Issue 115
August 2021
Division of Technical Resources
Office of Research Facilities
National Institutes of Health
Technical News BULLETIN

Standard Operating Procedures in Facilities Maintenance and Oversight of APFs

Introduction

In a current Good Manufacturing Practice (cGMP) environment, it is critical to ensure that all facility maintenance and oversight of an Aseptic Processing Facility (APF) is conducted in accordance with a multitude of regulatory requirements, good engineering practices, and manufacturer's recommendations. For instance, Section 211.68 of the Code of Federal Regulation (CFR) states that equipment "...shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance." Establishing and implementing Standard Operating Procedures (SOPs) helps personnel keep an APF in compliance with the numerous requirements it must follow; properly developed facility SOPs provide a standard for how to perform a task or routine activity with the intent to produce consistent results and reduce mistakes.

Facility SOPs for APFs

Thorough, quality SOPs are particularly critical for APFs because there are many processes that can impact various aspects of the facility's functionality. Procedures required for APF maintenance include those impacting operations such as entry exit, preventative maintenance schedules, work order processes, calibration, emergency work, material management, and training programs. Quality Assurance (QA) oversight of the facility provides additional procedures such as compliance monitoring of cGMP facilities and processes, including continuous monitoring of critical parameters, tracking of incidents, System Discrepancy/Deviation (SD), Corrective Action Preventative Action (CAPA), Root Cause Analysis (RCA), managing change controls and facility audits.

Development

In some cases, SOPs are specific, step-by-step technical instructions; in other cases, it may be more appropriate to use general language, or reference the User's site-specific SOPs, particularly regarding things like gowning requirements. Regardless, a well-written SOP should be clear, concise, and simple to ensure it is easily replicated every time. A consistently executed SOP contributes to product quality.

During the development of each SOP, the author collaborates with key players (e.g., end user, Subject Matter Experts (SMEs), facility QA, DFOM, etc.) to define the SOP's requirements, including execution verification. SOPs should be concise, and shall address the following:

- Objective
- Scope or purpose
- Step by step process
- Responsibilities
- Training
- Review & approval
- Management controls

In addition, SOPs often include reference documents (e.g., Work Instructions (WI), forms, and templates) to help achieve consistency and document tasks.

Training

A training program helps management identify the need for additional training, when and how often to provide refresher courses, and who requires training when there is a new or revised SOP. SOPs are used to develop and conduct the relevant training; a training coordinator shall document training on effective SOPs. Personnel must demonstrate competence by reviewing an SOP using a system which documents that the employee read and understood the procedure, or they may attend a classroom training session, which can include an exam. This process allows for management to ensure trainees have a clear understanding of the procedures and address any questions or concerns that may arise. An effective training management program should maintain auditable training records to ensure competency and compliance.

Implementation

An SOP becomes effective once it is approved and staff have received initial training; the document's effective date need not be the issue date. APF personnel shall follow the effective processes to prevent potential negative impact on the product being produced, or damage to the facility, as stated in DRM Section 13.20.1. A well written and implemented SOP can help a QA team provide compliance oversight and support for the operation and maintenance of APF facility systems and equipment.

Audits

When a facility is audited, auditors review SOPs that are in effect to ensure compliance; this review includes an inspection of training records and may include interviewing staff and/or other steps to ensure that effective SOPs are being followed. SOPs help achieve the goal of an audit by identifying if quality systems have been implemented, maintained, and remain effective. Audit observations of SOP violations require immediate action to rectify deficiencies.

Summary

SOPs play a crucial role in APF facilities by making sure the necessary maintenance, QA work, and training are performed and documented based on written procedures. As these documents are developed, reviewed, implemented, and maintained, they become an integral component of the APF's quality system. Consistent and proper use of SOPs will ensure the work performed for the maintenance and QA purposes does not alter the qualified state of the equipment and validated state of the process and/or room.