



SOPs: Least Understood, Most Important Tool to Ensure Regulatory Compliance

By Mukesh Kumar, PhD, RAC

Written standard operating procedures (SOPs) are the foundation of any drug development, testing, manufacturing and marketing program. SOPs strengthen compliance not only with US Food and Drug Administration (FDA) requirements but also with international requirements. Ideally, SOPs should describe everything that occurs at a facility in sufficient detail to ensure all tasks are conducted consistently, repeatedly and accurately. SOPs are among the first documents to be reviewed by auditors and are an integral component of an organization's demonstrated compliance with regulations.

Although most organizations appreciate the importance of SOPs, they may have a poor understanding of many aspects of SOP creation, maintenance, training and organization, leading to many errors with regulatory compliance identified during FDA audits. This article discusses the most common issues with SOP creation, management and implementation and suggests solutions to create one of the best regulatory compliance tools available to an organization.

SOPs are Required by Law

Many parts of Title 21 in the *Code of Federal Regulations* (CFR), such as 21 CFR Parts 11.10, 11.30 and 56.108, describe requirements for written procedures. The regulations describe that a facility must have written procedures, i.e., SOPs, with documentation to support conformity with the same. Similarly, requirements for written SOPs are frequently mentioned in the ICH guidelines and ISO requirements.

However, since the regulations do not provide guidance on the format of SOPs or their specific style and content, companies can design their SOPs in the way they believe is best to ensure process control and compliance. Once an organization defines its specific procedures via SOPs, it is responsible for complying with them. In other words, SOPs define the commitments made regarding conduct of processes and organizations are required to demonstrate conformance to those processes.

It may sound simple to follow a set of written procedures that define the way an activity is to be completed, but if those procedures are not written clearly and comprehensively or are not current, there are likely to be deviations in practice, which may lead to quality issues. That is the reason why SOPs play a central role in compliance audits by regulators. Most audit findings can be attributed to noncompliance with SOPs or inadequate SOPs. Frequently, Form 483s and Warning Letters from FDA cite inadequate SOPs or noncompliance with the company's own procedures.

SOPs Should be Clear

Although each SOP is unique to the organization, certain attributes are common to all SOPs (see **Figure 1**). An SOP should be task-specific. It

should address only one or a few closely related tasks.

Ideally, the lead employee responsible for conducting or overseeing a given task should create the document. The procedure should be described in sufficient detail so an employee with the proper qualifications can perform the procedure appropriately.

Tasks should be split into short, discrete steps and sub-steps to make the procedure as reader friendly and easy to follow as possible. Diagrams or flowcharts should be used when needed. For example, use a flowchart to define the sequence in which steps should be completed and show alternate pathways.

Another way to encourage precision in SOPs is to write in plain language. This means using bullets and numbers when possible, keeping the step descriptions short and the entire procedure as concise as possible.

SOPs should be written in the language of its users; it is not necessary to have the SOPs only in English. A common audit finding is poor compliance with SOPs due to employees' unfamiliarity with their content. For example, if manufacturing facility personnel can only read and speak Spanish, yet the SOPs are written in English, there is sure to be an issue with understanding and complying with the SOPs.

Since FDA auditors mostly request a certified translation of non-English SOPs for review, it is best to create SOPs in English as well as the language(s) used by employees. It is also wise to list the job titles of staff who are responsible for each procedure step. To avoid the need for frequent revisions to the SOPs, it is advisable not to list the names of individuals who currently hold these positions.

SOPs Should be Maintained

SOPs are living documents. As procedures change with time and experience, so should their SOPs. Most deviations from the processes described in a given SOP can be attributed to procedural changes that have not been formalized in the current version of the SOP. On the other hand, an organization with evolving SOPs typically learns from experience, adapts to developments in related fields and acquires in-depth knowledge of the processes it conducts.

In addition to reflecting the current practices used to complete a given task, the SOP should include a history of changes. An organization with evolving SOPs is an organization that learns from its experience, adapts to developments in related fields, indicates in-depth knowledge of the processes it conducts, and is perceived as more credible by auditors.

An easy method to document the evolution from previous to current procedures is to properly annotate the SOP with version number, effective dates and categorization. It is also a good idea to have a summary section at the

beginning of the SOP listing the changes from the previous versions. Needless to say, SOPs should be formatted professionally using pagination, headers and footers on all pages, with identifiers and other measures to ensure appropriate identification.

SOP maintenance should be formalized in—what else?—an SOP. Many organizations do not formally define their process for updating SOPs in a written document. For an auditor, any process that is not written is a process that was not conducted. An SOP that defines the practices for revising existing SOPs, creating new ones and training, retraining and authorizing employees in all processes is a must to demonstrate timelines.

To meet regulatory requirements, companies should define a system of reviewing and revising their SOPs. A good standard practice is an annual or biannual review, but at a minimum, a company should review its SOPs every three years. Revisions should take place immediately if there are any major changes in procedures. Once a revision is made, all personnel responsible for the procedure must be retrained. This training should be documented in personnel files to show that employees have been trained on the most current processes.

Just as it is a good practice to have the SOPs written by the person(s) responsible for a given task, it is important that the same individual(s) be asked to track any changes to the process and determine the need for revising or replacing a given SOP. Most commonly, SOPs are maintained by the Quality Assurance (QA) department of an organization. This approach ensures uniformity in SOP format and style across the organization, control over access and editing privileges, and regular monitoring of training and revisions.

SOPs need to be guarded like trade secrets as they describe activities critical to the compliance status of an organization. Auditors usually look for processes that balance control over integrity of an SOP with ease of access to relevant SOPs for all employees.

Organizations can achieve this balance by using position-specific SOP binders or electronic documents. This ensures that employees have access to the relevant SOPs whenever they need to reference them.

On the other hand, it is important for a company to control and limit access to the SOPs. There should be limits on editing capabilities so that processes are changed only by authorized personnel. Within an organization, unauthorized



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access to non-relevant or older SOP versions should be prohibited so outdated processes are not mistakenly followed.

One last piece of advice for creating the perfect document to impress the FDA auditor is to create a master table of contents. This will serve as a great reference tool. The table of contents should list all company SOPs, organized by department and including the title and a short description/purpose of the procedure. With the table of contents and short summaries, an auditor can see all processes covered by SOPs and decide which ones to review in greater detail.

SOP Training Should be Extensive

Without adequate training of personnel, SOPs do not mean much. Taking the time to train employees and confirm that they have read and understood the SOPs for which they are responsible is very important. Auditors have been known to gauge employees' understanding of processes by asking them to describe the contents of SOPs and demonstrate performance of the tasks. Also of key interest to auditors are personnel training records.

There are several ways to evaluate employee conformance to SOPs such as administering

Figure 1: Best Practices for SOP Creation

- **Task specific:** one or few closely-related tasks
- **Have sufficient details to complete the task:** step-by-step instructions
- **Written in "plain" language:** easy to understand by the user
- **Define responsible personnel:** assignment by position or job title, not name
- **Appropriately annotated:** tracking number, checklists, dates
- **Current:** updated when the processes change, with modifications documented
- **Accessible to relevant personnel:** not all employees need all SOPs
- **Documentation-centric:** create documentation of performance conformance

quizzes, assigning mentors and documenting performance reviews. Additionally, checklists and other forms are very helpful tools to monitor and assist with compliance. Not only do the checklists verify that employees are performing the tasks appropriately, but they also serve to document compliance. Remember to require signatures and dates on any documentation associated with SOPs. Good documentation and organization for the completed checklists and documents go a long way to make FDA auditors comfortable with the compliance status of an organization.

Conclusion

Most organizations take SOPs for granted, yet good SOPs are the foundation for effective regulatory compliance. A company that has well-written and designed SOPs supported by a strong process of training, documentation and ongoing updates is well on its way to impressing FDA.

While some companies use outside vendors to create sophisticated SOP documents, simpler techniques can ensure good-quality, FDA-compliant documents.

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