Operational Considerations for Sterile Compounding During COVID-19 Pandemic

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This document is for informational purposes only and is intended to address operational considerations during the COVID-19 pandemic. This does not reflect the Compounding Expert Committee's opinions on future revisions to official text of the *USP-NF*. USP is actively monitoring the evolving situation and will update this document accordingly. Parties relying on the information in this document bear independent responsibility for awareness of, and compliance with, any applicable federal, state, or local laws and requirements.

Background and Introduction

USP General Chapter <797> *Pharmaceutical Compounding – Sterile Preparations* provides official standards for compounding quality sterile preparations. The chapter sets forth standards to minimize the microbial contamination risk for compounded sterile preparations (CSPs).[1]

In light of the rapidly evolving COVID-19 pandemic, the demand on compounding operations is expected to continue to increase and impose challenges on compounding entities. During this pandemic, USP supports State Boards and other regulators using **risk-based enforcement discretion** related to the implementation of USP compounding standards.

The USP Compounding Expert Committee (CMP EC) has developed the operational strategies below based on stakeholder input and in anticipation of challenges that may arise during the COVID-19 pandemic. In light of the public health emergency posed by COVID-19, this document was developed without a public comment period. This document is not a USP compendial standard; rather, it reflects options developed by the USP CMP EC, based on their scientific and professional expertise, and with input from stakeholders and regulatory agencies at the federal and state level.

Facilities should carefully consider the impact on the CSP and the environment and implement risk-mitigating strategies to help ensure quality CSPs. USP recommends that compounders also check with State Boards and other regulatory bodies to determine the existence of waivers or interim requirements.

[1] Free digital access to <797>: https://www.usp.org/compounding/general-chapter-797

Assignment of Beyond-Use Dates

The global drug supply chain is impacted by the COVID-19 pandemic, leading to supply disruptions and shortages of drug products. In consideration of the current resource constraints and increased waste of drugs, compounders should apply Beyond-Use Dates (BUDs) conservatively based on both chemical and physical stability and microbiological considerations. The currently official General Chapter <797> does not prohibit longer BUDs after sterility testing and when justified according to the section titled *Storage and Beyond-Use Dating*. To help manage drug supply and patient access to essential medications, the CMP EC is providing as guidelines the following BUDs, which are based on stakeholder input received by the CMP EC during the COVID-19 pandemic, as well as stakeholder comments that were received during two previous public comment periods on proposed revisions to General Chapter <797>, all of which were thoroughly evaluated by the CMP EC during the revision process. The BUDs below may be assigned if compounding does not otherwise deviate from General Chapter <797> standards:

- For low- and medium-risk level compounded sterile preparations (CSPs) prepared in a segregated compounding area, apply BUDs conservatively, not to exceed:
  - 12 hours at controlled room temperature
  - 24 hours in a refrigerator
- For low- and medium-risk level CSPs prepared in a cleanroom suite, apply BUDs conservatively, not to exceed:
  - 4 days at controlled room temperature
  - 10 days in a refrigerator for medium-risk level CSPs
  - 14 days in refrigerator for low-risk level CSPs
  - 45 days in a solid frozen state at −25° to −10° or colder
- If a single-dose container is entered or punctured only in ISO Class 5 or cleaner air, it may be used up to:
  - 12 hours after initial entry or puncture, as long as the storage requirements during that 12-hour period are maintained.
  - Opened single-dose ampules must not be stored for any time period.
- When assigning these BUDs, considerations should be given to:
  - Ensuring personnel monitoring (e.g., gloved fingertip and thumb sampling) is successfully completed every 6 months.
  - Increasing frequency of surface sampling in the primary engineering control to determine effectiveness of cleaning procedures and work practices.

Considerations for Certification and Recertification

- Primary and secondary engineering controls should not be used without initial (i.e., startup) certification.
- Understanding resource constraints during the COVID-19 pandemic, facilities may consider delaying recertification of primary and secondary engineering controls if they are served by a continuous monitor. The continuous monitor may help assure that a state of control is established and maintained from the previous certification.
  - The interval between certification should not exceed 12 months.
  - Consider increased environmental monitoring and applying shorter beyond-use dates (BUDs) if certification is delayed.

Cleaning and Disinfecting

In addition to the cleaning and disinfecting standards in <797> to help ensure quality CSPs, the Centers for Disease Control (CDC) has published considerations for cleaning and disinfecting the facility when someone is sick.[2]

- Follow facility policies and procedures for environmental cleaning and disinfection consistently and correctly.
- Routinely clean and disinfect frequently touched surfaces and objects.
- Use soap and water or detergent prior to applying an Environmental Protection Agency (EPA)-registered disinfectant (or equivalent).
  - Follow manufacturer-recommended contact times.
- Refer to List N on the EPA website for EPA-registered disinfectants that have qualified under EPA's emerging viral pathogens program for use against SARS-CoV-2.[3]
  - Consider surface materials when selecting agents.
- Dispose of cleaning supplies according to facility procedures.

[2] Adapted from CDC Cleaning and Disinfecting Your Facility, accessed April 6, 2020 at https://www.cdc.gov/coronavirus/2019-ncov/community/disinfecting-building-facility.html
[3] EPA List N: Disinfectants for Use Against SARS-CoV-2 at https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2