Bullet Proofing Your Calibration Program
Calibration Audits

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Abstract

Audits from customers or the FDA are looking for faults within a calibration program. This session, Bullet Proofing Your Calibration Program, includes an in-depth explanation of the steps required for successful calibration audits. This session details discussions of procedures, calibration reporting, and equipment files and how they relate to audits. Examples of FDA 483's and warning letters pertaining to calibration audits are presented. This session also addresses:

Writing calibration reports and deviation reports
Scheduling and tracking calibrations
Ensuring documentation is cGMP compliant

Introduction

The basis for pharmaceutical calibration audits by the Food & Drug Administration (FDA) is governed by the Code of Federal Regulations (CFR). There are many different sections of the CFR. For the manufacturing of finished pharmaceuticals, CFR 211.68(a) is applicable. The regulation is not detailed and allows for individualization of your calibration program. It only states the bare minimum requirements.

CFR 211.68(a) is titled, "Automatic, mechanical, and electronic equipment." The regulation states; "Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product. F such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance. Written records of those calibration checks and inspections shall be maintained." [43 FR 45077, Sept. 29, 1978, as amended at 60 FR 4091, Jan. 20, 1995].

PROCEDURES

As written, the CFR for calibrations in regards to finished pharmaceuticals does not define exactly how a calibration program operates. Procedures are developed that dictate how the calibration program should operate. Development of procedures that describe the calibration program is the written program that CFR 211.68 indicates.

Procedures should be written in a fashion that is consistent. Most companies have a written program on how to produce procedures. Procedures are a common cause of 483 citations. Most commonly, the auditor will discover that the procedure is not followed properly or not performed at all. Always review procedures and don't assume the content is correct.

The umbrella procedure or master calibration procedure is a procedure that describes how the calibration program operates at a facility. Some of the common sections within a procedure are; purpose, scope, responsibility, procedure, references, attachments, review cycle, and revision history. The procedure should identify how to assess the instrumentation or classify the instrument into a category. Common categories are critical, non-critical and reference. The procedure should describe how instruments will be identified and how calibration intervals will be established. This procedure should address contractor control, calibration labeling, procedures, calibration practices, documentation / change control, forward and reverse traceability.

The best concept in writing procedures and developing a calibration program is to keep it simple. Do not institute change unless regulations, quality, or safety are driving the change. The more simple the program, the more likely the technicians will follow the written procedures.

DOCUMENT, DOCUMENT, DOCUMENT

In the pharmaceutical calibration world, an instrument is not calibrated unless the documentation is complete. The only evidence of the calibration performed is the calibration report and calibration label. Very seldom does an FDA inspector watch someone perform a calibration to ensure that a proper calibration is being performed per an approved procedure. That is not to say that an inspector can not request to watch a technician perform a calibration and then verify if the technician performs the calibration per the approved procedure. Procedures and calibration reports are commonly audited items by an inspector.

Specifications and change control generated should have the approval signature of the technician, user and QA. If changes are warranted, then approvals must be obtained prior to making the change. A specification form or Equipment Master Specification is a form that can be used to obtain approvals for such parameters as; calibration tolerance, calibration interval, operating range, etc. Such parameters can have an extreme impact on the quality of the products produced therefore it is always best to have the input and approvals of Production, Engineering, and Quality.

The calibration report is one of the most significant documents produced by a pharmaceutical calibration group. The calibration report should be a self explanatory document that does not leave any unanswered questions. The calibration report should describe the instrument in detail. Every instrument should have a unique identification number which will appear on the calibration report and serve as the identification for the report also. The calibration report should describe such things as; manufacturer, model number, serial number, calibration procedure, operating range, calibration tolerance, interval, and description of the instrument. The calibration report is where the data is recorded during the actual calibration. As Found data is

the data taken prior to any adjustments being made. As Left data is the data taken after adjustments are made to the instrument. This data is what is used to determine if the instrument is within calibration tolerance or not. The calibration date and due date for next calibration, should be present on the report. The standards used for the calibration are to be listed on the report along with their identification number and due date of calibration. An indication of whether the instrument was found in or out of tolerance is another item that should be indicated on the report. Finally, the technician should sign and date the report along with an approver signing and dating the report. The approver is normally the supervisor.

The deviation report is a report that is used to describe and resolve a calibration deviation. A calibration deviation occurs when a critical instrument is found to be out of tolerance. This report will indicate the instrument identification number, date of deviation, a description of the deviation, resolution of the deviation, and approval signatures. Normally the approval signatures will be the Technician, Calibration Supervisor, Production Manager, and Quality Assurance. This is another report that is an auditable report.

EQUIPMENT FILES

Equipment files or instrument files should be kept in a neat and orderly fashion. The following items are examples of things in an equipment file; Instrument Master Specifications, Calibration Reports, Deviations, Purchasing Information, Manuals, etc. The equipment or instrument file should tell a story about that instrument. The story could begin with the purchasing information, specification approval, manuals and then calibration reports showing calibrations performed at predetermined intervals. If the interval is not met then the calibration report should indicate why. Documentation prevent any questions from arising, making the files self explanatory.

SUMMARY

Are your procedures adequate to perform quality calibrations? Are your procedures reviewed on a regular basis? Verify that procedures truly indicate the work being performed and there are adequate instructions on how to document the calibration. Is your calibration documentation compliant? Make sure that all calibration documentation is understandable, clear and self explanatory. We do not want questions to be raised and create other auditable documents based on an unclear calibration document. Are equipment files complete? The files should tell a story of the life of an instrument. There should be no hidden chapters. How are calibrations scheduled and tracked? If you utilize software to track your instruments, is the software validated? If you know that an audit is to be conducted then a walk through of the facility can identify some potential problems. Calibration labels are like a giant flag to an inspector. Make sure that all labels reflect the proper dates and information. Many investigations start by examining a calibration label in the field.

References:

1. Code of Federal Regulations – 21 CFR Part 211.68
2. GAMP Guide to Calibration Management