5 ROLES AND RESPONSIBILITIES

5.1 Test Facility Management

The test facility management should:

- Designate personnel with specific responsibility for the management of the electronic archives. Such personnel should be qualified, and have relevant experience and appropriate training to perform their duties in accordance with the GLP Principles. If parts of the archiving process are not covered by the personnel of the test facility, the test facility management has to ensure that GLP Principles are fulfilled by the service provider, e.g. via a service level agreement [8].
- Ensure that appropriate facilities, equipment, materials and SOPs are available and that the electronic archiving systems are suitable for their intended purpose and are validated, operated and maintained in accordance with the Principles of GLP.
- Establish procedures for all aspects of the life cycle of archived electronic raw data, i.e. archiving, amending, maintaining, migration, reformatting, conversion, retrieval and deletion.

5.2 Study Director

The study director should ensure the proper archiving of all data related to the study, including any electronic raw data [1, 3]. The final report should specify where all data (including electronic data) related to the study are stored.

5.3 Archivist / IT Personnel

The archivist is responsible for all aspects of electronic archiving and should have full control of all activities within the archiving process. If there is external IT involvement (service provider), the archivist has to ensure that the procedures are followed as described in the relevant service level agreements or contracts [4, 8].

5.4 Quality Assurance (QA)

The QA is responsible for inspecting all aspects of archiving for compliance with GLP. This includes the inspection of archiving procedures for electronic raw data, IT infrastructure, electronic archives, archived studies and documents concerning the personnel. If there is external IT involvement, their activities should be included in facility based inspections [8]. All findings should be reported to the test facility management.

The QA should be qualified in terms of IT knowledge and properly trained in the corresponding archive systems to be able to inspect electronic archiving procedures.

6 ARCHIVING OF ELECTRONIC RAW DATA

6.1 Electronic Archiving

The GLP Principles for archiving must be applied consistently to electronic and non-electronic data.

The archiving of electronic raw data means the process of protection against loss, modification, and unauthorised access. The availability of controlled amendment procedures and readability should be assured at any time during the required retention period.

Electronic raw data should be archived after completion of the study (final report signed by study director) as for all other study raw data (paper, slides etc.).

6.2 Archiving Options

It must be ensured that archived electronic raw data are never changed even not by the system administrator. In any case, the archived electronic raw data should have read-only status for all system users.

6.2.1 Off-line Archiving

Electronic raw data should be stored on data media (e.g.CD-Rom, DVD, USB sticks, external hard drive). The media should be protected against deletion and change and archived.

The stored electronic raw data should be well protected against accidental data changes and physically separated from the productive system. The types of medium selected should provide long-term readability (magnetic media are less favourable in this respect). Due to the physical separation of the data media, the maintenance of the overall index and the amending procedures may be difficult. In addition, direct access to the data for any form of data warehousing or data mining is not feasible.

6.2.2 On-line Archiving

On-line archiving can be achieved either using a dedicated electronic archive system (physically separated) or a productive system, in which the archived electronic raw data are explicitly marked (logically separated).

The requirements for archiving systems with respect to physical access to the system, restricted numbers of system administrators, system maintenance, and data protection will be more easily achievable using a dedicated electronic archive system. Both options allow that historical electronic data are directly accessible for further evaluation purposes.

6.3 Archiving Process

The system of indexing employed should facilitate the retrieval of all information required to reconstruct a study from both the study and the facility records.

- For each study, the order of the study director to archive study data should include a full index of the electronic raw data and their storage location.
- The status of the electronic raw data should be changed from “productive” to “archive” (on-line).
- In case of physical separation of the electronic archive the electronic raw data should be moved from the source to the archive destination and set to read-only.
- In case of logical separation of the electronic archive the electronic raw data should be set to read-only.
- The proper and secure transfer of electronic raw data to the archive has to be verified and documented.
- The index of the archive inventory should be updated.
- The archivist should give confirmation to the study director that the archiving process has been completed.

It is recommended that all information is frozen at the time of archiving. For on-line archiving, it is important to freeze historical results and report formats, including company name, department names, user names, etc.

The archiving process for electronic raw data should be described in an SOP and performed by validated procedures.

Interactions between the study director, the archivist and IT personnel involved at any stage of the archiving process should be documented.

7 OPERATION OF ELECTRONIC ARCHIVES

The usual archiving requirements for paper archives also apply to electronic archives. Specific aspects for the archiving of electronic raw data should be considered.

7.1 Requirements for Storage Conditions

- Storage conditions should be appropriate with respect to the particular sensitivity of the media to heat, humidity, and electromagnetic radiation.
- Data media (off line archiving) should be stored in a GLP archive.
- In case of on-line archiving it has to be ensured that the storage locations fulfil the requirements for a GLP archive. It is recommended that security copies (backups) of archived electronic raw data be kept off-site under suited conditions.

7.2 Specific Activities for the Archiving of Electronic Raw Data

- Any checking in and checking out of data and/or data media (who, what, when) should be documented in the electronic archive system.
- It should be checked that user access to the archived data is restricted to read only, to prevent any changes.

- The readability of the archived data should be checked at appropriate intervals.
- Depending on the storage media used, these should be renewed at appropriate intervals.

7.3 Long-term Availability of Archived Electronic Raw Data

Long-term access to archived data requires processes to copy, convert or migrate archived data to newer technologies. When there are software changes in the productive systems, or a system will be retired, procedures have to be in place to initiate a risk assessment of the readability and retrieval of archived data. Based on the result of the risk assessment, the test facility management should decide on any measures necessary for the archived data. A general SOP should be established for the processes mentioned below.

7.3.1 Copying Archived Data

The copying of archived data is considered to have the least impact on their integrity. This should be carried out if there is a need to copy electronic data from their current storage medium to a new medium, i.e. change of medium (tape to CD), medium refreshment (tape to tape, CD to CD) or a change in the location of the archives (server to server).

Suitable methods and processes should be used and verified for the intended purpose. The time schedule for a medium refresh should be appropriate to specifications of medium degradation, ensuring the minimum loss of records kept in long-term storage. In any case the replication should not result in any loss of content, structure, or context of the archived data.

7.3.2 Migrating Archived Data

Data migration is the activity of e.g. transporting electronic data from one computer system to another, transferring data between storage media or simply the transition of data from one state to another [e.g. conversion of data to a different format]. The term "data" refers to "raw data" as well as "metadata". The main objective of a migration strategy should be to preserve the integrity and usefulness of the data [2].

Data migration efforts may vary greatly in complexity and risks. Data migration requires the development of software or procedures to interpret the data structure of the legacy system and convert them to the format of the new system.

Data that have been migrated should be readable, identifiable, retrievable, and interpretable. There is a considerable risk that some information may be lost during migration. It is an essential objective of the validation of the migration process to determine the impact of this potential loss on data interpretation.

7.4 Retrieval of Archived Data

For audits and inspections carried out by the authorities or by QAs, electronic raw data and audit trails should be made available in a human readable form in good timely manner.

7.4.1 Regulatory and/or Internal Requirements for Further Data Processing

If regulatory and/or internal requirements make further data processing/interpretation necessary, the electronic raw data should be copied to a productive system. Data processing should be performed only on the copied data.
If the new evaluation results in a different interpretation of the original study outcome, an amendment process should be initiated. All data generated during such a process should be archived in addition to the original raw data.

7.4.2 Deletion of Archived Data

The process of deleting archived data should be described in an SOP. It is recommended that the archivist notifies the test facility management after the defined retention period, which is at least 10 years according to the Swiss GLP Ordinance [1]. It should be taken into account that in other countries the retention period may differ. The test facility management should decide on the further retention of the electronic raw data or initiate their deletion. In any case, this decision should be documented.

8 RETIREMENT OF A COMPUTERISED SYSTEM

If the archived electronic raw data are only interpretable by the original application software, the following options should be considered prior to the retirement of the computerised system.

8.1 Data Migration to a Follow-up System

Data migration is considered as the preferred option, thereby keeping both the electronic raw data and the possibility of generating a human readable form.

8.2 Maintaining Retired Systems

If the result of the risk assessment concludes that an unacceptable change of data integrity may occur after data migration, or if a follow-up system is not available, the conservation of the computerised system (hardware and/or software) may be appropriate. However, this option is considered as unsuitable for long-term storage of electronic raw data, since maintaining outdated systems involves increasing effort, cost, and risk during the retention time.

8.3 Maintaining Electronic Raw Data Only in Human Readable Form

In case the storage of electronic raw data in human readable form is the only alternative, it should be considered that this approach might not be accepted by all registration authorities.
The amount of archived electronic raw data that has to be transferred into a human readable form may create a substantial effort. Therefore, it may be appropriate to store at the time of archiving both the proprietary and the human readable form of the electronic raw data.

9 REFERENCES

[1] Ordinance on Good Laboratory Practice of 18 May 2005 [RS 813.112.1] as last amended on 1 December 2012. (OGLP)

[2] OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring No. 1: OECD Principles of Good Laboratory Practice (as revised in 1997). Environment Directorate, OECD, Paris, 1998. (OECD)

[3] OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring No. 17: Advisory Document of the Working Group on Good Laboratory Practice. Application of GLP Principles to Computerised Systems. Environment Directorate, OECD, Paris, 2016. (OECD)

[4] OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring No. 15: Advisory Document of the Working Group on GLP: Establishment and Control of Archives that Operate in Compliance with the Principles of GLP. Paris 2007. (OECD)

[5] Electronic Records; Electronic Signatures; 21 CFR Part 11 (Rule 11), US Food and Drug Administration, 20 March 1997.

[6] Guidance for Industry – Part 11, Electronic Records; Electronic Signatures – Scope and Application, US Food and Drug Administration, August 2003.

[7] Bundesgesetz über Zertifizierungsdienste im Bereich der elektronischen Signatur und anderer Anwendungen digitaler Zertifikate vom 18. März 2016 (Stand 1. Januar 2017). (link)

[8] Working Group on Information Technology (AGIT): Good Laboratory Practice (GLP); Guidelines for Collaboration with External IT Service Providers Supporting a GLP Environment. (AGIT)

[9] Working Group on Information Technology (AGIT): Good Laboratory Practice (GLP); Guidelines for the Acquisition and Processing of Electronic Raw Data. (AGIT)

10 WORKING GROUP ON INFORMATION TECHNOLOGY

The Working Group on Information Technology (AGIT) was founded on 27 March 1998 with the objective of discussing relevant topics of Good Laboratory Practice (GLP) in the field of information technology between industry and the monitoring authorities.
The AGIT intends to set up guidelines based on legislative requirements and practical experience to support test facilities introducing information technology tools to computerised systems in practice. OECD GLP Advisory Document number 17 on the *Application of the Principles of GLP to Computerised Systems* is used as a basis for discussion.

The members of the AGIT are representatives of the Swiss GLP monitoring authorities (Olivier Depallens, Swiss Federal Office of Public Health; Elisabeth Klenke and Daniel Roth, Swissmedic, Swiss Agency for Therapeutic Products; Christoph Moor, Federal Office for the Environment), and invited experts from industry (Peter Esch, Novartis Pharma AG; Stephan Hassler, Innovative Environmental Sciences Ltd.; Silvio Albertini, F. Hoffmann-La Roche AG; Christine Wurz, Idorsia Pharmaceuticals Ltd.).

For the convenience of users, AGIT publications are available on the Swiss GLP website (see Good Laboratory Practice (GLP)). The Swiss GLP homepage also provides links and references to guidelines, laws and regulations, definitions etc.

AGIT Publications:

- Guidelines for the Validation of Computerised Systems
- Guidelines for the Management of Electronic SOPs in a GLP Environment
- Guidelines for the Archiving of Electronic Raw Data in a GLP Environment
- Guidelines for the Acquisition and Processing of Electronic Raw Data in a GLP Environment
- Guidelines for the Development and Validation of Spreadsheets
- Guidelines for Change Management and Risk Assessment of Validated Computerized Systems in a GLP Environment.
- Position Paper 1: Is it acceptable to destroy the paper originals of raw data and related study documentation, if an image of the paper is captured in an electronic form (e.g. scanned)?
- Guidelines for Collaboration with External IT Service Providers Supporting a GLP Environment