EXCEPTIONS VS DEVIATIONS:

DO I HAVE TO PUT THAT ON MY COMPLIANCE STATEMENT?

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IMPORTANCE OF GLP COMPLIANCE

1. Data Reliability: GLP compliance ensures data generated from laboratory studies are reliable and can be trusted by regulatory authorities when assessing the safety of chemicals and products.
2. Market Access: GLP Compliant data is accepted by countries who adhere to the mutual acceptance of data (MAD) agreement.
3. Regulatory Requirements: Many regulatory agencies require GLP compliance for studies submitted for product approvals, ensuring the safety and data is generated under controlled and standardized conditions.

EFFECTS OF NON-COMPLIANCE

§160.17 Effects of non-compliance

- EPA may refuse to consider reliable for purposes of supporting an application for a research or marketing permit any data from a study which was not conducted in accordance with this part.
- Submission of a statement required by §160.12 which is false may form the basis for cancellation, suspension, or modification of the research or marketing permit or denial or disapproval of an application for such a permit under FIFRA section 3, 5, 6, 18, or 24 or FFDCA section 406 or 409, or for criminal prosecution under 18 U.S.C 2 or 1001 or FIFRA section 14, or for imposition of civil penalties under FIFRA section 14.

GLP COMPLIANCE STATEMENT

§160.12 Statement of compliance or non-compliance:

- Any person who submits to EPA an application for a research or marketing permit and who, in connection with the application, submits data from a study to which this part applies shall include in the application a true and correct statement, signed by the applicant, the sponsor and the study director, of one of the following types:
  - A statement that the study was conducted in accordance with this part; or
  - A statement describing in detail all differences between the practices used in the study and those are required by this part; or
  - A statement that the person was not a sponsor of the study, did not conduct the study, and does not know whether the study was conducted in accordance with this part.

EXAMPLE FROM PR2011-3

Pesticide Registration (PR) Notice 2011-3 Standard Format for Data submitted under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

Example 1:

This study was conducted in accordance with 40 CFR 160.

Study Director: _____*signature*_____ Date: _____
Typed Name of Signer: _____
Typed Name of Laboratory: _____

Sponsor: _____*signature*_____ Date: _____
Typed Name of Signer: _____
Typed Name of Company: _____

Submitter: _____*signature*_____ Date: _____
Typed Name or Signer: _____
Typed Name of Company: _____

EXAMPLE FROM PR2011-3

Example 2:

The following is a detailed description of all differences between the practices used in the study and those required by 40 CFR 160:

_____

_____

Study Director: _____*signature*_____ Date: _____
Typed Name: _____
Typed Name of Laboratory: _____

Sponsor: _____*signature*_____ Date: _____
Typed Name of Signer: _____
Typed Name of Company: _____

Submitter: _____*signature*_____ Date: _____
Typed Name of Signer: _____
Typed Name of Company: _____

EXAMPLE FROM PR2011-3

Example 3:

The submitter of this study neither sponsored this study nor conducted it and does not know whether the study was conducted in accordance with 40 CFR 160.

Submitter: _____*signature*_____ Date: _____
Typed Name of Signer: _____
Typed Name of Company: _____

DIFFERENCE BETWEEN DEVIATION AND EXCEPTION

GLP Compliance Exception:

A GLP compliance exception is a deviation or excursion from a regulatory requirement.

SOP / METHOD / PROTOCOL DEVIATIONS:

A deviation is an excursion from a procedure described in the protocol, SOP, method or guideline.

HOW TO HANDLE SOP / PROTOCOL / METHOD DEVIATIONS?

- SOPs should be in place on how to handle SOP / Protocol / Method Deviations.
- Identify and document the deviation! As soon as a deviation is discovered, document what happened (reference SOP / Protocol / method).
- Type of deviation: Was it an administrative error (minor)? Did the deviation impact data quality, study conduct or GLP compliance?
- Impact assessment:
  - Data integrity (accuracy, completeness, traceability)
  - Study validity and interpretation
  - Regulatory compliance


GLP COMPLIANCE EXCEPTION

HOW TO HANDLE GLP COMPLIANCE EXCEPTIONS

- GLP compliance exceptions must be promptly identified, documented, and evaluated to assess their potential impact on study integrity and data reliability.
- In the final report, each exception should be clearly described, including the nature of the deviation, affected phases of the study, and any data involved.

ASSESSING EXCEPTIONS TO GLP COMPLIANCE

- Identify and describe the regulation. Clearly state what did not meet the regulatory requirements and when it occurred.
- Assess impact to study integrity. Evaluate whether the exception affects:
  - Data integrity (accuracy, completeness, and traceability).
  - Ability to reconstruct the study.
- Do the study conclusions remain scientifically valid?

STUDY DIRECTOR AND SPONSOR: WHAT HAPPENS IF THEY ARE NOT ON THE SAME PAGE

"I DON'T WANT TO PUT THAT ON MY COMPLIANCE STATEMENT" – STUDY DIRECTOR

"I DON'T WANT YOU TO PUT THAT ON YOUR COMPLIANCE STATEMENT" – SPONSOR

SPONSOR AND STUDY DIRECTOR

- Both the sponsor and study director sign off on the GLP compliance statement.
- What happens if one party does not agree with including or removing something from a draft GLP compliance statement.

Correspondence documentation is key. You would expect there to be communication between the study director, sponsor and the QAU.

GROUP DISCUSSION

For the following scenarios: Would you handle this as a protocol / method / SOP Deviation or address as an exception to GLP Compliance?

EQUIPMENT IDENTIFICATION & LATE ENTRY

While weighing soil, an analyst inadvertently did not record the balance ID / Cal due date on the day of weighing. The laboratory only has one balance that could have been used. The study director directs the analyst to add the balance ID and Cal Due date with a "Late Entry" error code and added clarification that the balance was within calibration date and verified the day of use.

§160.130 (e) All data generated during the conduct of the study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data.

TEMPERATURE RECORDS

§160.190 Storage and retrieval of records and data (a)all raw data, documentation, records, protocols, specimens and final reports generated as a result of a study shall be retained.

Lack of retrievable raw data is considered an exception to GLP compliance record retention and data integrity requirements.

Temperature Monitoring Records: it was identified that temperature data for the period of 29 hours was no longer available. The electronic temperature monitoring system automatically overwrote historical data once its storage capacity was reached. As a result, original temperature records for the affected period cannot be retrieved or reviewed.

REFERENCE SUBSTANCE CHARACTERIZATION

Characterization of one of the reference substances used in the study was incomplete at the time of use. The documentation supporting identity, purity, concentration, stability, or expiration was not fully available prior to sample analysis.

§160.105 Test, control, and reference substance characterization (a) The identity, strength, purity, and composition, or other characteristics that appropriately define the test, control, or reference substances shall be determined for each batch and shall be documented before its use in the study.

STABILITY OF TEST, CONTROL, REFERENCE SUBSTANCE

§160.105 (e) The stability of the test, control and reference substances under the conditions at the test site shall be known for all studies.

Study Director receives a delayed test substance shipment and all dry ice has sublimed. The certificate of analysis lists the storage conditions as frozen. Study Director verified the purity before and after dosing.

PIPETTE VERIFICATIONS

SOP says to verify the pipette at n=10. A pipette used for dosing was actually verified at n=7 replicates.

SOP Deviation

QA PHASE INSPECTIONS

Study #0000123

Study Nature: 120-day aerobic soil degradation in four soils with analytical method validation

This was the following QA Statement list of inspections:

Date(s)	Type	Date distributed to study director & management
24 AUG 2025	Protocol	24 AUG 2025
03 SEP 2025	**Phase Inspection: Soil #1 & #2 weighing**	03 SEP 2025
26-28 JAN 2026	Report / Raw Data	28 JAN

§160.35 Quality Assurance Unit (b)(3) Inspect each study at intervals adequate to ensure the integrity of the study and maintain written and properly signed records of each periodic inspection showing the date of the inspection, the study inspected, the phase or segment of the study inspected, the person performing the inspection, findings and problems, action recommended and taken to resolve existing problems, and any scheduled date for reinspection. Any problems which are likely to affect study integrity found during the course of an inspection shall be brought to the attention of the study director and management immediately

SPONSOR'S SIGNATURE ON PROTOCOL

A study director signs the protocol prior to receiving the sponsor's signature. The sponsor has emailed the study director to proceed with signing the protocol and initiating the study.

§160.120(a)(14) The date of approval of the protocol by the sponsor and the dated signature of the study director.

BALANCE PRINT OUTS

SOP states that you have to use a balance printer for microbalances. While analyst was weighing test substances, they went to print and the printer had run out of paper. The analyst had manually recorded the data visible on the balance but was unable to capture the balance print out.

SOP Deviation

PIPETTE

- §160.63 Maintenance and Calibration of Equipment (1) Equipment shall be adequately inspected, cleaned, and maintained. Equipment used for the generation, measurement, or assessment of data shall be adequately tested, calibrated, and/or standardized.

The impact should be investigated and documented. Did the calibration curve pass linearity test? Can a calibration test be performed after the deviation and exception occurred? Did that pipette pass calibration testing?

A pipette was used to prepare dilutions of calibration standards within the pipette's verification period in June. The pipette was due for verification in July. The pipette was verified according to SOP, but it was determined that the pipette did not pass verification as per SOP. The pipette was tagged out of order and sent to manufacturer.

REFERENCE SUBSTANCE

Name	Glyphosate
CAS Number	1071-83-6
Lot #	XXXXXXXX123456
Molecular Formula	$C_3H_8NO_5P$
Molecular Weight	169.07
Storage Temperature	20ºC±4ºC
Expiration Date	26 JAN 2027
Purity	98.70% (g/g)
Water Solubility	12 g/L at 25ºC
Reference Material Statement	This certificate is designed in accordance with ISO 17034 and ISO Guide 31. This reference material (RM) was designed, produced and verified in accordance with ISO/IEC 17025, ISO 17034 and a registered quality management system ISO 9001. The producer certifies that this reference material meets the specification stated in this certificate until the expiry date, provided it is stored unopened at the recommended temperature herein. Product warranties for this reference material are set out in the terms and conditions of purchase.

§160.105(a) The identity, strength, purity, and composition, or other characteristics which will appropriately define the test, control, or reference substance shal1 be determined for each batch and shall be documented before its use in a study. Methods of synthesis, fabrication, or derivation of the test, control, or reference substance shall be documented by the sponsor or the testing facility, and the location of such documentation shall be specified.

TRAINING RECORDS

An analyst did not have documented training on the latest version of the sample preparation and analytical method being performed in a GLP study.

§160.29 Personnel

(a) Each individual engaged in the conduct of or responsible for the supervision of a study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned functions.

(b) Each testing facility shall maintain a current summary of training and experience and job description for each individual engaged in or supervising the conduct of a study.


THANK YOU FOR YOUR TIME!