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QUALITY SYSTEMS AND STANDARD OPERATING PROCEDURES – A REVIEW

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Abstract:

It is mandatory for sponsors of clinical trials and contract research organizations alike to establish, manage and monitor their quality control and quality assurance systems and their integral standard operating procedures and other quality documents to provide high-quality products and services to fully satisfy customer needs and expectations. Quality control and quality assurance systems together constitute the key quality systems and parts of quality management. Quality control is focused on fulfilling quality requirements, whereas quality assurance is focused on providing confidence that quality requirements are fulfilled. The quality systems must be commensurate with the company business objectives and business model. Top management commitment and its active involvement are critical in order to ensure at all times the adequacy, suitability, effectiveness and efficiency of the quality systems. Effective and efficient quality systems can promote timely registration of drugs by eliminating waste and the need for rework with overall financial and social benefits to the Company. The mission of a quality assurance department is to provide an effective and efficient quality assurance system and counsel for the operational units. The development and use of SOPs are an integral part of a successful quality system as it provides individuals with the information to perform a job properly, and facilities consistency in the quality and integrity of a product or end result.

Keywords: *Quality systems, Quality assurance, Quality control, Quality management, Standard Operating Procedure*

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INTRODUCTION:

High levels of quality are essential to achieve company business objectives. Quality, a source of competitive advantages, should remain a hallmark of company products and services. High quality is not an added value; it is an essential basic requirement. Quality does not only relate solely to the end products and services a company provides but also relates to the way the company employees do their job and the work processes they follow to produce products or services. Each employee in all organisational units is responsible for ensuring that their work processes are continually improving quality. Top management should provide the training and an appropriate motivating environment to foster teamwork both within and across organisational units for employees to improve processes. Ultimately, everyone in a company is responsible for the quality of its products and services. A company in the role of a sponsor of clinical trials can best achieve its business objectives by establishing and managing robust quality systems with their integral quality documents including standard operating procedures (SOP).[1]

QUALITY SYSTEMS:

A Quality system is defined as the organisational structure, responsibilities, processes, procedures and resources for implementing quality management. Quality management includes those aspects of the overall management function that determine the implementation of the company quality policy and quality objectives. Both quality control and quality systems are parts of quality management. The 13th principle in the International Conference on Harmonisation Good Clinical Practices [ICH GCP] guideline clearly states the systems and procedures that assure the quality of every aspect of clinical trials should be implemented. The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented [recorded] and reported in compliance with the protocol, Good clinical practice [GCP] and the clinical requirements. Although a sponsor may transfer any or all of its trial-related duties and functions to a Contract Research Organisation [CRO], the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. However, the CRO is also required in its own right to implement quality assurance and quality control. Both quality control and quality assurance systems must be commensurate with the company business objectives and business model. The two together constitute the key quality systems.

Responsibilities of quality systems:

Responsibilities for developing the quality strategy, policies, processes, standard and systems for the company its supply chain to operate within. This may include auditing to and supply ensure compliance although this may be carried out by a third-party accredited body. Will have people and budgetary management responsibility.

Processes of quality systems:

A quality management process is a workflow mechanism in an organisation for ensuring that a team's deliverables are **"fit for purpose".** A quality management system is a collection of business processes and procedures which aims to ensure the quality of products or services.

Procedures and quality systems:

This quality system procedure describes methods of working, individual responsibilities, standards of woman ship, retained records, and arrangements for corrective and preventive action used to control quality system documentation and data approval, revision, and issue. The quality system resources is to check that your organisation has identified which resources it needs to make available in order to ensure the effective operation of the QMS. Resources will often include raw materials, infrastructure, finance, personnel and IT, all of which can be either internally or externally provided.

Top management commitment and active involvement in the establishment, management and monitoring of quality systems is critical and is achieved.

- Defining and documenting a quality policy and quality objectives and ensuring that both the policy and objectives are understood and implemented by all employees at all levels.
- Ensuring that appropriate processes are implemented to fully satisfy customer needs and expectations and company objectives;
- Defining and documenting the responsibility, authority, and interrelation of key personnel managing the quality systems;
- Providing adequate resources for implementing and maintaining the quality systems.
- Conducting scheduled management reviews of the quality systems to assess their continued suitability, adequacy, effectiveness and efficiency; and
- Deciding on actions for continual quality improvement.

Quality control is focused on fulfilling quality requirements, and as related to clinical trials, it

encompasses the operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled. Quality assurance, on the other hand, is focussed on providing confidence that quality requirements are fulfilled. As related to clinical trials, it includes all those planned and systemic actions that are established to ensure that the trial is performed and the data are generated, documented and reported in compliance with Good Clinical Practices (GCP) and the applicable regulatory requirements.

Quality control is generally the responsibility of the quality assurance department. The mission of a quality assurance department is to provide an effective and efficient quality assurance system and counsel for the operational units. The quality assurance department must be manned by an adequate number of dedicated and adequately qualified and trained personnel with well-developed interpersonal skills. The well-developed interpersonal skills will provide the quality assurance personnel with persuasive, diplomatic, tactful, and resilient qualities generally required of them. The quality assurance department must operate independently from the operational units and it must regularly perform quality review activities [self-inspection audits\ internal audits] to ensure compliance within operational units with company quality standards, good working practices (current good manufacturing practices, Good laboratory practice [GLP],[GCP] and local national , regional and international legal , ethical and regulatory requirements.

STANDARD OPERATING PROCEDURES:

A Standard Operating Procedures (SOP) is a set of written instructions that document a routine or repetitive activity followed by an organisation.[2]. Back bone of pharmaceutical industries. The development and use of SOPs are an integral part of a successful quality system as it provides individuals with the information to perform a job properly, and facilities consistency in the quality and integrity of a product or end result. The term SOP may not always be appropriate and terms such as protocols, instructions, worksheets, and laboratory operating procedures may also be used. SOPs describe both technical and fundamental programmatic operational elements of an organisation shown in figure 1. Since each institute operates and functions differently depending on varying circumstances, and has its own ways of carrying out certain procedures, the SOPs in different factories will differ. However, the basic content, structure, and the concepts of SOPs will obviously be the same.[3]

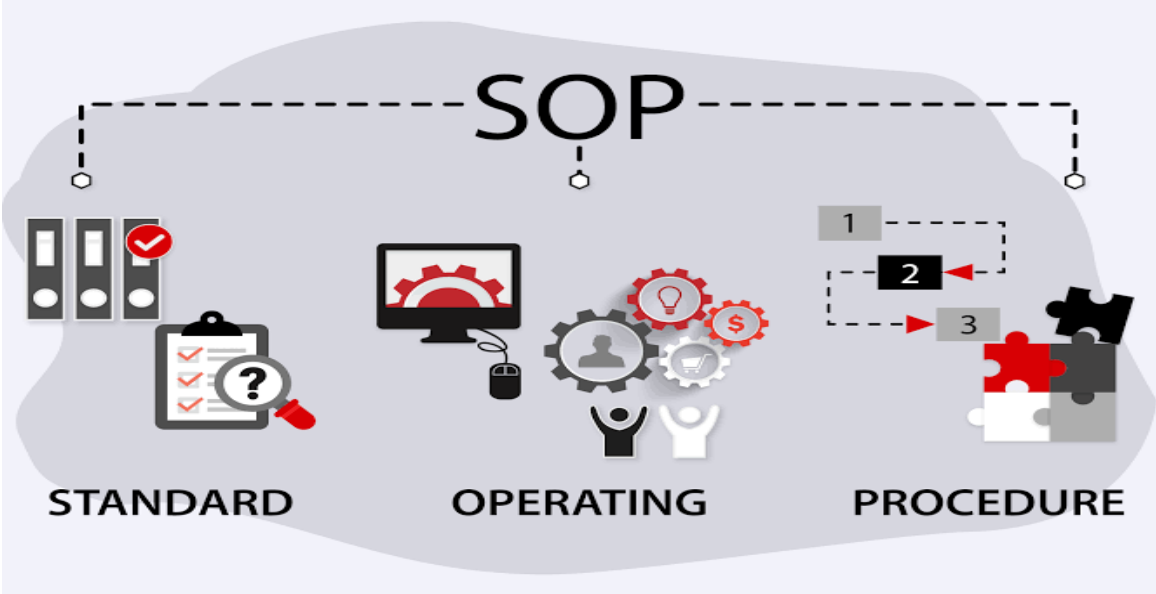

Figure: 1 Showing Standard Operating Procedure

Objectives:

To describe the responsibilities of the coordinating centre for managing and monitoring the participating sites. To provide guidelines for accurate and timely data collection, resolution of data clarification (queries). Detailing the regularly recurring work processes that are to be conducted or followed with an organisation and to facilitate consistent conformance to technical and quality system requirements and to support data quality. Maintain their “quality control”

and "quality assurance" processes. To ensure compliance with governmental regulations. To serve as a training document for teaching users about the process for which the SOPs are written shown in figure 2.[4]

Some of the important contents of SOPs are:

- Name & Address of the company
- SOP number, and Date when the SOP was prepared /reviewed.
- Aim or objective of the SOP
- Scope of the SOP (area which will be covered by the SOP)
- Process/steps to be carried out, in sequential order.
- Whose responsibility is to carry out the SOP
- 7.Any other useful information
- Name and signature of the person/s who made/ reviewed and the SOPs, along with date of review.[5]

figure: 2 Showing Areas of Standard Operating Procedure

PURPOSE of SOP:

SOPs detail the regularly recurring work processes that are to be conducted or followed within an organisation. They document the way activities are to be performed to facilitate consistent conformance to technical and quality system requirements and to support data quality. SOPs are intended to be specific to the organisation or facility whose activities are described and assist that organisation to maintain their quality control and quality assurance processes and ensure compliance with governmental regulations. If not written correctly, SOPs are of limited value. In addition, the best written SOPs will fail if they are not followed. Therefore, the use of SOPs needs to be reviewed and re-enforced by management, preferably the direct supervisor. Current copies of the SOPs also need to be readily accessible for reference in the work areas of those individuals actually performing the activity, either in hard copy or electronic format.[6]

Benefits:

The development and use of SOPs minimises variation and promotes quality through consistent implementation of a process or procedure within the organisation, even if there are temporary or permanent personal changes. When historical data is being evaluated for current use, SOPs can also be valuable for reconstructing project activities when no other references are available. Ultimately, the benefits of a valid SOP are reduced work effort, along with improved comparability, credibility, and legal defensibility. SOPs are needed even when published methods are being utilised. For example, if an SOP is written for a standard analytical method, the SOP should specify the procedures to be followed in greater detail than appear in the published method. Provides information to perform a job properly with all safety, health, environmental and operational environmental and operational information necessary to perform a job properly. Giving information in order to achieve predetermined specification and quality end-result. Minimises variation and promotes quality. Steps can be reviewed in accident investigations. Serves as a training document for users and to ensure that GMP is followed and achieved at all times. SOPs assist pharmacy personnel to know who does what, and when, thus avoiding confusion, and function overlapping. This also takes care of accountability and responsibility. SOPs help to ensure the quality and consistency of the service, and thus minimise harm to the patient and are useful tools for training new members of staff. SOPs give clarity to the pharmacy personnel, to follow steps / procedures, systematically, and uniformly.[7]

Sop writing style:

- SOPs should be written in a concise, step-by-step, easy-to-read format.
- The information presented should be unambiguous and not overly complicated.
- The active voice and present verb tense should be used, but implied.
- The document should not be wordy, redundant, or overly lengthy.
- Routine procedures that are short and require few decisions can be written using simple steps format.
- Procedures that require many decisions should be written along with flowchart.
- In addition, follow the style guide used by your organisation,eg..,font size and margins
- Requirements for documentation identification and control, accountability and traceability responsibility must be included with every SOP; this can be achieved by providing consistent format.[8]

Types of sops:

SOPs may be written for any repetitive technical activity, as well as for any administrative or functional programmatic procedure that is being followed within an organisation.[9]. The types of SOPs are :

Technical SOPs:

SOPs instructing the user how to perform a specific analytical method to be followed in the laboratory and how to collect a sample in order to preserve the sample integrity and representativeness. Also cover data processing and evaluation (including verification and validation), modelling, risk assessment

Administrative SOPs:

SOPs generated for administrative tasks. Reviewing documentation such as QA project plans and QMP, Writing contracts, Performance assessment. Also includes how to coordinate the activity and record and results as well as coordinating the team efforts.[10]

Master sop:

In addition to the various SOPs that are required, the company has to first make an SOPs that defines how the various SOPs will be made, what kind of information, structure and numbering system will be included in various SOPs. It should also contain a time frame for revision of SOPs. It should identify the persons authorised for each activity (creating, checking, verifying, and implementing).

Sop preparation:

The organisation should have a procedure in place for determining what procedure or processes need to be documented. Those SOPs should then be written by individuals knowledgeable with the activity and the organisation's internal structure. A team approach can be followed, especially for multi-tasked processes where the experiences of a number of individuals are critical. 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 of personnel qualifications. For example, if a basic chemistry or biological course experience or additional training is required that requirement should be indicated.[11]

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 finalised. The finalised SOPs should be approved as described in the organisation's Quality management plan or its own SOP for preparation of SOPs.

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 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.

Implementing sop:

- The most important step for implementing the SOP is in the working area, training or retraining the user. Everyone should follow the procedure exactly with each and every step in detail, it is very important to train the user otherwise individuals may interpret meaning in different ways.
- While training the user trainer should share the reason why, SOP will be performed correctly. People have much more to follow when they understand the importance of procedure.

- Trainer should explain and demonstrate how each step in the SOP will be performed and should assure them this will increase quality of product by providing safety and accuracy which will ultimately increase the confidence of the user.

Management of sop:

- Organisation shall have SOP on preparation, approval, revision and control of Standard Operating Procedure for better control and management of SOPs.
- Generally, administrative aspects of the SOPs system such as distribution and filing are well managed. On the other hand, overall system management, frequently characterised by the lack of a system owner, is generally poor. If a system owner exists at all, his or her responsibilities are limited.[12]

Ideally a system owner:

- Eliminates obsolete SOPs.(which is not needed)
- Ensures that SOPs meet their quality requirements and are user friendly.
- Manages SOPs change controls.
- Distributes SOPs.
- Ensures that SOPs are current.
- Ensures that new or changed SOPs are valid only after training has occurred and provides training about the SOP system.
- Measures system performance and periodically reports results to management.
- Continuously improves the system.[13]

REASONS FOR HAVING SOPs:

- To provide people with all the safety, health, environmental and operational information.
- To ensure that processes continue uninterrupted and completed on a prescribed schedule and maintain quality control of processes and products.
- To ensure that no failures occur in any processes.
- To ensure that approved procedures are followed in compliance with company and government regulations.
- To serve as an historical record of the whole process which is done and have a basis of that when the process is changed.
- Provide training and guidance for new staff.[14]

It is essential for:

- An integral part of a successful quality system.
- Plant's effectiveness and efficacy.
- Regular requirement.
- To ensure that production operations are performed consistently to maintain quality control of processes and products.
- To ensure that processes continue uninterrupted and are completed on a prescribed schedule.[15]

INSIDE THE SOP:

Company name and pagination:

The company name and pagination must appear on every page

Title:

The title should be descriptive. The title should be directive language to declare what is being done to what.

Identification

Procedures must be easily identified by giving a unique number and version number. The identification number of SOP supports accountability of the document throughout the facility and over time as it changes.[16]

REVIEW AND APPROVAL:

All SOPs shall have space for signature of initiator (the person who has written SOP) , reviewer (the person who has reviewed the SOP) and approver (Quality Assurance head of the organisation). The purpose or objective of the procedure should restate and expand a well written title. Expand or qualify the directive language used in the title (e.g. to describe the operation procedure of a compression machine).

SCOPE:

The scope should provide limits to the use of procedure. The scope shall be written in such a way that it answers the following questions.

- Are there certain samples that are appropriate to test this method?
- Do these operations apply only to certain equipment or certain departments?
- Is there a limit to the capacity, volume, or throughout the procedure?
- State to what areas this procedure does apply and does not apply.

Describing the procedure in a step by step, chronological manner. Use active verbs and direct statements. SOP general format shown in annexure I.

ANNEXURE I

Name of facility_____ **page ..... of....**

SOP Number _____ Title _____
Revision number _____
Written by _____ Edited by _____
Authorization signature _____ Department _____ Date_____
Effective date _____Replaces _____

Purpose:
WHY:
Why is this procedure written.
Why is it being performed.

Scope
WHEN:
Indicate when this procedure needs to be performed.
WHERE:
Indicate where this procedure applies.

Responsibility
WHO:
Who performs the procedure, who is responsible to see it is performed correctly.

Materials and equipment
WHAT: What is needed to perform the test. The list should be completely specific.

SOPs should be organised to ensure ease and efficiency in use and to be specific to the organisation which develops it. Where possible break the information into a series of logical steps to avoid a long list.

SOP generally consists of

Title page:

The first page or cover page of each SOP should contain the following information:

a) A title that clearly identifies the activity or procedure.
b) An SOP identification (ID) number
c) Date of issue and / or revision
d) The signature and signature dates of those individuals who prepared and approved the SOP.

Table of contents:

a) A table of contents may be needed for quick reference, especially if the SOP is long.
b) To locate the information
c) To denote changes or revisions made only to certain sections of an SOP.

Text:

Well written SOPs should first briefly describe

a) The purpose of the work or process
b) The scope of the work or process
c) Responsibilities and applicabilities
d) Summary of the method/procedure
e) Definition of any specialised/unusual terms and explanation of abbreviations
f) Health and safety cautions
g) QC section: used to check the quality of the work that includes specific assessment criteria and appropriate QC procedures.
h) Attach any appropriate information, e.g., an SOP may reference other SOPs.

CONCLUSION:

It is mandatory for sponsors of clinical trials and contract research organizations alike to establish, manage and monitor their quality control and quality assurance systems. Their integral standard operating procedures and other quality documents to provide high-quality products and services. To fully satisfy customer needs and expectations. Quality control and quality assurance systems together constitute the key quality systems and parts of quality management. Quality control is focused on fulfilling quality requirements, whereas quality assurance is focused on providing confidence that quality requirements are fulfilled.

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