Good Laboratory Practice

GUIDELINES FOR THE MANAGEMENT OF ELECTRONIC STANDARD OPERATING PROCEDURES (SOPs) IN A GLP ENVIRONMENT

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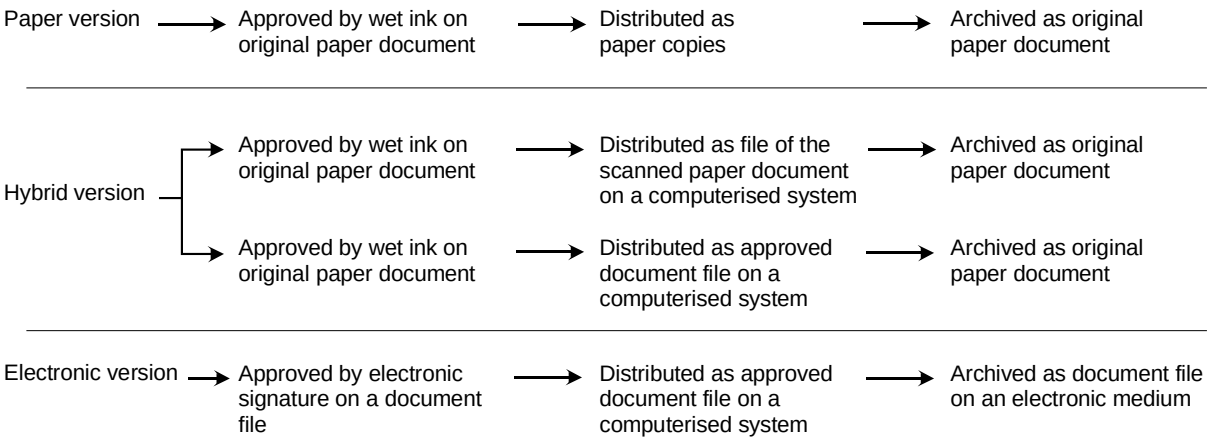
1 FOREWORD

The aim of this document is to provide guidance on the application of the OECD's Principles of Good Laboratory Practice (GLP) [1,2] to the implementation and management of electronic Standard Operating Procedures (SOPs). The document intends to promote a common standard and support test facilities in setting up their own system, but should not be considered as legally binding. Different approaches may be used as long as they are in compliance with the GLP Principles.

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 Management of electronic standard operating procedures (SOPs) in a GLP environment was issued in July 2001. 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 commonly used in the GLP environment. The GLP Principles [2] have therefore been adapted to this situation, and the OECD has published the Advisory Document No. 17 "*Application of GLP Principles to Computerised Systems*" [3] which replaces since April 2016 the previous OECD Consensus Document No. 10. In spite of these documents, interpretation of the Principles is still necessary. This paper intends to give guidance on how to manage electronic SOPs, as there are several advantages of such systems over the use of paper versions. Electronic documents with electronic signatures are common practice, however a hybrid version might be appropriate as a preliminary step, but should not be regarded as a long-term solution. The following table gives an overview of the different possibilities:



The management of SOPs as electronic and semi-electronic (hybrid) versions offers several advantages over paper versions:

- The burden of administration and distribution can be reduced. There can be automatic alerts for SOPs becoming due for revision. More flexible updating is possible, thus enabling continuous improvement. An SOP index can be generated and updated automatically. An electronic indexing and searching mechanism can help to save time.

- The review process can be carried out more efficiently.
- If electronic records with electronic signatures are used, records are linked to the corresponding signature. Any subsequent change of data is therefore impossible or at least detectable, depending on the system used.
- Technologies, e.g. video and audio, may be used as media for SOPs in addition to written text.

3 SCOPE

This document intends to give guidance on

- How electronic SOPs are prepared, approved, distributed in a controlled manner, periodically reviewed/revised, and archived.
- How the integrity of electronic SOPs is ensured.
- How the accessibility of electronic SOPs is optimised in a laboratory environment.
- How version control of electronic SOPs is ensured.

4 GENERAL REQUIREMENTS

"*All computerised systems used for the generation, measurement, calculation, assessment, transfer, processing, storage or archiving of data intended for regulatory submission or to support regulatory decisions should be validated, and operated and maintained in ways that are compliant with the GLP Principles. The same requirement also applies to computerised systems used to produce other GLP-relevant data such as records of raw data, environmental conditions, personnel and training records, maintenance documentation, etc*." [3].

Therefore, a computerised system intended for the operation of an electronic SOP system should be developed, validated, operated and maintained in accordance with the Principles of GLP, considering AGIT guidelines [4, 5].

All procedures, functions and roles, e.g. electronic signature, scanning of documents, storage, maintenance, and distribution of new SOP versions, user information, and archiving should be described in SOPs.

Access rights to the SOP system need to be managed and documented. Administration of access to the SOP file or data system, which includes the rights of read, write, create, and delete, should be limited to the SOP system administrator role. Clear definition of roles and responsibilities (e.g. system owner versus SOP system administrator) should be described in an SOP and/or in a corresponding service level agreement (SLA). User access to the SOP system should be limited to read-only access. Printouts may be allowed under restricted conditions. The electronic SOP system should be organised in a structured and indexed form, which enables easy retrieval of SOPs by users. Training of users is essential to optimise the use of an electronic SOP system.

A periodic review at regular intervals should ensure that performance criteria are met, e.g. reliability, responsiveness, capacity, network connections, ready and easy access for the user. Security measures should be taken to ensure data integrity in the event of failure, unauthorised access or corruption of data, e.g. by viruses. A backup of the electronic SOP system should be established to allow its recovery following any failure that might compromise the system's integrity.

A contingency, disaster, and recovery plan should ensure that in case of system breakdown the electronic SOP system is restored within an adequate timeframe or an alternative access to SOPs should be available.

5 ROLES AND RESPONSIBILITIES

5.1 Test Facility Management

Test facility management should ensure that appropriate SOPs are established, distributed and followed by personnel generating GLP study data. The test facility management must approve all SOP versions. This can take place either by signing a paper copy or by applying an electronic signature to an electronic version of an SOP.

The test facility management should ensure that an appropriate and validated computerised system is available for the management of electronic SOPs and designate a SOP system administrator and a system owner.

5.2 SOP System Administrator

The SOP system administrator is responsible for management of the SOPs, which includes ensuring that the effective version of an SOP is accessible on the system, and that invalid SOPs are clearly identified. The administrator should inform users of any change to the active SOP system, i.e. new, updated or invalid SOPs.

Where there is an electronic SOP system, the administrator is responsible to initiate the archiving process of all historical versions of SOPs.

5.3 System Owner

The system owner is responsible for ensuring that the computerised system is validated, operated and maintained according to the Principles of GLP [2].

The system owner should make the SOP system administrator aware of any changes that may have an impact on the use or operation of the SOP system, according to AGIT *Guidelines on Change Management and Risk Assessment of Validated Computerized Systems in a GLP Environment* [5]. If IT service is provided by a third party, a corresponding SLA between IT service provider and test facility management should be established [6].

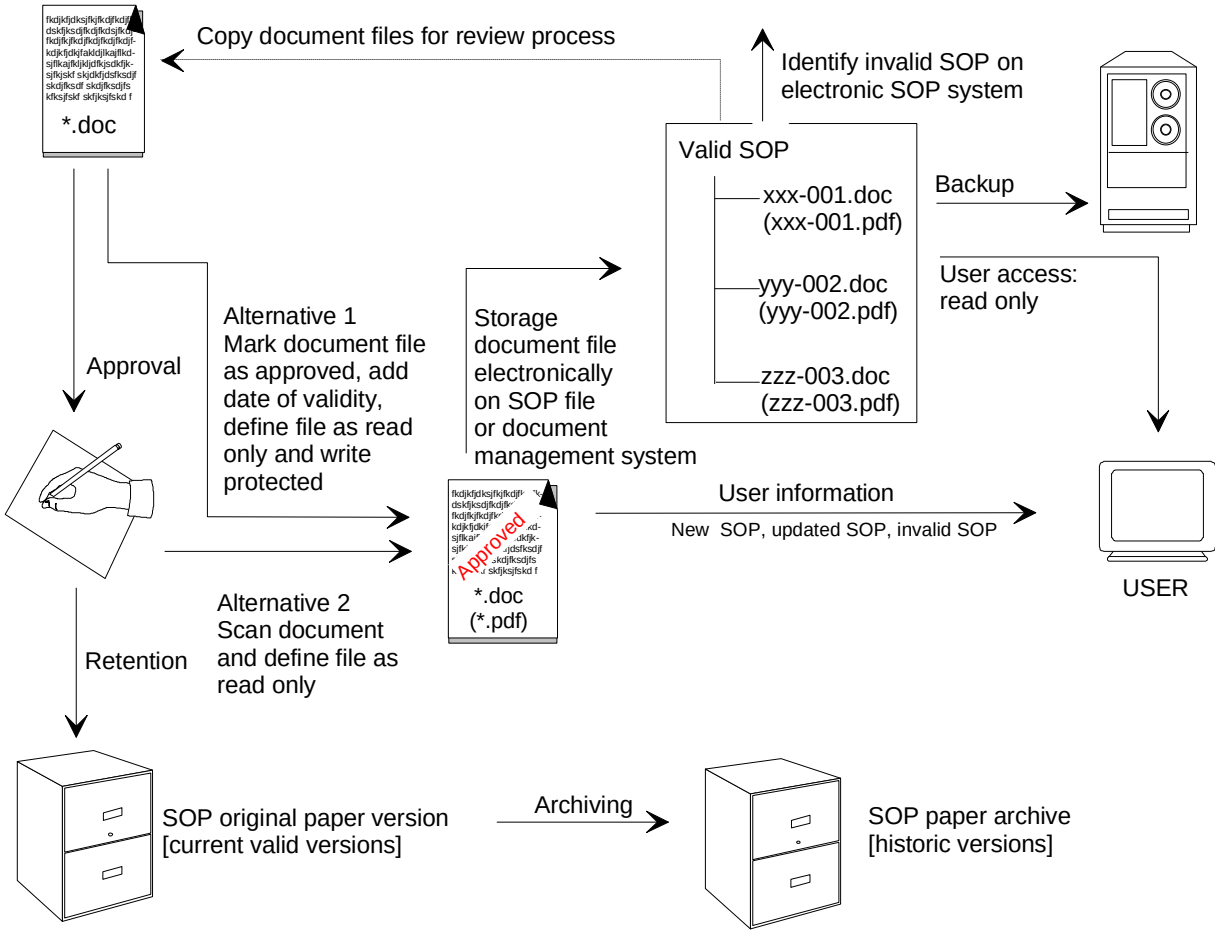
The system owner is responsible for assigning user access and privileges and should ensure that access to the system is controlled.

5.4 Users

All users of computerised systems are responsible for using these systems in compliance with GLP Principles. Users of the SOP system should have read-only access.

6 PROCESS DESCRIPTION AND SPECIFIC REQUIREMENTS

6.1 Hybrid Version



Preparation and Distribution
A printout of the SOP is signed by the test facility management with a dated, handwritten signature.

The signed SOP is scanned to an electronic version, or the document file is converted to an electronic version that can only be read but not changed by the user. The approval should be indicated e.g. by a scanned, handwritten signature, or the name of the authorised person who signed.

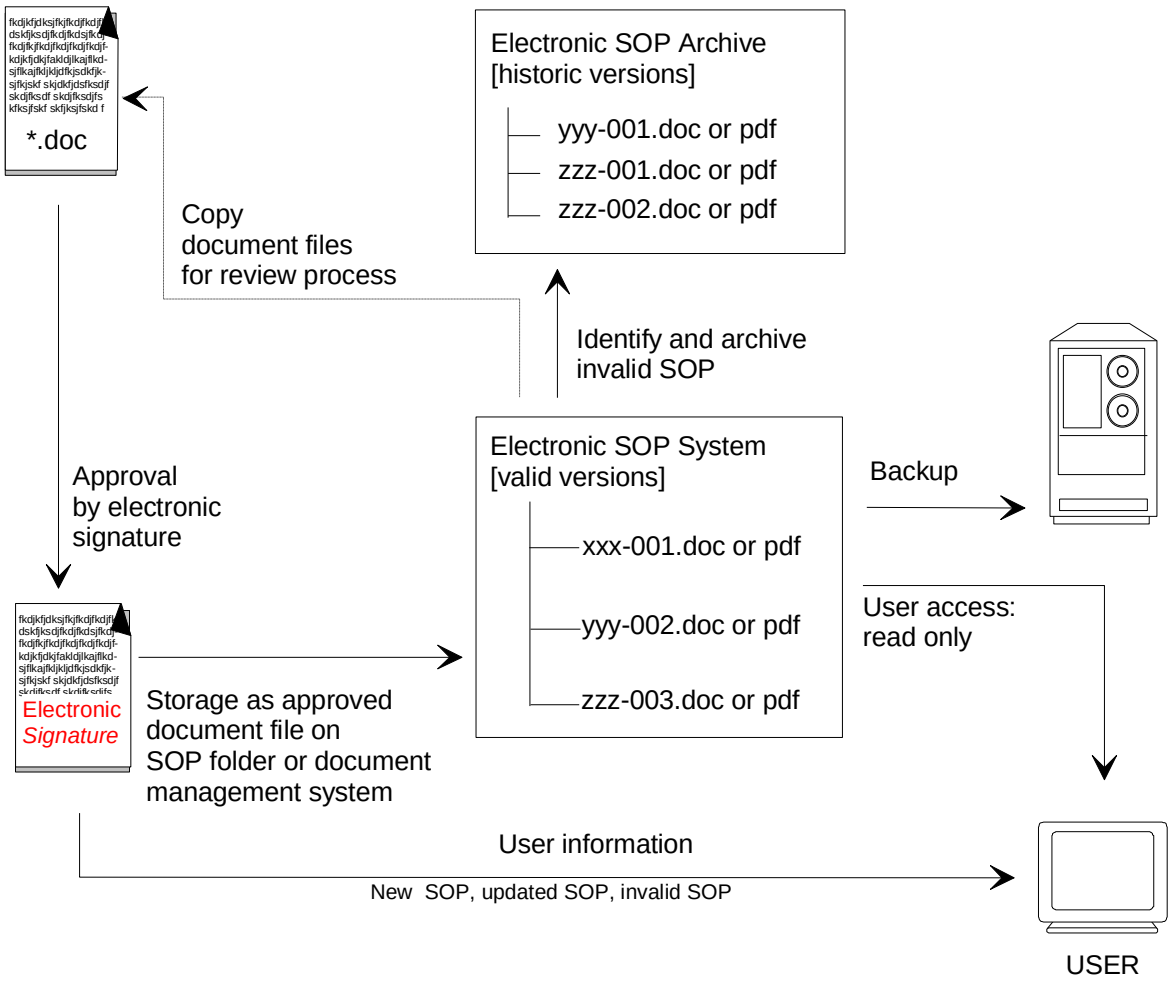
Procedures should be established to scan and store the approved SOPs in electronic form as write-protected documents at the corresponding SOP folder or document management system. The corresponding original document file should be stored for future review of the SOP. Access to this file should be limited to the SOP system administrator. Furthermore, procedures should be established to inactivate invalid SOPs. Backup procedures should prevent any loss of data.

Users should be informed about any changes, i.e. new, updated or invalid SOPs.

Review
SOPs should be reviewed periodically. For this purpose, the SOP system administrator contacts the authors to review and update the documents.

Archiving
All historical original SOPs paper versions should be kept in an archive in compliance with OECD Advisory Document No.15 [7].

6.2 Electronic Version



Preparation and Distribution
Test facility management approves the SOP by electronic signature. The document file should be protected as read only and write protected after electronic signature. The approved file should be stored in a SOP folder or document management system.

Users should be informed about any changes, i.e. new, updated or invalid SOPs.

Review
SOPs should be reviewed periodically. For this purpose, an automated process or the SOP system administrator contacts the authors to review and update the documents.

When the revision is completed, test facility management signs electronically the new version, which is then made available in the system. The superseded version should be set to invalid and users are informed that a new version is effective and available in the system.

Archiving
Historic versions of SOPs should be stored in an electronic SOP archive, which is in compliance with the GLP Principles and the OECD Advisory Documents No. 15 and 17 [7, 3]. The archiving process for electronic SOPs should be described and validated.

The archivist is responsible for the archiving process. Duties and activities may be covered by system owner, SOP system administrator and IT personnel [7].

7 OTHER OPTIONS

Printouts
If electronic SOPs are used, no printouts are necessary.

If SOPs are frequently needed at different locations or at locations with unfavourable environmental conditions, mobile devices may be an option or a limited number of controlled paper copies may be used.

There should be an SOP available describing in which case and under what conditions printouts are allowed, as well as which procedures to follow. Responsibilities must be clearly assigned.

Downloads
SOPs should not be downloaded and stored on a personal directory.

As downloading might be necessary for a revision of an SOP, such a document should be clearly marked as a draft version. The corresponding file location of the draft SOP should be strictly separated from the location of the valid SOP file.

8 REFERENCES

[1] Ordinance on Good Laboratory Practice (GLP) 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] Working Group on Information Technology (AGIT): Guidelines for the Validation of Computerised Systems. (AGIT)

[5] Working Group on Information Technology (AGIT): Guidelines for Change Management and Risk Assessment of Validated Computerised Systems in a GLP Environment. (AGIT)

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

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

9 WORKING GROUP 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