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Guidance for Preparing Standard Operating Procedures (Sops)

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ABSTRACT: *SOPs are living documents that detail written instructions describing specific steps to follow in all activities under defined conditions. SOPs are necessary to ensure the continuity of processes to achieve quality performance and quality products/preparations. The purpose statement identifies the goal of the SOP. It answers the question of why the SOP is being written. For example, "The purpose of this Standard Operating Procedure (SOP) is to specify the processes used to manage SOPs". The Purpose statement needs to be detailed enough so that the intended user can recognize what the document covers.*

KEYWORDS: *Standard operating procedures (SOPs), Pharmaceutical industry*

I. INTRODUCTION

In the face of a challenging regulatory environment, some leading Pharmaceutical companies have found ways to improve quality and costs significantly. To drive this kind of beneficial change, companies must first create a culture where quality objectives are transparent, well understood, and undoubtedly these goals can be achieved by following certain sets of procedures called as "Standard Operating Procedures" *(SOP)*. Procedures are essential for any plant's effectiveness and efficiency, and they are regulatory requirement in the Pharmaceutical Industry. A typical Pharmaceutical Industry has an average of 1200- 1300 SOPs. A Parenteral Drug Association (PDA) survey found that a typical pharmaceutical company must manage an average of 1250 CGMP-required SOPs and that the average maintenance burden is 15,000 h per firm.

A Standard Operating Procedure (SOP) is a set of written instructions that document a routine or repetitive activity which is followed by employees in an organization. The development and use of SOPs are an integral part of a successful quality system. It provides information to perform a job properly, and consistently in order to achieve pre-determined specification and quality end-result.

SOPs should allow for the continual improvement of standards of service, and provide evidence of commitment towards protecting patients. Additional benefits are:

Help to assure quality and consistency of service;
Help to ensure that good practice is achieved at all times;
Provide an opportunity to fully utilize the expertise of all team members;
Enable pharmacists to delegate;
Help to avoid confusion over who does what (role clarification);
Provide advice and guidance to locums and part-time staff;
They are useful tools for training new members of staff;
Provide a contribution to the audit process.

II. BENEFITS OF SOP

Benefits of Sop

- **To provide people with all the safety, health, environmental and operational information necessary to perform a job properly.** Placing value only on production while ignoring safety, health and environment is costly in the long run. It is better to train employees in all aspects of doing a job than to face accidents, fines and litigation later.
- **To ensure that production operations are performed consistently to maintain quality control of processes and products.** Consumers, from individuals to companies, want products of consistent quality and specifications. SOPs specify job steps that help standardize products and therefore quality.
- **To ensure that processes continue uninterrupted and are completed on a prescribed schedule.** By following SOPs, you help ensure against process shut-downs caused by equipment failure or other facility damage.
- **To ensure that no failures occur in manufacturing and other processes that would harm anyone in the surrounding community.** Following health and environmental steps in SOPs ensures against spills and emissions that threaten plant neighbors and create community outrage.

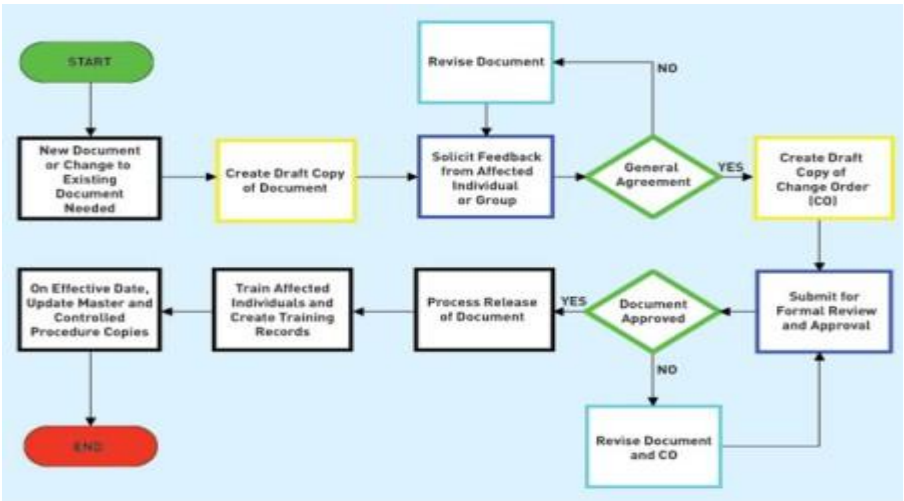
- **To ensure that approved procedures are followed in compliance with company and government regulations.** Well-written SOPs help ensure that government regulations are satisfied. They also demonstrate a company's good-faith intention to operate properly. Failure to write and use good SOPs only signals government regulators that your company is not serious about compliance.
- **To serve as a training document for teaching users about the process for which the SOP was written.** Thorough SOPs can be used as the basis for providing standardized training for employees who are new to a particular job and for those who need re-training.
- **To serve as a checklist for co-workers who observe job performance to reinforce proper performance.** The process of actively caring about fellow workers involves one worker coaching another in all aspects of proper job performance. When the proper procedures are outlined in a good SOP, any co-worker can coach another to help improve work skills.
- **To serve as a checklist for auditors.** Auditing job performance is a process similar to observation mentioned in the previous item only it usually involves record keeping. SOPs should serve as a strong basis when detailed audit checklists are developed.
- **To serve as an historical record of the how, why and when of steps in an existing process so there is a factual basis for revising those steps when a process or equipment are changed.** As people move from job to job within and between companies, unwritten knowledge and skills disappear from the workplace. Properly maintained written SOPs can chronicle the best knowledge that can serve new workers when older ones move on.
- **To serve as an explanation of steps in a process so they can be reviewed in accident investigations.** Although accidents are unfortunate, view them as opportunities to learn how to improve conditions. A good SOP gives you a basis from which to being investigating accidents.

Ten reasons for writing SOPs:

- To provide individuals who perform operations with all the safety, health, environmental and operational information required to perform a job properly
- To protect the health and safety of employees, and to protect the environment
- To protect the community
- To ensure that operations are done consistently in order to maintain quality control of processes and products
- To ensure that processes continue and are completed on a prescribed schedule
- To ensure that no failures occur in manufacturing and related processes that would harm employees or anyone in the surrounding community
- To ensure that approved procedures are followed in compliance with company and government regulations
- To serve as a training document for teaching users about a process
- To serve as an historical record of the how, why and when of steps in a process for use when modifications are made to that process and when a SOP must be revised
- To serve as an explanation of steps in a process that can be reviewed in incident investigations that seek to improve safety practices and operating.

III. SOP PROCESS

FIGURE 1. SOP Process



- **SOP Preparation**
  The organization should have a procedure in place for determining what procedures or processes need to be documented. Those SOPs should then be written by individuals knowledgeable with the activity and the organization's internal structure. These individuals are essentially subject-matter experts who actually perform the work or use the process. A team approach can be followed, especially for multi-tasked processes where the experiences of a number of individuals are critical, which also promotes "buy-in" from potential users of the SOP.
  SOPs should be written with sufficient detail so that someone with limited experience with or knowledge of the procedure, but with a basic understanding, can successfully reproduce the procedure when unsupervised. The experience requirement for performing an activity should be noted in the section on personnel qualifications. For example, if a basic chemistry or biological course experience or additional training is required that requirement should be indicated.
- **SOP Review and Approval**
  SOPs should be reviewed (that is, validated) by one or more individuals with appropriate training and experience with the process. It is especially helpful if draft SOPs are actually tested by individuals other than the original writer before the SOPs are finalized.
  The finalized SOPs should be approved as described in the organization's Quality Management Plan or its own SOP for preparation of SOPs. Generally the immediate supervisor, such as a section or branch chief, and the organization's quality assurance officer review and approve each SOP. Signature approval indicates that an SOP has been both reviewed and approved by management. As per the Government Paperwork Elimination Act of 1998, use of electronic signatures, as well as electronic maintenance and submission, is an acceptable substitution for paper, when practical.
- **Frequency of Revisions and Reviews**
  SOPs need to remain current to be useful. Therefore, whenever procedures are changed, SOPs should be updated and re-approved. If desired, modify only the pertinent section of an SOP and indicate the change date/revision number for that section in the Table of Contents and the document control notation.
  SOPs should be also systematically reviewed on a periodic basis, e.g. every 1-2 years, to ensure that the policies and procedures remain current and appropriate, or to determine whether the SOPs are even needed. The review date should be added to each SOP that has been reviewed. If an SOP describes a process that is no longer followed, it should be withdrawn from the current file and archived.
- **Checklists**
  Many activities use checklists to ensure that steps are followed in order. Checklists are also used to document completed actions. Any checklists or forms included as part of an activity should be referenced at the points in the procedure where they are to be used and then attached to the SOP.
  In some cases, detailed checklists are prepared specifically for a given activity. In those cases, the SOP should describe, at least generally, how the checklist is to be prepared, or on what it is to be based. Copies of specific checklists should be then maintained in the file with the activity results and/or with the SOP.
  Remember that the checklist is not the SOP, but a part of the SOP.
- **Document Control**
  Each organization should develop a numbering system to systematically identify and label their SOPs, and the document control should be described in its Quality Management Plan. Generally, each page of an SOP should have control documentation notation, similar to that illustrated below. A short title and identification (ID) number can serve as a reference designation. The revision number and date are very useful in identifying the SOP in use when reviewing historical data and is critical when the need for evidentiary records is involved and when the activity is being reviewed. When the number of pages is indicated, the user can quickly check if the SOP is complete. Generally this type of document control notation is located in the upper right-hand corner of each document page following the title page.
- **SOP Document Tracking and Archival**
  The organization should maintain a master list of all SOPs. This file or database should indicate the SOP number, version number, date of issuance, title, author, status, organizational division, branch, section, and any historical information regarding past versions. The QA Manager (or designee) is generally the individual responsible for maintaining a file listing all current quality-related SOPs used within the organization. If an electronic database is used, automatic "Review SOP" notices can be sent. Note that this list may be used also when audits are being considered or when questions are raised as to practices being followed within the organization.

IV. GUIDELINES FOR TECHNICAL & ADMINISTRATIVE OR FUNDAMENTAL PROGRAMMATIC SOP TEXT

Guidelines for Technical SOP Text

Technical SOPs can be written for a wide variety of activities. Examples are SOPs instructing the user how to perform a specific analytical method to be followed in the laboratory or field (such as field testing using an immunoassay kit), or how to collect a sample in order to preserve the sample integrity and representativeness (such as collection of samples for future analysis of volatile organic compounds or trace metals), or how to conduct a bio assessment of a freshwater site. Technical SOPs are also needed to cover activities such as data processing and evaluation (including verification and validation), modeling, risk assessment, and auditing of equipment operation.

Citing published methods in SOPs is not always acceptable, because cited published methods may not contain pertinent information for conducting the procedure-in-house. Technical SOPs need to include the specific steps aimed at initiating, coordinating, and recording and/or reporting the results of the activity, and should be tailored only to that activity. Technical SOPs should fit within the framework presented here, but this format can be modified, reduced, or expanded as required. Examples of technical SOPs are located in the Appendices A, B, and C.

In general, technical SOPs will consist of five elements: Title page, Table of Contents, Procedures, Quality Assurance/Quality Control, and References:

1. Title Page.
2. Table of Contents
3. Procedures - The following are topics that may be appropriate for inclusion in technical SOPs. Not all will apply to every procedure or work process being detailed.

a. Scope and Applicability (describing the purpose of the process or procedure and any organization or regulatory requirements, as well as any limits to the use of the procedure),

b. Summary of Method (briefly summarizing the procedure),

c. Definitions (identifying any acronyms, abbreviations, or specialized terms used),

Health & Safety Warnings (indicating operations that could result in personal injury or loss of life and explaining what will happen if the procedure is not followed or is followed incorrectly; listed here and at the critical steps in the procedure),

e. Cautions (indicating activities that could result in equipment damage, degradation of sample, or possible invalidation of results; listed here and at the critical steps in the procedure),

f. Interferences (describing any component of the process that may interfere with the accuracy of the final product),

g. Personnel Qualifications/Responsibilities (denoting the minimal experience the user should have to complete the task satisfactorily, and citing any applicable requirements, like certification or "inherently governmental function"),

h. Equipment and Supplies (listing and specifying, where necessary, equipment, materials, reagents, chemical standards, and biological specimens),

i. Procedure (identifying all pertinent steps, in order, and the materials needed to accomplish the procedure such as:

- Instrument or Method Calibration and Standardization
- Sample Collection
- Sample Handling and Preservation
- Sample Preparation and Analysis (such as extraction, digestion, analysis, identification, and counting procedures)
- Troubleshooting
- Data Acquisition, Calculations & Data Reduction Requirements (such as listing any mathematical steps to be followed)
- Computer Hardware & Software (used to store field sampling records, manipulate analytical results, and/or report data), and

j. Data and Records Management (e.g., identifying any calculations to be performed, forms to be used, reports to be written, and data and record storage information).

4. Quality Control and Quality Assurance Section - QC activities are designed to allow self-verification of the quality and consistency of the work. Describe the preparation of appropriate QC procedures (self-checks, such as calibrations, recounting, reidentification) and QC material (such as blanks - rinsate, trip, field, or method; replicates; splits; spikes; and performance evaluation samples) that are required to demonstrate successful performance of the method. Specific criteria for each should be included. Describe the frequency of required calibration and QC checks and discuss the rationale for decisions. Describe the limits/criteria for QC

data/results and actions required when QC data exceedQC limits or appear in the warning zone. Describe the procedures for reporting QC data and results.
5. Reference Section - Documents or procedures that interface with the SOP should be fully referenced (including version), such as related SOPs, published literature, or methods manuals. Citations cannot substitute for the description of the method being followed in the organization. Attach any that are not readily available.

Guidelines for Administrative or Fundamental Programmatic SOP Text

As with the technical SOPs, these SOPs can be written for a wide variety of activities, e.g., reviewing documentation such as contracts, QA Project Plans and Quality Management Plans; inspecting (auditing) the work of others; determining organizational training needs; developing information on records maintenance; validating data packages; or describing office correspondence procedures. Administrative SOPs need to include a number of specific steps aimed at initiating the activity, coordinating the activity, and recording and/or reporting the results of the activity, tailored to that activity. For example, audit or assessment SOPs should specify the authority for the assessment, how auditors are to be selected, what will be done with the results, and who is responsible for corrective action. Administrative SOPs should fit within the framework presented here, but this format can be modified, reduced, or expanded.
In general, administrative/programmatic SOPs will consist of five elements: Title page, Table of Contents, Purpose, Procedures, Quality Assurance/Quality Control, and References.
1. Title Page -.
2. Table of Contents -
3. Procedures -The following are topics that may be appropriate for inclusion in administrative SOPs:
a. Purpose – (identifying the intended use of the process)
b. Applicability/Scope (identifying when the procedure is to be followed),
c. Summary of Procedure,
d. Definitions (defining any words, phrases, or acronyms having special meaning or application),
e. Personnel Qualifications/Responsibilities (identifying any special qualifications users should have such as certification or training experience and/or any individual or positions having responsibility for the activity being described), Criteria, checklists, or other standards that are to be applied during the procedure such as citing this document as guidance for reviewing SOPs), and
h. Records Management (specifically, e.g., as forms to be used and locations of files).
4. Quality Control and Quality Assurance Section - Describe any control steps and provisions for review or oversight prior to acceptance of the product or deliverable. This can include test plans such as verification and validation plans for software or running a "spell-check" program on the finished document.
5. Reference Section - Cite all references noted in the body of the SOP. A copy of any cited references not readily available should be attached to the SOP.

V. POINTS TO BE CONSIDER DURING WRITING SOPs

1. How much someone knows about an entire process or job affects the way he or she does that job incorporate safety, health and environment into the traditional how-to-operate or how-to-do steps. This teaches the person comprehensively or holistically so that he or she has a complete picture of the responsibilities for doing a job properly. This simplifies follow-up training.
2. Write an SOP to be as long as necessary for a specific job. All jobs differ in the number of steps required to complete them properly. Short-changing someone by providing short and incomplete SOP sets up failure. Write an SOP to satisfy the definition of SOP, not a standard company format that no one has thought about in years.
3. People tend to ignore long SOPs because they cannot remember more than 6 to12 steps. If your SOP goes beyond 10 steps, consider these solutions:
   Break the long SOP into several logical sub-job SOPs,
   Write an accompanying shortened SOP that lists only the steps but not detailed explanations of those steps, and
   Make the long-form SOP a training document or manual to supplement the shorter sub-job SOPs mentioned earlier.
4. Prepare the longer comprehensive training SOPS first to get a picture of what training is needed. Then decide how to break it into shorter sub-job SOPs. Writing sub-job SOPs first, and then trying to put them together, may leave out linkage steps that make sub-jobs interdependent.
5. Write SOPs for people who perform under different interpersonal circumstances.

- Write some SOPs for people who work alone.
- Write some SOPs for two or more people who work together as a team.
- Write some SOPs for people who will supervise other people doing a job.

- Write some SOPs for people who not familiar with rules generally understood by your employees. For example, you may write for contractors, vendors or suppliers.

6. Consider the work culture within which people work. If you write for people in a culture in which shortcuts are accepted practice, explain the reasons behind certain steps so that SOP users will understand the importance of following all the steps in the proper order.
7. Consider the age, education, knowledge, skill, experience and training, and work culture of the individuals who will be performing the SOP steps.
8. Keep in mind that many people do not read all the steps before starting on step one. Many people read a step, perform it, read the next step, perform it, and soon. To try to get around this habit, forecast future effects and steps at certain points in the SOP to tell reader things they should know in advance, such as upcoming steps that require caution, precision, timing, assistance, and personal protective equipment.
9. Once you have completed writing an SOP, have several workers test it and give you feedback. If you did not consult safety, health and environmental experts prior to writing the SOP, have them observe the SOP being tested so they can add comments.
10. Review the effectiveness of SOPs after a few weeks and make necessary changes if in-the-field practice suggests that descriptions should be improved.

- Review SOPs when processes and equipment are changed.
- When new equipment is installed, take the opportunity to write a new SOP, incorporating the good from the old, and adding what is necessary to satisfy the new equipment

VI. DESIGNING OF SOP

In designing of SOP Following points are considered

OBJECTIVE:

To lay down procedure for the preparation of Standard Operating Procedures.

SCOPE:

This procedure is applicable to all the SOP's throughout the organization.

RESPONSIBILITY:

Person Performing: Respective HOD's of concerning departments

Person Monitoring: QA officer/ HOD QA

PROCEDURE:

All SOP's shall be computer typed using Times New Roman font.

Format of SOP shall be as per Annexure SOP/QA/002/1. Each SOP has:

I) Header,

II) Signature block and

III) Body.

Header: Present on all the pages of SOP and includes

Company Logo, Name, address & Concerned Dept.: Company Logo, (In capital bold letters of font size 16)

Document Type: Standard Operating Procedure (In capital bold letters of font size 14)

Ref. No.: It is like SOP/DC/YYY-Z Where DC depicts the department code as below:

PE: Personnel Department

PD: Production Department

MT: Maintenance Department

QA: Quality Assurance Department

QC: Quality Control Department

ST: Store Department

PU: Purchase Department

YYY is the sequential number starting from 001 for each department.

And Z is the revision status, starting from 0 for the original version and 1 for the next version and so on. (In capital letters of font size 12).

Supersedes: It is the Ref. No. of the earlier version. (In capital letters of font size 12).

Effective Date: It is the date from which the SOP shall be put in use. The date format has to be DD/MM/YYYY, where DD indicates the date, MM indicates the month & YYYY indicates the year (e.g. 01/11/2007). Date shall be written with blue indelible ink pen.

Review Date: It is the Month & Year during which the SOP shall be revised e.g. 21/2013, written with blue indelible ink pen. It shall be maximum 2 years from the effective date.

Page No.: It is like X OF Y. Where X is the individual page number and Y is the total number of pages. (In capital letters of font size 12)

Title: It shall be clear and descriptive. (In bold capital letters of font size 12).

Signature Block: It shall be below the header and only on the first page of the SOP.
(Titles in the rows & columns shall be in bold letters & other text in normal letters of font size 12. Name and designation shall be typed. And signature and date shall be put in blue indelible ink pen)
Prepared by: Signature with date, name and designation of the person from user department who has drafted the SOP.
Verified by: Signature with date, name and designation of the HOD or the person from user department who has verified the draft of the SOP.
Authorized by: Signature with date, name and designation of the person authorizing SOP, DGM QA or HOD QA.
Body: It shall contain the subject matter, which is written in the following Manner.
(Subtitles in capital bold letters and text matter in normal letters of font size 12).
OBJECTIVE: It shall define the purpose of the SOP.
SCOPE: It shall define the area of application.

VII. SOP CONTROL

Initially SOP is prepared by concern department as draft and draft is reviewed by dept. head and final draft is send to QA department that convert a draft to a final documents checked and approved by authorize person. Control copies are issued to concern department and issuance records are maintained. After approval of documents such as sops quality assurance must ensure that all users/concerned department gets training before the implementation of the sops record of such training must be maintained. A training co-coordinator preferably the head of user department or any designated individuals shall be responsible for organizing the training. After successful implementation of training on any sops, the sops become effective.
Original sops are stamped as "MASTER COPY" with red ink, master copy are stored under supervision and photocopy of master copy duly stamped as "CONTROL COPY" in blue color. Sops distribution list should be maintained for issuance records, change in sops need to initiated change request and all issue copies are retrieve and new one implemented with training.

- **SOP Record control**

GDP procedure should describe the types of workbooks/notebooks that may be used – typically these are hard-covered with sown/sturdy binding; avoid spiral bound workbooks or logbooks as pages may be removed.
In an emergency, if no official means to record an observation is available, then:

1. Initial, date and provide a comment on the paper record of the observation and attach to the official hardcopy record as soon as possible.
2. Transcribe and attach the data to the official record and annotate 'Transcribed, see attached original'. The transcription must be signed and dated by the Preparer and filed/stored together with the original record.
3. The data must be checked for accuracy by a second staff member.
4. Investigate why an official record was not available at the time. Implement corrective actions so that the same situation may not arise again, e.g. create a form for the record, amend the procedure, change the process so that the record is captured electronically etc.

- **Using true copies**

1. Sometimes there is a need to use a copy of an original document or record, e.g. attaching a copy of a report to a non-conformance record. So that it is apparent that the record is not the original:
2. Stamp or write on the front of the copied documentation, 'True Copy'.
3. Sign and date the 'True Copy' amendment.

- **Modifying records in a compliant manner**

The company GDP procedure should stipulate how data or entries may be amended. This should include details on:

1. Any standard abbreviations used, e.g. 'not applicable' (NA or N/A) etc.
2. Unacceptable practices, e.g. using 'ditto' marks (") to indicate the same entry as above, leaving empty fields in a form, etc.
3. Who is responsible for checking documentation amendments or general GMP compliance of logbook pages over time.

VIII. CONCLUSION

The Code of Federal Code Of Federal Regulations for drug product manufacture's states (Subpart F, CFR Part 211.100) "There shall be written procedure for production and process control designed to assure that drug product have the identity, strength, quality and purity, they purport or are represented to possess."
Regulations for medical device manufacturers and other related regulated entities (Title 21, CFR Part 820) states repeatedly that firms must "establish and maintain" procedures. To do so, companies should define,

document (either on paper or electronically), and implement standard operating procedures (SOPs). Additionally, companies must then follow up, review, and revise these documents as needed.

The intent here is simple: Companies must ensure that their organization develops and manages operationally sound procedures that are compliant with the law. FDA audit findings in 2006 clearly indicate that ensuring establishment and maintenance of procedures is fundamental in FDA's inspection strategy. During inspections in 2006, the agency commonly observed that companies failed to keep accurate records and that they neglected to establish and maintain procedures.

SOPs serve as a fundamental means of communication for all levels of the organization. Not only do they involve employees departmentally, but they also allow management and employees to gain a cross-functional view of the organization. This approach encourages employees to think about how process change may affect other functional areas. A good system forces Employee to think through processes and examine how Procedure might affect product, personnel, production, and equipment. ***It shall be noted that the Best written SOPs will fail if they are not followed.***

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