STANDARD OPERATING PROCEDURES

A standard operating procedure (SOP) is a document with detailed instructions and methodology to be followed, in order to maintain uniformity and consistency in results. The International Conference of Harmonization (ICH) defines SOP as, *"detailed written instructions to achieve uniformity of the performance of a specific function."*

One of the most important roles of SOPs is to institutionalize an individual experience or expertise. Often, one member of the staff sets up a procedure which is the most efficient way of performing a set task. When such an individual leaves the organization, or is off duty, the task would be performed using a different procedure which may not be equally efficient. If the original procedure was to be written down in simple steps (SOP), this could guide another individual to carry out the same function with equal efficiency. Thus by preparing an SOP, an individual's expertise becomes institutionalized, and the procedure can be carried out in the same way, even if the individual who developed the procedure is no longer with the organization.

SOPs answers 4 Ws and H concept i.e. who, what, when, where and how of the investigator's clinical trial management. In clinical research, it is extremely important to comply with the GCP protocols and procedures for two fold reasons. Firstly, any deviation from actual protocol will lead to an incorrect result. Secondly and most importantly, a human life is at stake. So, an SOP should be prepared with utmost care and then it should be followed religiously. Apart from all these, it also clearly defines the roles and responsibilities of people involved in conducting clinical trial, hence, making people accountable.

Standard Operating Procedures (SOPs) describe specific procedures performed during any operation including conduct of a clinical research study involving human subjects. SOPs are generally based on the ISO system, though they may be based on other systems too. Standard Operating Procedures should not be made for all procedures, but should be restricted to a certain type of procedures, these are:

1. Simple procedures.
2. Repetitive procedures.
3. Procedures that can be delegated from one individual to another.
4. Procedures that affect the quality of output, in this case data.

Any procedure which is not likely to affect the quality of data, does not require an SOP. A mistake which organizations often make is to create SOPs for every activity, thereby putting on the staff, an extra burden of reading and following these SOPs which have no bearing on the output.

Since, an SOP is a standalone document, certain parts of every SOP are repetitive. Reading a bunch of SOPs is one of the most uninteresting activities since there is little variety in the language for relief of boredom. However, the role of the SOP's is not to

entertain, but to help conduct the procedure in a standardized way. The trade off between boredom and utility is a fact to be remembered while preparing or following SOPs.

In all studies, the Principal Investigator has full responsibility for all the activities performed during the conduct of the study and must personally sign all major documents and correspondence. All activities detailed in these SOPs are to be completed under the supervision of the Principal Investigator. The Investigator may delegate activities to members of the research team. This delegation must be documented in writing.

The SOPs are provided in PDF format, are copyrighted and may not be modified, reproduced or used in other contexts. However, the templates which accompany the SOPs are provided in Microsoft Word so researchers may customize them for preparing new SOPS as and when required.

It is the responsibility of everyone (be it pharmaceutical company, contract research organization (CRO), sponsor, investigator, or any other party) involved in the process of drug development to prepare and follow good SOPs, in order to attain highest level of safety and efficacy of performed clinical trial. The Regulatory Authority should make it mandatory for all the parties involved or conducting Clinical Research and Clinical Trials to get their SOPs verified before getting a license to perform their operations or trials. Apart from this, every employee in the organization should be well trained to follow these SOPs. An organization following a standard procedure obviously has a competitive edge over those who are not following the standard operating procedure.

To summarize, the objectives of SOP are as follows:

1. Improve and maintain the quality of operations and hence affect the result positively.
2. Standardize the working practices.
3. Ensure quality, consistent and reproducible results.
4. Define the methodology to be followed.
5. Define the roles and responsibilities of the individuals and departments involved.
6. Ensure compliance to GCP and other regulatory guidelines.
7. Save time.

An effective standard operating procedure or SOP should:

1. Be written in a simple, easy to understand language.
2. Be a comprehensive document.
3. Differentiate between instructions and general information
4. Describe procedures in a familiar way.
5. Contain a descriptive title.
6. Contain an indication of SOPs position among other SOPs.

While preparing SOPs, the first SOP should be the SOP of SOPs. This SOP should describe how all the SOPs should be, and should specify the following:

1. The type and size of paper on which the SOP is printed.
2. The layout of the SOPs (Company logo, SOP title and number, version number, dates and signatures).
3. The font and the font size (should be an easily available and readable font).
4. All pages to be numbered (with the total number of pages as page 4 of 10).
5. Carry the names of the persons who have prepared the SOP and those who sanction the SOP.
6. Date of preparation and implementation of the SOP (leaving time for training of the staff on SOP).

Each SOP must have sections describing various aspects of the SOP, while the organization can decide these, the following as recommended:

1. Objective of the SOP.
2. Scope of the SOP.
3. Responsibilities.
4. Procedure (of the operation in question).
5. Signatures.
6. References.
7. Storage of the SOP.

Training

The staff for which the SOP is meant needs to be trained in the procedure ; this requires time and effort. There should be a provision for the same. A training log should be maintained so that at a glance, it becomes clear, which staff has undergone training and which has not.

Management

There should be a dedicated person whose job is to administer the quality system. The management has a specific responsibility of supporting the quality system and it should make resources available for this activity. A member of the quality team is responsible for the distribution and storage of SOPs.

The commitment of the management to support a quality system is essential for the working of the system. Establishing quality systems requires resources, man power and time. In the early stage of establishment, the system only consumes these resources without giving any benefit. Once the system is established and has been working for some time, it pays dividends to the organization. The commitments of the management are therefore, essential for supporting the system till it starts paying dividends.

Review of SOPs

SOPs are not permanent in nature and need to be reviewed periodically. Though some SOPs may remain unchanged for years, they should be periodically reviewed and the need to revise the SOPs is assessed. If no revision is made, the SOP may be revalidated with a revalidation stamp and the date of revalidation. Every SOP should carry the date for review, by which date the SOP must be reviewed.

Applicability of SOPs

The sponsor, the CRO and the sites must have their own SOPs. Yet, when a trial is to be conducted, the question as to whose SOPs are to be used, arises. The general answer would be, the sponsor's SOPs. There are two reasons for this ; firstly the sponsor is responsible for the quality of trial and the data is obtained. Since SOPs are an important part of the Quality System, the sponsor's SOPs should be followed. Secondly, the trial is financed by the sponsor, and the principle that whoever pays, dictates the conduct of the trial, holds good.

Standards, Procedures, Formats and Tests

The industrial model for production is worth emulating any process. Every process has raw materials or inputs, which are processed to get an output. The quality of the output depends both on the quality of inputs and process used.

It should be remembered that no engineer, however skilled, can produce a machine component unless provided with the right raw material. Hence, the quality of the raw material is of importance to obtain the right quality of the output. There is therefore the need to fix the standards of the raw material, these are often referred to as raw material specifications. So also the output must have defined standards by which the quality control judges the output.

When the raw material and the output have to be tested for conformance to the set standards, there would be need for test methods. These standard test methods ensure consistency in testing and therefore consistency in the quality of the output.

All information that has to be provided to or from the organization, must be in a specified form. If every employee were to apply for leave in a different format, the HR department would have a big problem on their hands. Similarly, if every employee's salary statement were to be made in different form, the employees would find it difficult to understand how much they were being paid. Standardization of the format for information is a part of the quality system and for this there are formats.

Formats are layouts for recording and transmitting information, and are an integral part of the quality system. Each organization must have its own formats for different purposes. It matters little what format is chosen for a particular type of information, the format must facilitate complete recording and transmission of information that is easy to understand.

The Format for an SOP is shown below :

<table>
<tr><td rowspan="4"> 
</td><td rowspan="2">Standard Operating Procedure</td><td>No :</td></tr>
<tr><td>Version :</td></tr>
<tr><td rowspan="2">Interim Monitoring Visits</td><td>Date :</td></tr>
<tr><td>Review Date :</td></tr>
</table>

1. Statement of Purpose
2. Scope

3. Procedure
    3.1
    3.2
    3.3
    3.4
    3.5
4. References
    1. Appendix

Signatures :

	Name	**Designation**	**Date**
Prepared by			
Reviewed by			
Authorized by			

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