STANDARD OPERATING PROCEDURE TITLE

SOP Subtitle

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1 PURPOSE

The purpose of a Standard Operating Procedure (SOP) is to describe complex routine procedures written in accordance with predetermined specifications. Each specification is critical to maintaining compliance with industry regulations and company standards. This template contains general examples and suggestions for writing an SOP for a nonclinical laboratory.

2 SCOPE

This template discusses qualities, considerations and examples of a well-written nonclinical laboratory SOP with a focus on chemical sciences. Laboratory SOPs provide step-by-step instructions on how to achieve consistent, quality results, reliable data and ensure employees follow good laboratory practices (GLP). GLP is touched upon in general terms and examples but this template should not be taken as a reference for industry requirements. Industry specific GLP guidelines are designated by regulatory agencies such as the EPA, FDA and OECD as noted in section 3. Good Clinical Laboratory Practices (GCLP) are not discussed within the context of this SOP. Section 3 provides definitions for uncommon terms, but some preexisting knowledge of analytical terminology is required to make the most use of this template.

3 DEFINITIONS

Instead of a definitions section, laboratory SOPs typically provide detailed descriptions of the instrumentation, matrix spikes and standards utilized during the procedure.

Blank (or Method Blank) refers to an analyte free sample matrix similar the matrices of the samples being tested for an analyte. The blank is used to evaluate contamination in the analytical procedure.

Environmental Protection Agency (EPA) is the US federal organization with authority over studies relating to health effects, environmental effects and chemical fate testing. The EPA requires all data developed under section 5 of the Toxic Substances Control Act (TSCA) to be in accordance with EPA GLP to be considered a reliable evaluation of a chemical substance's health and environmental effects.

Federal Drug Administration (FDA) is the US federal organization with authority over nonclinical laboratory studies supporting applications for research or marketing permits for products regulated by the FDA. Medical products or devices, cosmetics and biological products typically fall within the FDA's jurisdiction and should adhere to the FDA GLP guidelines.

Lowest Limit of Detection (LLD) is the lowest concentration of an analyte which can be distinguished from a blank, or the absence of the analyte, with a certain degree of confidence.

Lowest Limit of Quantitation (LLOQ) is the lowest limit in which quantitative results can be reliably obtained within a certain degree of confidence, or the lowest concentration of an analyte that can be accurately measured.

Matrix Spike (MS) refers to a type of quality control sample used to evaluate the effects of a sample matrix on the performance of an analytical method. Matrix spikes consist of a sample injected with a prepared standard solution of known analyte concentration. The same standard

solution is also used in the laboratory control sample (LCS) which does not have a sample matrix. The LCS demonstrates the analytical method's performance when unaffected by the sample matrix; the MS demonstrates the analytical method's performance when effected by the sample matrix. These results are compared to evaluate the significance of matrix interference on the data.

Organization for Economic Co-operation and Development (OECD) is an international organization which sets a wide range of standards to promote global economic and social well-being. Unless specifically exempted by national legislation, OECD GLP apply to all non-clinical health and environmental safety studies related to licensing pharmaceuticals, food, cosmetics, drug products, industrial chemicals, etc. OECD guidelines were created in the context of standardizing testing procedures for the Mutual Acceptance of Data (MAD).

Upper Limit of Quantitation (ULOQ) is the highest limit in which quantitative results can be reliably obtained within a certain degree of confidence, or the highest concentration of an analyte that can be accurately measured.

4 RESPONSIBILITIES

4.1 Analysts

Analysts are responsible for following the procedure as written unless authorized by their supervisor for one-time-only deviations. The analyst generates the data or product featured in the project deliverables and performs the first level review. The second level review may be performed by a fellow analyst or supervisor.

4.2 Supervisors

Supervisors are responsible for documenting nonconformances, training certifications, procedural deviations, incident reports and for notifying appropriate persons per company form management guidelines. The supervisor ensures analyst success while prioritizing safety. The second or third level review may be performed by the supervisor, provided they do not perform both the second and third level reviews. The third level review may be performed by a fellow supervisor or qualified staff member.

4.3 Project Managers

Project Managers are responsible for communicating client needs to supervisors and analysts while keeping the client abreast of any deviations or nonconformances which influence deliverables. The project manager performs the final data review before organizing and submitting project deliverables to the client.

4.4 Quality Assurance (QA) Managers

Quality Assurance Managers are responsible for ensuring all analysts, supervisors and project managers are well-informed of company policies related to quality assurance. Quarterly or annual internal audits are conducted by QA managers to evaluate staff QA compliance and identify training insufficiencies for correction. QA managers are responsible for SOP accessibility, maintenance, revision and validation.

4.5 All Personnel

All personnel are responsible for conforming to the safety and ethics guidelines outlined by federal, state and local regulatory agencies as well as company policy.

5 SAFETY

5.1 OSHA Requirements

OSHA requirements are not detailed in length, but a SOP should reference employee legal rights and applicable regulatory laws. SOP instructions must be written with the goal of ensuring compliance with OSHA standards throughout the procedure. The company can be held liable for SOP instructions which disregard or conflict with OSHA law.

5.2 Safety Equipment

Safety equipment is vital to the health of employees and must meet, or exceed, OSHA requirements for mitigating exposure. Descriptions and locations of safety equipment must be clearly communicated to the analyst prior to any work action. Decontamination procedures should be documented and clearly referenced within the SOP in case of emergency.

5.3 MSDS/SDS

Materials Safety Data Sheets (MSDS), or Safety Data Sheets (SDS), must be provided for any known hazardous material an analyst may encounter in the lab. Easily accessible intranet resources or hazard notifications in project descriptions are strongly advised. The SOP should make note of where MSDS/SDS information is available.

5.4 Waste

Waste collection, storage and disposal procedures are typically outlined in a separate SOP maintained by the Environmental, Health and Safety (EHS) administrator. The SOP should reference the specific location of relevant documentation and provide an overview of which waste disposal practices are most relevant to the procedure.

6 STANDARDS

Data Quality Indicators (DQI) must be established and documented for field and laboratory data collection SOPs. The EPA requires that DQIs include precision, accuracy, representativeness, comparability and completeness (PARCC) at minimum. The following are three suggestions of how a SOP might meet some of those requirements.

6.1 Calibration

Sensitivity for an instrument or method is assessed by the detection limit, the analyte concentration that can be reliably measured. There are various detection limits including LLD, LLOQ and ULOQ as defined in section 3. Detection limits and sensitivity are verified by regular calibration and validation of the instrument and method. Calibration details for all instruments utilized during the procedure should be accounted for in the SOP. The SOP should distinguish specific success or failure criteria for a calibration and describe the appropriate actions to take in the event of calibration failure. The SOP should also detail how calibration information is to be included in project deliverables.

6.2 Laboratory Control Sample (LCS)

Accuracy is the degree to which a measured result agrees with an accepted reference value. Analytical accuracy is verified for an instrument or method when a detected analyte concentration matches a known analyte concentration in a sample called the LCS. The LCS is a matrix free sample spiked with a lab-prepared standard solution. The SOP should reference the standard solution's composition, distinguish specific success or failure criteria and describe the appropriate actions to take in the event of a LCS failure. The LCS also provides valuable sample matrix information when used in conjunction with a blank and matrix spike as defined in section 3. The SOP should describe how LCS results are used for data review and validation if applicable.

6.3 Relative Standard Deviation (RSD) and Relative Percent Difference (RPD)

Precision is the degree to which a measured result agrees with repeated or duplicate measurements. Laboratories most commonly evaluate analytical precision by calculating the RSD and RPD. RSD is calculated for multiple duplicates; RPD is calculated for a single duplicate. RSD and RPD statistics are also used to evaluate the success or failure of standards such as the matrix spike and its duplicate (MS/MSD) or a laboratory control sample and its duplicate (LCS/LCSD). The SOP should specify the success or failure criteria of these standards and how the RSD and RPD are calculated.

$$RSD = \frac{\sigma}{\bar{x}}$$

Standard Deviation (σ)

$$\sigma = \sqrt{\frac{\sum(x-\bar{x})^2}{n-1}}$$

Mean ($\bar{x}$)

$$\bar{x} = \frac{\sum(x)}{n}$$

Where: x = the measurement

n = the number of measurements

$$RPD = \frac{|S-D|}{(S+D)/2} \times 100$$

Where: S = the Sample measurement

D = the Duplicate measurement

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7 PROCEDURE

The procedure section lists the step-by-step instructions and process details in chronological order. Directions should be concise, easy-to-read and unambiguous. Refer to complex information in appropriate sections, appendices or indexes to avoid redundancy and lengthy deviations from the described task. The preferable writing style uses active voice and present tense verbs. Information must be clearly conveyed to remove any doubt about procedure requirements.

8 REFERENCES

The references section includes the bibliography as defined by company style guidelines. The most common citation styles are APA, MLA, IEEE or Chicago. Appendices and indexes follow the references section unless directed otherwise.