Audits: Why They Aren't Enough

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Abstract

Organizations have many ways to evaluate or determine their ability to conform to quality requirements, whether those requirements are internally (i.e. corporate policy) or externally imposed (i.e. regulatory law, etc).

One method in through audits. Calibration/metrology labs will be periodically audited to determine the level of compliance to their own quality manual (policies) and to regulatory requirements, if they apply. Of particular interest are audits required by the Food and Drug Administration. The products regulated by the FDA have a direct affect on society whether they are food, medicine, or medical devices. Failure to comply with regulatory requirements could result in serious and significant harm to the public.

Is it possible for a lab to pass audit after audit and still have "holes" in their quality program? Could they be compliant with their own quality policies yet fail to meet regulatory requirements?

These are just some of the questions to be discussed in this paper.

Disclaimer:
This paper is based on research of documents and discussions with metrology individuals from different companies and industries and does not depict any particular company's quality system or auditing organization.

Introduction

I started in metrology while in the Air Force. At that time we had a very detailed (and labor intensive) auditing process. The internal process was one of inspection and it audited documentation, calibration accuracy, and technical competence. In those days it also used the multi-level random sampling method. Every calibration document, label, and asset record was reviewed for accuracy. Based on the random sampling level, equipment would be re-calibrated by a quality assurance person. Calibration technicians were evaluated for their technical competence via an "over-the-shoulder" evaluation.

This continuous auditing could be more aptly described as an inspection system for quality assurance. In this case, there was 100% inspection of all criteria except for calibration accuracy which was performed on a percentage basis. Needless to say, this required personnel resources which usually were one or more full time employees.

The goal in the Air Force was to support the mission. There was much consideration given to cost and eventually the quality assurance inspection system gave way to a less comprehensive program focused less on inspection and more on continuous improvement.

I have found in commercial (public sector) industry that auditing is not as aggressive or as comprehensive. With in-house calibration departments in a manufacturing environment or a third party calibration service supplier, the bottom line is still measured in dollars – one as an expense and the other as profit. In any case, the cost of quality affects the level of auditing.

This paper is written primarily for in-house calibration/metrology departments supporting a manufacturing activity. Also, it focuses on regulated industries, particularly organizations regulated by the US Food and Drug Administration (FDA).

Some topics will not apply to external vendors or calibration service suppliers unless they are contracted as the sole supplier for a company (outsourced service).

Audits – What are they?

What an audit is varies with the application or the purpose of the audit. The basis of all audits is to *determine compliance to a requirement*. According to Merriam-Webster, this is done through "a methodical examination and review".

For the purposes of this paper we will be viewing audits as equipment audits – determining if equipment meets requirements. Particularly, does the calibrated equipment used to manufacture or test product meets specifications (range, accuracy, precision) for its intended use. As stated above, this will primarily apply to an in-house calibration activity. Most external calibration service suppliers will not know what the intended use is for their customer's equipment. And in many cases the customer will not specify what the requirements are – they will rely on the supplier to calibrate the equipment to manufacturer's specifications.

Attachments 1 through 6 contain the requirement for calibration from 21 CFR Part 211 and 820, ISO Standard 13485 and the Audit sections from ISO Standards 17025 and 10012.

The following are some definitions or purpose of an audit (also referred to as a quality audit):

Merriam Webster defines "audit" (noun) as:
2 : a methodical examination and review

ANSI/NCSL Z540-1-1994
Quality Audit - A systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these arrangements are implemented effectively and are suitable to achieve objectives.
NOTE: The quality audit typically applies to, but is not limited to, a quality system or elements thereof, to processes, to products, or to services. Such audits are often called *quality system audit[s], process quality audit[s], product quality audit[s],* and *service quality audit[s]*.

FDA QSR Manual Ch 17 Quality System Audits
Audit Requirements:
…To assure that company quality goals will be routinely met and to comply with the QS regulation, quality system audits should:

- measure the effectiveness of the quality system;
- provide objective evidence that adequate controls are in place; and
- assure that products and processes conform with specifications.

Quality Assurance versus Audits

While writing this paper I realized that I may be intertwining quality assurance and auditing. This may be confusing, however the intent is to identify the potential gaps in a quality system.

The QA program is intended to assure quality on a day to day basis while the audit function is performed periodically and is intended to assure that the quality program is being followed according to the organization's quality manual.

Considering this, quality assurance can be considered as the process of determining the quality of the product or service. In our case, the quality of the documentation (procedures and calibration records), calibration accuracy of the equipment, and the technical competence of the personnel. This is usually done through the use of inspection, either continuous (100%) or sampling.

But how many companies have a QA program that performs these functions? Do they inspect 100% of the calibration documentation? Such as calibration label, calibration certificate, the physical condition of the equipment, etc. Is it feasible to re-calibrate a sample (percentage) of the equipment calibrated by your personnel?

For many organizations this is not feasible (cost affective). It is difficult to inspect a calibration label when the technician is at the customer's site which could be hundreds of miles away. Is your quality manager able to review every calibration certificate prior to giving it to the customer? For the on-site technician this would mean having to withhold the certificate until the quality manager can review it. For some customers this may be undesirable in which case the quality manager will have to review the electronic document or a copy of the original certificate.

What is the quality reviewer (manager usually) looking for when inspecting the calibration certificate? In most cases they are looking for the required entries on the document which may be defined by a standard (such as ISO 17025) or by agreement with the customer (contract).

One, if not the most important item to be audited is whether or not the equipment is suitable for its intended use.

Suitable for Use Determination

Ensuring that calibrated equipment is suitable for its intended use or performs its function satisfactorily is the basis for 21 CFR parts 820 and 211 – medical device and pharmaceutical manufacturing. This should be the basis for all calibration activities supporting the manufacture of any product.

Yet, most internal and external auditors focus on the *Control of inspection, measuring, and test equipment.* How do auditors assure control? This is usually accomplished by taking the calibration information from the label on a number of pieces of equipment from the production floor and comparing it with the calibration management system's (CMS) record. The CMS may be paper documents or electronic records. If the data matches, it is assumed that there is adequate control.

Having control is certainly an important and critical aspect of the quality system. It is also the easiest to verify. The assumption is, if the organization can make the information on the label match the information in the CMS that they have adequate control. If they can't, dig deeper because there will be other, possibly more serious, problems.

This is potentially the largest and yet easiest "hole to plug". The best method being automation where the calibration label is printed by the software that determines the new calibration date. The accuracy can be verified by the quality manager if the system saves a copy of the label image. This doesn't ensure that the new label was applied to the equipment, however, failure to apply a label is not as common as making a clerical or typographical error on a label. One way to decrease the uncertainty of failure to apply the label is to remove and retain the old label. Not something that is easily managed, particularly if you are trying to achieve a paperless CMS.

The calibration certificate is another potential audit issue. This is usually printed by the CMS also, but there are still some hand written calibration certificates. The certificate is usually audited for traceability. Does it show what calibration standards used in the calibration of the equipment? The auditor will then look up the calibration certificate for the calibration standards used. The most critical elements here is the date the standards were calibrated. Were the standard's calibration due dates expired? This potential "hole" can be plugged with an electronic CMS that will not allow the technician to enter the standard if the due date is passed. The downside here occurs when the calibration technician finishes the calibration and then attempts to enter the calibration standards and the CMS won't let them. Implementing a calibration process that requires the technician to begin the CMS record prior to the start of the calibration will solve this issue. Barcodes and scanners simplify this process if the software can accommodate them.

The most critical, yet least verified, item is whether or not the equipment is suitable for its intended use. There are several factors to consider:

a. Is it the correct function or parameter (temperature, force, pressure, etc)
b. Does the range of the instrument encompass the product or process range
c. Is the accuracy or tolerance ratio equal to or greater than 1:1
d. Are all product/process parameters calibrated.
e. Is the calibrated component capable of producing valid results.

So, what does it mean?

"calibrated equipment is suitable for its intended purposes and is capable of producing valid results"

- How do we verify this?
- Where is the trail from product/process specifications to calibration results?
- If there is a calibration label on the machine, does the equipment owner know that the parameters needed to make good product were calibrated?
- Concerning producing valid results - If a device/process requires a specific temperature shouldn't the temp at the device location be within specs. Should this be a calibration or a validation? What if the individual validating the equipment assumes that this was a calibrated function if there is a calibration label on the machine?

There are many factors or decisions involved in determining suitability for use and producing valid results. This paper cannot review all of them. The intent is to make you aware that this is a critical function and should be part of your internal auditing process.

How do you verify suitable for use and valid results?

The primary method is to have a document which links the process or product specifications with the production equipment. This may also be used to identify or create a calibration procedure for the machine.

Who performs this?

Identifying process or product specifications is the equipment owner's responsibility who is usually an engineering function (Equipment Engineering, Manufacturing Engineering, etc) in a manufacturing company.

This document (which may be called an Equipment Calibration Specification or ECS) would be the link between the customer's process/product requirements and calibration specifications. Any other factors or parameters which could affect the calibration should be identified on this document. It may also be a good place to document risk factors which can be used to select an adequate calibration interval. In a high volume, high cost production environment the calibration interval may be shorter due to risk (monetary losses or risk to life or health).

This document may contain the process/product range and tolerance to encompass all products or processes it is used for. If there are multiple processes/products there should be another document (controlled and listed on the ECS) which links all of the process/products it produces to the ECS.

Depending on your industry or regulatory requirements there may be other controls you'll need to demonstrate and the ECS is an excellent place to document them. Factors such as: storage and handling precautions, hazardous material notice, when to perform a calibration verification (after moving, software changes, etc) may be included on the ECS.

Conclusion

Are your internal audits and inspections just verifying control?

Have external auditors only verified control or do they dig deeper?

Do you rely on your customer to identify their calibration requirements or do you work with them to develop requirements and have documented evidence that the calibration of their equipment meets its intended use?

There is more to auditing than just verifying that there are controls in place. Review your regulatory requirements and look for potential "holes" in your quality system.

Its been said that the simpler the system the less there is to audit. This may be true, but are you truly meeting all of your customer's or your company's needs and regulatory requirements?

Attachment 1

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of 2006]
[CITE: 21CFR820.72]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

Part 820 - Quality System Regulation

G -- Subpart G--Production and Process Controls

Sec. 820.72 Inspection, measuring, and test equipment.

(a) *Control of inspection, measuring, and test equipment.* Each manufacturer shall ensure that all inspection, measuring, and test equipment, including mechanical, automated, or electronic inspection and test equipment, is suitable for its intended purposes and is capable of producing valid results. Each manufacturer shall establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked, and maintained. The procedures shall include provisions for handling, preservation, and storage of equipment, so that its accuracy and fitness for use are maintained. These activities shall be documented.

(b) *Calibration.* Calibration procedures shall include specific directions and limits for accuracy and precision. When accuracy and precision limits are not met, there shall be provisions for remedial action to reestablish the limits and to evaluate whether there was any adverse effect on the device's quality. These activities shall be documented.

(1) *Calibration standards.* Calibration standards used for inspection, measuring, and test equipment shall be traceable to national or international standards. If national or international standards are not practical or available, the manufacturer shall use an independent reproducible standard. If no applicable standard exists, the manufacturer shall establish and maintain an in-house standard.

(2) *Calibration records.* The equipment identification, calibration dates, the individual performing each calibration, and the next calibration date shall be documented. These records shall be displayed on or near each piece of equipment or shall be readily available to the personnel using such equipment and to the individuals responsible for calibrating the equipment.

[QSR Manual http://www.fda.gov/cdrh/qsr/07.html#measuring_equipment]

Attachment 2

[Code of Federal Regulations]
[Title 21, Volume 4]
[Revised as of April 1, 2005]
[CITE: 21CFR211.68]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER C--DRUGS: GENERAL

PART 211 -- CURRENT GOOD MANUFACTURING PRACTICE FOR FINISHED PHARMACEUTICALS

Subpart D--Equipment

Sec. 211.68 Automatic, mechanical, and electronic equipment.

(a) 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. If 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.

(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.

[43 FR 45077, Sept. 29, 1978, as amended at 60 FR 4091, Jan. 20, 1995]

Attachment 4

ISO 13485:2003 Medical devices - Quality management systems – Requirements for regulatory purposes

7.6 Control of monitoring and measuring devices

The organization shall determine the monitoring and measurement to be undertaken and the monitoring and measuring devices needed to provide evidence of conformity of product to determined requirements (see 7.2.1).

The organization shall establish documented procedures to ensure that monitoring and measurement can be carried out and are carried out in a manner that is consistent with the monitoring and measurement requirements.

Where necessary to ensure valid results, measuring equipment shall

a) be calibrated or verified at specified intervals, or prior to use, against measurement standards traceable to international or national measurement standards; where no such standards exist, the basis used for calibration or verification shall be recorded;

b) be adjusted or re-adjusted as necessary;

c) be identified to enable the calibration status to be determined;

d) be safeguarded from adjustments that would invalidate the measurement result;

e) be protected from damage and deterioration during handling, maintenance and storage.

In addition, the organization shall assess and record the validity of the previous measuring results when the equipment is found not to conform to requirements. The organization shall take appropriate action on the equipment and any product affected. Records of the results of calibration and verification shall be maintained (see 4.2.4).

When used in the monitoring and measurement of specified requirements, the ability of computer software to satisfy the intended application shall be confirmed. This shall be undertaken prior to initial use and reconfirmed as necessary.

NOTE See ISO 10012 for guidance related to measurement management systems.

Attachment 5

ISO 10012:2003 Measurement management systems — Requirements for measurement processes and measuring equipment

8.2 Auditing and monitoring

8.2.1 General

The metrological function shall use auditing, monitoring and other techniques, as appropriate, to determine the suitability and effectiveness of the measurement management system.

8.2.2 Customer satisfaction

The metrological function shall monitor information relating to customer satisfaction as to whether the customer's metrological needs have been met. The methods for obtaining and using this information shall be specified.

8.2.3 Measurement management system audit

The metrological function shall plan and conduct audits of the measurement management system to ensure its continuing effective implementation and compliance with the specified requirements. Audit results shall be reported to affected parties within the organization's management.

The results of all audits of the measurement management system, and all changes to the system, shall be recorded. The organization shall ensure that actions are taken without undue delay to eliminate detected nonconformities and their causes.

Guidance

Measurement management system audits may be carried out as a part of the audits of the organization's management system.

ISO 19011 provides guidance on auditing systems.

Audits of the measurement management system may be carried out by the organization's metrological function, or by contracted or third-party personnel. Auditors should not audit their own areas of responsibility.

8.2.4 Monitoring of the measurement management system

Within the processes comprising the measurement management system, the metrological confirmation and measurement processes shall be monitored. Monitoring shall be in accordance with documented procedures and at established intervals.

This shall include determination of applicable methods, including statistical techniques, and the extent of their use.

Monitoring of the measurement management system shall provide for the prevention of deviations from requirements by ensuring the prompt detection of deficiencies and timely actions for their correction. This monitoring shall be commensurate to the risk of failure to comply with the specified requirements.

The results of monitoring of the measurement and confirmation processes and any resulting corrective actions shall be documented to demonstrate that the measurement and confirmation processes have continuously complied with the documented requirements.

Attachment 6

ISO/IEC 17025:2005 General requirements for the competence of testing and calibration laboratories

4.14 Internal audits

4.14.1 The laboratory shall periodically, and in accordance with a predetermined schedule and procedure, conduct internal audits of its activities to verify that its operations continue to comply with the requirements of the management system and this International Standard. The internal audit programme shall address all elements of the management system, including the testing and/or calibration activities. It is the responsibility of the quality manager to plan and organize audits as required by the schedule and requested by management. Such audits shall be carried out by trained and qualified personnel who are, wherever resources permit, independent of the activity to be audited.

NOTE The cycle for internal auditing should normally be completed in one year.

4.14.2 When audit findings cast doubt on the effectiveness of the operations or on the correctness or validity of the laboratory's test or calibration results, the laboratory shall take timely corrective action, and shall notify customers in writing if investigations show that the laboratory results may have been affected.

4.14.3 The area of activity audited, the audit findings and corrective actions that arise from them shall be recorded.

4.14.4 Follow-up audit activities shall verify and record the implementation and effectiveness of the corrective action taken.