The 5 Areas of Laboratory Compliance

Jan 7, 2014 6:31 am PST

Courtesy of Getty Images

Editor's Note: Compliance in the manufacturing laboratory is a multi-faceted and often elusive goal. Alice Krumenaker, in her presentation from IVT's Laboratory Week, offers tips and suggestions for achieving compliant personnel, procedures, lab instrumentation, and methods.

1. Personnel

Be able to confirm that employees are qualified for their positions by having a current curriculum vita on file. Ask employees to update it periodically (annually, biannually, etc.) and as responsibilities change (for example, after a promotion). Accurate training records should be on file that are easily retrieved. Frequent refresher training on quality and safety topics should be conducted.

2. Procedures

Approved procedures need to be in place for method validation and transfer requirements.

Have approved procedures in place for regarding instrument qualification, calibration, and preventive maintenance. Instructions for qualification and calibration should be written out even if this is typically done by the vendor or an outside contractor. If using a protocol from a vendor or outside contract, ensure that it is aligned with your procedure. Include the actions to be taken when an instrument fails calibration.

Have an approved procedure for out-of-specification/out-of-trend results, deviations, and investigations. Include some type of root cause analysis steps to help identify the cause of the issues and prevent it from occurring in the future.

Have procedures in place regarding the use and security of lab software, including data acquisition software and laboratory information management system; a procedure should also be in place to define how raw data and lab documentation is handled. Furthermore, have a procedure in place to define the process for receiving samples and how samples are managed within the laboratory.

3. Laboratory Instrumentation

New instruments should be appropriately qualified before use (see USP general chapter <1058> for instrument categories).

Instruments should have a logbook for recording maintenance and calibration (an instrument usage logbook is not a requirement; however, it may be a handy way to track down information during an inspection if they have been used routinely).

Instrument calibration status should be clearly displayed on the instrument, including the calibration and preventive maintenance (if applicable) dates and the next due date.

Instruments requiring repair or are out-of-calibration should be placed out-of-service and should be clearly labeled so that they are not used for any type of GMP work. Out-of-calibration instruments may be used for non-GxP work if your procedures include this instruction; however, measures must be taken to ensure that these instruments are not used for any GxP testing if both types of work is done in your laboratory.

Laboratory Investigation Preparation Guide

4. Investigations

Unexpected results and/or events should be documented and thoroughly investigated. It is not sufficient to determine that additional training is required for the analyst or glassware wasn't adequately cleaned.

Regardless of the method used, the investigation steps and results need to be clearly documents. Include supporting documentation so that anyone reading the investigation report understands the actions taken and the corresponding results. In the event that the cause cannot be identified, be sure the investigation report illustrates that adequate measures were taken to attempt to identify the cause.

Don't stop at identifying the root cause. Put a plan in place to resolve the issue in the current situation and prevent it from occurring in the future, then follow through to initiate the plan and evaluate if it has the desired results. (For a guide on investigation preparation, see the Table).

5. Methods

Accurately record actions taken during method validation. The project status may change and if the work needs to be resumed at a later date, time won't be lost repeating work that was already completed.

Write method development reports to describe what worked and what didn't when developing the method. This is not a regulatory requirement, however, it is a good practice. This report doesn't need to be formal (it may just be a notebook reference, in fact that's fine), but it should follow a consistent format to make it easy to read. This information may be useful in the future when developing a method for a similar drug substance or product.

Internal procedures should align with compendial and ICH guidelines for method validation. Be thorough in validating methods. Use care to thoroughly demonstrate forced degradation. If the substance doesn't break down under the recommended conditions, obtain standards of known impurities, if possible, to demonstrate specificity of the method.

Use clearly written, reviewed, and approved protocols for method validation and be sure reports include all necessary notebook references and supporting information. The goal is for someone not related to the project to be able to read and understand the documents and know the appropriate measures were taken to validate the method.

Facebook Twitter Pinterest Email Add This

Tags:
GLP, Method Validation

- Are all protocols, methods, reports, etc. written, reviewed approved and filed where they are secure, but easily retrieved?
- Are training records up-to-date, securely filed, and available for review as necessary?
- Are instrument qualification protocols on file for lab instrumentation and software as necessary?
- Are logbooks in use and reviewed as defined in company procedures? Are they replaced as specified and completed contemporaneously?
- Are data and lab notebooks reviewed routinely and errors corrected promptly using good documentation practices? Are completed notebooks closed and filed securely?
- Do lab instruments clearly display calibration status? Are instruments that are due for calibration clearly labeled to ensure they are not used for GMP work?
- Is lab software validated? Is it password protected, with each user having an individual password that is not shared with other analysts? Is data backed up and able to be restored? Is there a disaster recovery plan? Is an audit trail being used? Can files be overwritten? Do calculations performed by software conform to the company's rounding procedures?
- Are lab investigations thorough, identifying the root cause, and closed in a timely manner?
- Do methods and procedures accurately reflect the way processes are actually being done? Be sure to update methods and procedures as soon as possible when updates are necessary. You are expected to be doing what is written in these documents; updating them as needed isn't just a good practice, it is a necessity.
- Have internal audits and address items that are identified as soon as possible. It is much better to resolve issues internally before a regulatory inspection takes place.
- Conduct "mock inspections" within the department to help employees feel more comfortable with the expectations of the inspection process.