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6 Tips for a Compliant Laboratory

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There are some common trends in US Food and Drug Administration citations and observations in the laboratory. While issues in these areas consistently appear in FDA Warning Letters and FDA 483s each year, there are some best practices that can be implemented to ensure that you do not incite regulatory action. Taken from an Alice Krumenaker presentation given at IVT's Method Validation and Development conference, the following are six keys to laboratory compliance.

1. Robust Documentation

Good Documentation Practices (GDP) should be the foundation whenever you record data. In the analytical laboratory, everything is important; otherwise you wouldn't be doing it! GDP requires that you have a written procedure that defines how data will be recorded. It is also advisable to use stamps and pre-printed worksheets or forms to minimize transcription errors or templates for electronic documentation.

In the regulated laboratory, you can't skimp on recording data; it must be recorded thoroughly and accurately. This is especially true for method development. Thus, it is important to record what doesn't work as well as what does work; project teams and priorities may change, and this information could avoid wasted time. This information may be captured in a method development report.

Time for review should be built into the documentation process. A review time can catch errors and allow them to be corrected before reports are issued. If you have reviewer familiar with the subject, a peer review or a dedicated document reviewer can be effective. You cannot wait too long to implement the review. It is easy to re-inject a sample, but this can't be done months after the assay was done.

As with anything in the laboratory, standardization can improve efficiency and increase compliance. Standardizing the way data is documented and filed will make it easier to record and filed. Even during research, while there needs to be some flexibility, having general expectations in place will make the data easier and more efficient to review and retrieve.

2. Laboratory Data Systems

You must know how calculations are done in your data system. You cannot just assume the calculations are correct; computers can make mistakes too! Ask yourself:

- Is rounding done in accordance with your procedures?
- If you have/ a procedure that specifies how rounding is done, does your data acquisition system follow your procedure?
- If there are inconsistencies, are you able to resolve them, or do you need vendor assistance?

The lab data system security has to be a major concern; it is a key part of quality and 21 CFR Part 11 compliance. Password protection, accurate audit trails, the frequency and manner of backups, and disaster recovery all need to be considered and implemented in a data security plan.

3. Laboratory Instrumentation

IQ/OQ/PQ should be performed using protocols that have been reviewed for technical content and compliance prior to execution. Once executed, protocols should be reviewed by a person familiar with the system, reviewed by the quality unit, and then filed so that they may be easily retrieved.

The procedures for qualification, calibration, and preventive maintenance should include actions to take when calibration or qualification tests fail. The frequency of calibration and preventative maintenance should be scheduled on a routine. The date should be allowed to extend to the end of the scheduled month, rather than expire on a given date. If an outside vendor typically does the calibration and preventive maintenance, the requirements should still be covered in the procedures.

Instruments labeled clearly with calibration status. The labels should be clear and easily read and include identification of person performing calibration. The labels should be attached using adhesive that will stick to instrument surface and constructed with a material that will not be damaged by chemicals. You should also label instruments that are out of calibration or being serviced. Periodically check the laboratories to ensure the labels are still in place.

Using logbooks during calibration, preventive maintenance, and repairs; while not a not a requirement; may be helpful when asked for information during an FDA inspection. Having accurate records for an FDA inspector displays a state of control. When using logbooks, an established procedure for reviewing logbooks can ensure that entries are made contemporaneously and that errors are corrected and vendors make appropriate entries in instrument logbooks.

4. Laboratory Training

Adequate training is key component of FDA inspections. Training records help demonstrate that employees are qualified for the work they are doing. For laboratories, you need to demonstrate training for new employee orientation, standard operating procedures (SOPs), techniques and analytical methods, quality and safety, and management.

Although labs are doing the same types of work, each company has different ways of getting the work done. New employee training should include orientation topics; for example, where to find methods and procedures, use and storage of logbooks, lab book documentation, and specific lab requirements for instrument usage. This is not a direct GMP requirement, but it will help employees adjust quicker and help minimize errors.

For many manufacturers, “Read and Understood” SOP training is commonly used because of ease and efficiency. However, it is often not effective. You must implement adequate measures demonstrate that SOP training is hitting the mark.

Training on techniques and analytical methods can be difficult. For specific techniques such as pipetting and

balance usage, you should have training and/or proficiency assessments. For analytical methods, the training type depends on the complexity. It could be a “read and understand”, a demonstration by author, or one-on-one instruction. Compendial methods and/or techniques should be included in training plans, if appropriate.

Quality and safety should be “built in” to all procedures and methods, but sometimes they get pushed to the side in a desire to complete projects. Thus, refresher quality and safety training should be conducted on a regularly scheduled basis and should be included in training file.

Management is often good at being sure department training is current, but they may not keep up with their own training requirement. Delicately, someone should be sure that management has realistic requirements and keeps their training up-to-date.

5. Mistake-Proofing

Lean techniques are commonly used in manufacturing to prevent or greatly limit the possibility of operators performing an act incorrectly. An effective technique, originating in Japan, is 5S. This is a lean technique that reduces errors by keeping work spaces uncluttered and maintaining a state of organization. The fives steps of 5S are:

- Separate: Separate items that are needed from items that may be discarded
- Sort: Place items where they may be located easily
- Shine: Wash, sweep clean work area
- Straighten: Clean continuously rather than at the end of the shift or end of the day
- Sustain: Maintain the state of organization and monitor to find ways to improve

5S tools that may be helpful in the analytical laboratory include:

- Force Field Analysis: Determine forces for and against a change to determine how to remove barriers.
- RACI Matrix: A matrix used to assign responsibilities and accountabilities during a project.
- Kaizen: A short-term improvement project that has a large benefit.

6. Compliant Methods

Incomplete, inadequate, or non-existent method validations are a common source of observations. You must use solid scientific knowledge and build in quality when developing methods. You must also remain aware of compendial changes to methods! Many USP methods are being updated and this may impact testing that’s being done in your laboratory.

Don’t create a scenario in which the method can be validated and transferred easily only to find issues when it is actually being used for testing in the lab. Consider where and how the method will be used when developing and validating. Use ruggedness testing to stress factors that will be used in actually testing the product rather than following a validation template.

Don’t stop at method transfer! Periodically evaluate your methods. Lab environments, manufacturing processes, and products may change through the course of years. Don’t be resistant to change if improvements are needed.

When working on new projects, consider knowledge gained from similar projects in the past to create a more solid framework for method development and validation. In addition to saving time, this helps you to have a more practical recognition of real world applications.

Tags:

GMP - Laboratory Controls, Method Validation
