

Calibration Management of Outsourced Calibrations

In today's fast paced biopharmaceutical manufacturing environment, "speed to market" is the hallmark catch phrase. Many companies are focusing only on the processes that add the most value and are outsourcing the rest. This focus on core competencies has some biotech companies reevaluating their calibration practices. Many are contracting more of that workload, from both laboratory and production facilities, to calibration service laboratories.

Outsourcing and cGMP Records

Requirements for calibrating instrumentation used in the manufacturing and quality control of drug and biotech products are well defined in 21 CFR 211, Current Good Manufacturing Practices (cGMP). The regulation allows flexibility in how, where, and by whom calibrations are performed, provided that the industry-accepted practices are followed.

The decision to outsource is usually driven by budgeting constraints and can be made using typical "make vs. buy" analyses. Some variables used in those analyses are the complexity of the instrumentation, the quantity and diversity of the instrument inventory, the expense of calibration standards, and the availability of technical expertise. A low-volume, complex instrument such as a high-performance liquid chromatograph (HPLC) requires different skill sets and instrumentation for calibration from those needed with higher-volume, less sophisticated instruments like thermometers, balances, and micropipettes.

A company may outsource all or only a few calibration services, which fall into several categories. The first category consists of using a particular laboratory to calibrate specific instruments, for example micropipettes, which are gathered and routinely sent off-site. The second involves having a company, such as the manufacturer, service and calibrate equipment (HPLC, for example) on site. The third category of outsourcing is contracting a calibration lab to calibrate your entire inventory on site. Many larger organizations have dedicated, full time calibration technicians outsourced from service labs. Most companies use a combination of these categories

Vendor Qualification

One important consideration before hiring

a contract calibration service is evaluating the company and its ability to provide the required service. 21 CFR 211 describes this requirement and makes it the responsibility of the regulated company (sponsor). Qualifying a calibration service is similar to qualifying other GMP vendors and should include a review of several areas specific to calibration. Some areas of particular interest to FDA and typically asked about during field inspections include calibration procedures, standards traceability, technician training, and calibration documentation.

Regulations do not require a vendor audit; however, that may be advisable depending on the level of service required. Often an evaluation survey will be sufficient for service companies that calibrate a small volume. As you move up the scale in both volume and complexity of instruments to be calibrated, a vendor audit may be justified.

Calibration Management

Regardless of who provides calibration services, the biotech company is ultimately responsible for managing and recording equipment calibrations. A good calibration management system (CMS) should track the instrument inventory, schedule the calibrations and record the histories.

CMSs can be manually tracked, tracked using an internally developed database, or a commercial software package. Each type of system offers advantages, depending on the scope of the operation. An important aspect of any GMP software system is that it must be validated as required by the cGMP. That is also a prerequisite for the use of electronic records and electronic signatures under 21CFR Part 11.

Validation of a GMP software database consists of three steps. The first is to define systems requirements. The Good Automated Manufacturing Practice (GAMP, www.ispe.org) guide calls them the "User Requirements Statements" (URS). These are numbered, discrete statements describing how software should function. The URS are used either to determine how software is to be developed internally or to determine whether a commercially available package meet your requirements.

The next step in the validation process is determining the capabilities of your development staff or outside supplier. Requirements include a software development life cycle, software quality assurance plans, testing, and maintenance. At this point, many companies defer to an outside developer with experience in developing GMP applications because the systems needed can stretch the limited internal IT resources.

The final step in the validation process is performing installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) for the software under your specific application environment.

Service History Records

With a CMS in place and validated, you can manage both your internal and external calibrations. Control of calibration certificates or histories is a special concern when using an outside calibration service. Many companies that use a CMS will maintain a database record including who did the calibration, when it was done and what standards and procedures were used. Many companies will also file the hard copy in the instrument's history folder.

An added benefit of some CMS packages is their ability to attach external electronic files to the database records, typically done through what is called an OLE link. Attached documents usually can be in any format, but the most popular being word processing, spreadsheet, PDF, and scanned graphic images.

By working with a calibration service company ahead of time, you can save time and resources by identifying or specifying the history record format.

Outsourced calibrations are becoming more popular in the biopharmaceutical industry, allowing companies to save both time and money. It is important to take certain steps when outsourcing calibrations, including qualifying the vendor, choosing and validating a CMS, and maintaining the database of calibration events.

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