Good Laboratory Practice

POSITION PAPER 2:

Is a formal validation of spreadsheets used for data processing in a GLP study in any case mandatory?

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1 OBJECTIVE

The aim of this document is to take position on the issue regarding the validation of spreadsheets.

Spreadsheets are widely used in GLP studies, e.g. for acquisition of raw data, for data transfer from LIMS and instrument systems and for processing of data. A common approach to develop and validate spreadsheets is described in the correspondent AGIT Guidelines [1].

Is a formal validation of spreadsheets used for data processing in a GLP study in any case mandatory?

Answer: **No**

In case a spreadsheet is repeatedly used in the same setting, a validation according to AGIT Guidelines for the Development and Validation of Spreadsheets [1] is highly recommended. However, if spreadsheets are only used for data processing purposes, verification of the spreadsheets may be sufficient. Figures 1 and 2 on raw data capturing and processing should support test facilities with their decision on how to handle spreadsheets used in GLP studies.

This position paper specifies AGIT's position and its rationale for the approach without validation.

2 GLP REQUIREMENTS

Test facilities can use this approach of verified but not validated spreadsheets only if the raw data are stored for subsequent archiving according the AGIT guidelines [2,3]. These data are then copied (e.g. entered manually or uploaded) to a spreadsheet for processing. During this step, the raw data need to remain unchanged.

In case non-validated spreadsheets are used, data transfer and processing need to be verified for each study under the responsibility of the SD. QA should have the possibility to check this during data inspection.

According to the Principles, the final report should contain a presentation of the results, including calculations and determinations of statistical significance [4]. QA should verify and confirm that the final report reflects the raw data. As usual, the reported raw data should allow a re-calculation of the results based on the formulas/equations given in the report.

It is recommended to archive the spreadsheets electronically or print-outs thereof as part of the study documentation to ensure traceability.

3 RECOMMENDATIONS AND CONSIDERATIONS

The following elements/approaches/aspects are recommended:

- Data and values on spreadsheets should be organized in a clear structure.
- All values given on the spreadsheet should be assigned to a unique study identifier and the corresponding sample definition (e.g. sample type, sampling time point, group number and should be assigned to the corresponding unit, e.g. mL, g/L, dpm, g/cm^2, %).
- Values used for calculations should be visible/readable on the sheet (see figure 3).
- Calculations across files should be avoided. If data from other files are needed, these data should be imported and then processed.
- The use of macros should be kept to a minimum. If macros are needed a validated approach is recommended [1].
- The use of an "empty" template is encouraged to avoid erroneous calculations due to data from previous use.

- Files and calculations should be protected in such a way that formulas are not accidentally overwritten.
- The read-write access of template should be restricted to a limited number of users.
- Any recognized error or malfunction in a template should be subject to an impact analysis to allow identification of potentially impacted studies and correction measures. This is particularly relevant for multiple used spreadsheets.
- An appropriate quality check should be conducted prior to release of data. The extent of this check should be defined in an SOP and consider critical steps e.g. changes in number of samples, missing samples, handling of outliers, hidden areas.
- If a spreadsheet is repeatedly used without changes, a validation may be a better approach than the study-specific verification.

The following aspects should be considered since they might be critical:

- In general, spreadsheets in an open file system have poor security and no audit trail.
- Formulas can be accidently added to spreadsheets using simple menu functions.
- After reformatting of spreadsheets (e.g. hidden column but formula not adapted), reference areas may be no longer correct.
- Access control: unauthorized use of open sessions should be prevented.
- Changes in computer configuration/operating system/version of spreadsheet program: spreadsheets are developed on a specific computer configuration, with specific operating system and version of the spreadsheet program, therefore the impact of such changes should be evaluated.
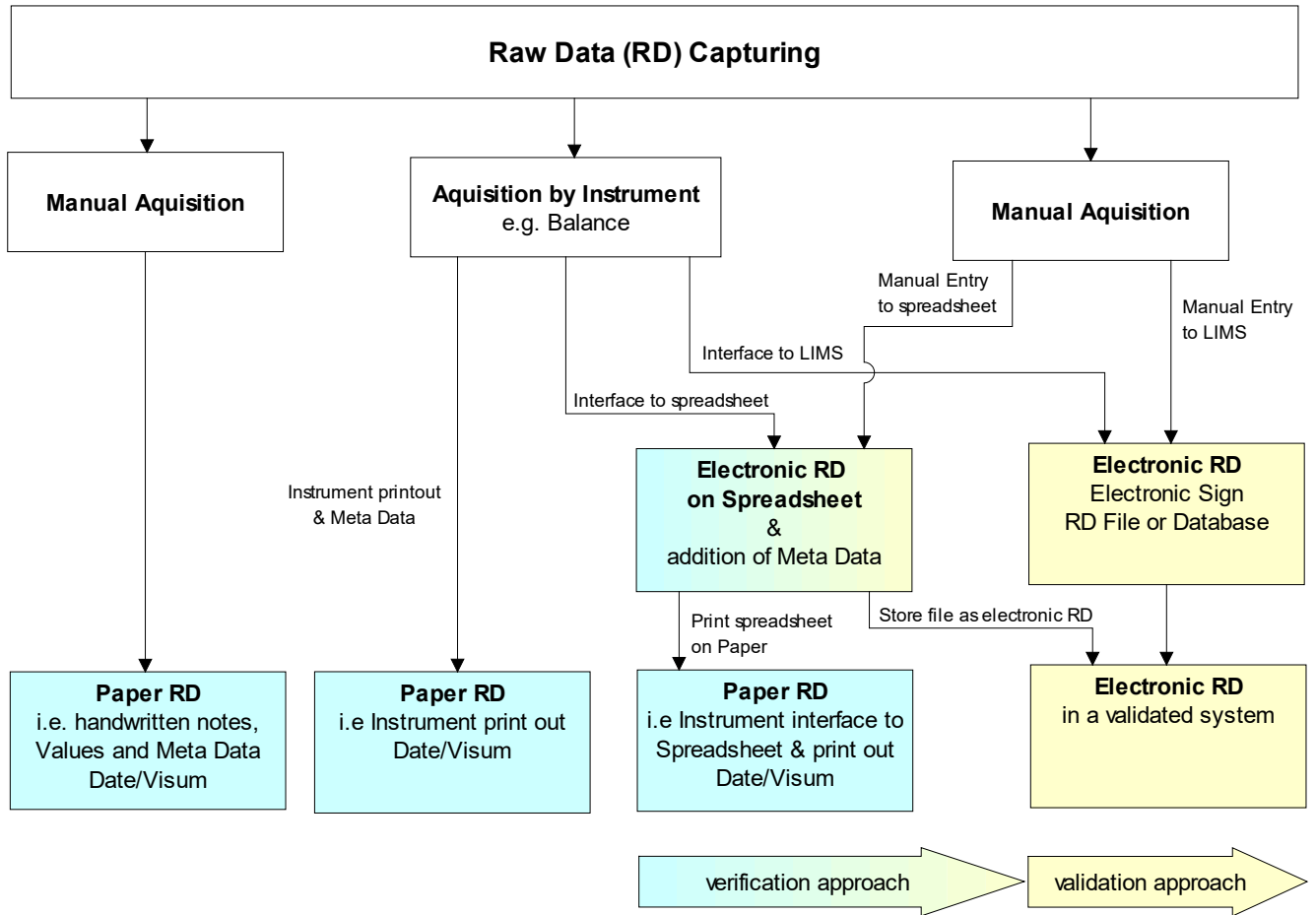
Figure 1: **Raw Data Capturing**

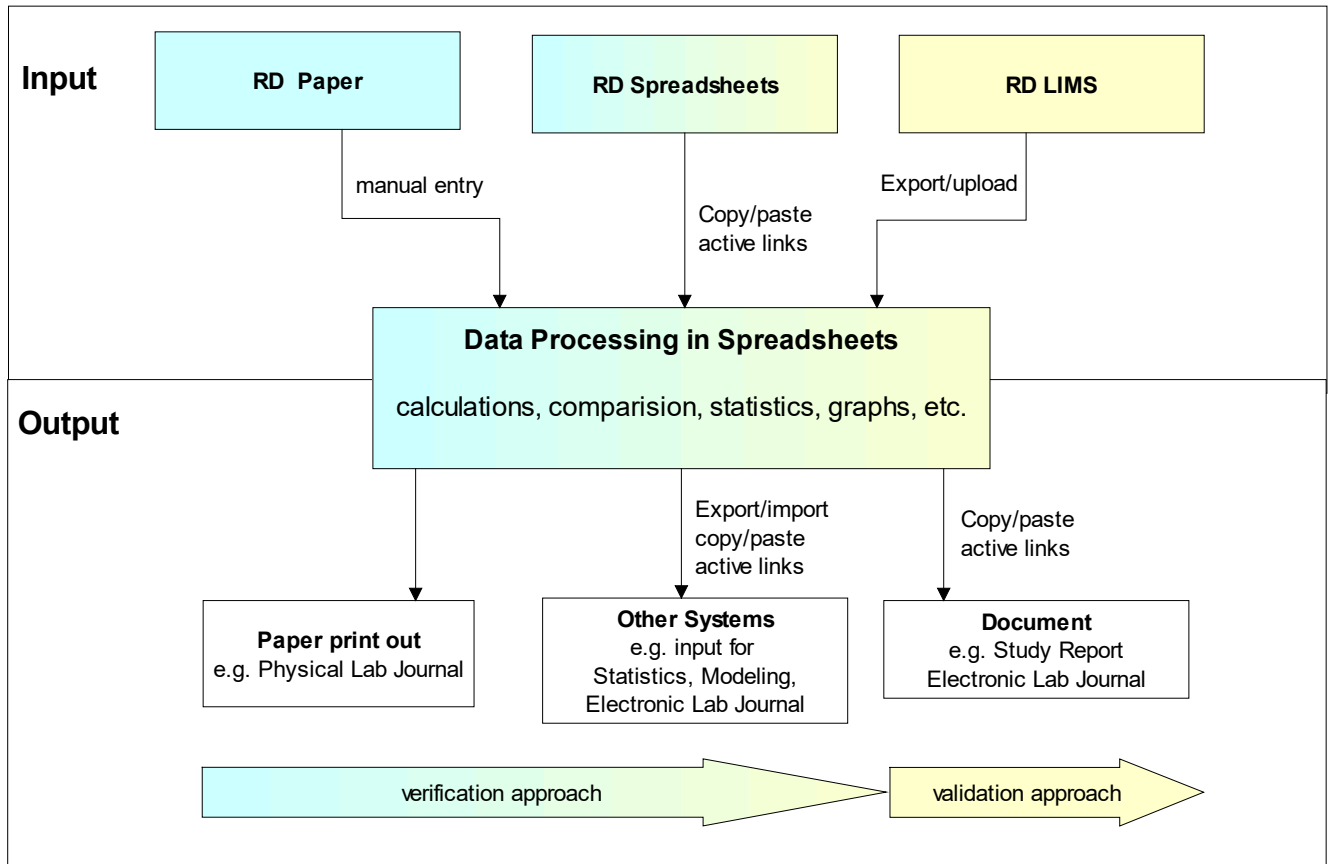Figure 2: **Data Processing using Spreadsheets**

Figure 3:

Example: Spreadsheet Print Out for Lab Journal

07-11-2019/

Tank Water Analytics

Study   2019008 ✔

Sample   Tank Water Day 4, HD ✔

SP Column   Isolute SPE Column C18 (Lot 17256706MA) ✔

Size   5g / 25ml ✔

Meta Data Describing DATA

Solid Phase Extraction

Fraction No.	Eluent	Volume [ml]	Aliquot [µl]	Activity [dpm]	Total-Activity [dpm]	[%] of Total
1	Tank Water ✔	1000 ✔	5000 ✔	2 ✔	400 ✔	0.5 ✔
2	Acetonitrile ✔	5.1	250	192	3917	5.1
3	Acetonitrile	5.3	250	71	1505	1.9
4	Acetonitrile	5.1	250	14	286	0.4
5	Acetonitrile	4.8	250	9	173	0.2
6	Methanol ✔	5.8 ✔	250 ✔	2417 ✔	56074 ✔	72.5 ✔
7	Methanol	5.6 ✔	250 ✔	501 ✔	11222 ✔	14.5 ✔
8	Methanol	5.8	250	64	1485	1.9
9	Methanol	5.9	250	56	1322	1.7
10	Acetone ✔	5.5	250	42	924	1.2
Sum					77308 ✔	100.0

Calculated Data

Raw Data Measured Values

Appr. 7/11/19

4   REFERENCES

[1] Working Group on Information Technology (AGIT): Good Laboratory Practice (GLP); Guidelines for the Development and Validation of Spreadsheets (AGIT)

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

[3] Working Group on Information Technology (AGIT); Good Laboratory Practice (GLP); Guidelines for the Archiving of Electronic Raw Data in a GLP Environment. (AGIT)

[4] 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)

5   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 members of the AGIT are representatives of the Swiss GLP monitoring authorities and invited experts from industry.

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.