GLP Compliance – Myth, Mysteries, Real Regulations or Somewhere In-Between

NAICC 2018 – Renée Daniel

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Let's Get Real

- Common things that QA auditors, Test Facility Management or Study Personnel may think are "required" by GLPs but….
- Are they myths, mysteries, real regulations or somewhere in-between (i.e., industry standards).
  - Myth – Not required although some may disagree
  - Mystery – Who knows where this came from?
  - Real Regulation – 40 CFR 160 says to do it
  - Somewhere In-Between – Some/Many auditors have interpreted the regulations to require it so it has become industry standard
- How much do we, as QA Auditors, make up as we go along?

GLP Compliance

- If someone forgets to record data or date a data entry then records/dates it later with a “late entry” error code this should be included on the GLP compliance statement
  - Real Regulation – Since all data must be recorded promptly and dated **ON** the day of entry there is no way to make this compliant with a “late entry” code. (160.130)
- If a sponsor sends their own SOPs to a CRO it is a compliance issue if they are not followed
  - Myth, maybe? – If the CRO has their own management approved SOPs that are followed this is compliant. However, if the protocols specifies that sponsor SOPs must be followed or references specific sponsor SOPs then it would be a compliance issue if not followed.

Organization Charts

- Are required by the regulations
- Must have job titles and personnel names
- Must include all personnel at the facility
- Must be signed and dated by management
- Need to be retained

Myth – There is no mention in the GLPs of organization charts.

Mystery - EPA and sponsors expect them to be available to use as a tool for determining adequacy of resources (e.g., who reports to whom, training, number of staff). Specific format dictated by facility SOPs.

CVs, Training Records and Job Descriptions

- Must include all personnel
  - Mystery – Technically only requires GLP personnel but some QAs expect to see non-GLP personnel also
- Must be signed and dated
  - Mystery, but is typical since it shows "ownership"
- Must be reviewed/updated annually
  - Somewhere In-Between, but is a way of demonstrating that the record is current
- Annual GLP training is required
  - Myth – TFM gets to decide how much GLP training is required
- Meeting attendance should be included in training records – YES!

Equipment

- Check weights need to be stainless steel
  - Myth, Mystery, Somewhere In-Between – Dictated by facility SOPs
- Weights/balances need to be verified by outside service annually
  - Myth, Mystery, Somewhere In-Between – Dictated by facility SOPs
- GLPs require that target weights be bracketed with check weight masses
  - Myth, Mystery, Somewhere In-Between – Dictated by facility SOPs
- A checkmark can be used to indicate that balance was checked instead of recording theoretical and actual masses?
  - No, Real Regulation – Results are data that must be recorded
- Every measuring device needs to be calibrated (checked for accuracy) including graduated cylinders
  - Mystery – No requirement to calibrate measuring devices that are purchased with expectation of accuracy which is not expected to change

Labeling

- If test substance arrives without expiration date and storage conditions on label, this information doesn't need to be added
  - Somewhere In-Between – Although 160.105(c) requires "expiration date, if any" and "storage conditions necessary to maintain identity…", EPA has indicated that they expect labels to always contain this information
- If a test substance arrives at a field site without an expiration date, the PI can assign one based on facility SOPs
  - No, Somewhere In-Between – EPA has indicated that the PI cannot assign their own expiration date as this should be based on storage stability data and should be assigned by the study director.
- Equipment cleaning solutions need to be labeled with identity, concentration, expiration date and storage requirements
  - Real Regulation – 160.83 requires this for ALL solutions!
- Collection dates are required to be on the sample label
  - Myth – 160.130(c) allows for collection date to be on label or to accompany the sample in a manner that precludes error in recording or storage of data

Freezers

- Sample freezers have to be locked
  - Mystery – If building is locked then this may not be necessary, not specific required by GLPs
- Alarms required for freezers
  - Mystery – Typically samples are stored at CROs very short term and personnel are onsite a lot of that time so this may not be necessary and is not specifically required by GLPs
- Untreated and treated samples can be stored in same freezer and shipped in same box
  - Mystery – An untreated sample for one study could have maintenance chemicals that are the test substance for another study so key is just adequate separation (e.g., bags)
- Tank mix, test substance samples or spiking solutions can be stored in same freezer as residue samples
  - Mystery – see above, key is adequate separation

Quality Assurance

- Contract QA SOPs, CV, and QA reports should be kept at field site
  - Somewhere In-Between – US GLPs allow flexibility in QA records storage location but all need to be available onsite for an EPA or sponsor facility audit
- QA must keep master schedule up to date and all studies conducted at facility need to be on it
  - Myth – Must be current but QA doesn't have to make entries and technically only GLP studies are required
- GLPs require at least 1 critical phase inspection for each **trial in a study**
  - Myth – 160.35(b)(3) requires each **study** to be inspected at adequate intervals but sponsors get to decide how to interpret (i.e., # of inspections for each study)
- GLPs require that study director and management sign the inspection report
  - Myth – GLPs do not require any signatures (but EPA likes to see them)

Quality Assurance

- US GLPs require that inspection be reported to the PI
  - Myth –US GLPs do not mention PIs but OECD GLPs requires this reporting
- GLPs require that separate QA reports be submitted to study director and management
  - Somewhere In-Between – Requirement is for any problems to be brought to the attention of SD and TFM immediately
- Field site QA must submit separate status reports to management and the study director
  - Myth – According to EPA, sponsor QAs are responsible for status reports
- US GLP regulations require QA statement to indicate the date inspections were reported to PI
  - Myth – US GLPs only require date reported to SD and TFM to be on QA statement. However, many sponsors request this on QA statement but be careful when choosing which date to use so that it is not a date before the date reported to SD

Contact Info

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Questions, Audience Participation

- Questions about presentations?
- Audience participation – No personnel or company names when sharing stories please
  - What potential myths and mysteries have you encountered? Please share
  - As a CRO, are there any things that a visiting QA has told you that you feel might be a myth?