CETA Application Guide
CAG-011

Gloved Fingertip Testing for Sterile Compounding Personnel

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The CETA Board of Directors thanks the Action Committee members that contributed to this Guide.

Abby Roth, Chair

Jeremy Mahurin, Vice Chair/Secretary

Sharon Danko

Ronald Dewalt

Jared Eberly

Anthony Grilli

Kyle Mulder

Denise Rodriguez

CAG Administrator: R. Vijayakumar

CAG Administration Committee Chair: Tony Caughron

CETA Board Approval

Committee	Title	Signature	Name	Version	Date
Executive	President		Shawn Windley	01:2021	February 2021

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Foreword

The Controlled Environment Testing Association (CETA) is an international organization. One of CETA's objectives is to promote quality assurance through the review of existing standards and the development of new methodologies. One of the main vehicles for obtaining this goal is our CETA Application Guides (CAGs). The CETA Application Guides have proven to be an immeasurably valuable tool to a wide variety of professionals in our industry. They have been used by many safety professionals, industrial hygienists, facility engineers and quality control personnel.

The standards and other documents normatively referenced, in whole or in part, in this CETA Application Guide are indispensable for its use and application. The content of this CAG has its origin in material found in these reference documents. Preparation and development of these guides are the outcome of work completed by technical committees that are formed by the CETA Board of Directors.

Abstract

Sterile compounding personnel pose the greatest risk to the microbial integrity of a compounded sterile preparation (CSP) through inherent bioburden and improper garbing practices. Gloved fingertip testing evaluates a compounder's competency in performing hand hygiene and garbing based on the facility's standard operating procedures.

1 Introduction

The purpose of this guide is to establish an industry-based methodology for complying with the sterile compounding personnel gloved fingertip testing requirements addressed in USP Chapter <797> *Pharmaceutical Compounding - Sterile Preparations* and USP Chapter <825> *Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging*. This guide can assist in developing procedures to establish a robust personnel testing program for facilities in which sterile compounding is performed. This guide utilizes traditional microbiological methods as indicated in USP standards.

The individual State Boards of Pharmacy, Departments of Health, and other inspection agencies enforce USP standards or their own versions of the standards. When individual state or agency standards conflict with USP Chapter <797> or USP Chapter <825>, the standards which the facility is inspected against must be used and clearly identified in any documentation. The United States Pharmacopeia is updated and revised annually. Verify each year that no changes have been made to relevant chapters before proceeding.

2 Scope

This CETA Application Guide (CAG) is designed to provide a uniform approach for consistent and reproducible gloved fingertip testing evaluation for compliance with USP Chapters <797> and <825>.

2.1 Limitations

This guide does not cover specific information that the sterile compounding facility may require of a third-party vendor. A third-party vendor is expected to adhere to the service agreement and applicable facility SOPs.

This guide does not meet the needs of a facility that must comply with the current good manufacturing practices (CGMP).

3 Target Audience

Sterile compounding industry professionals.

4 References

For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

4.1 Reference Documents

Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice (2004). U.S. Department of Health and Human Services Food and Drug Administration, Silver Spring, MD, US.

USP General Chapter <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging. USP 42-NF 37 (2019). United States Pharmacopeial Convention, Inc., Rockville, MD, US.

ISO Standard No. 17025: General Requirements for the Competence of Testing and Calibration Laboratories (:2017). International Organization for Standardization, Geneva, CH.

4.2 Cited Bibliography

The following documents are cited in the guide. They may be obtained from the source of the publication.

USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. USP 41-NF 36 (2008) United States Pharmacopeial Convention, Inc., Rockville, MD, US.

The Revision to USP General Chapter <797>, USP 42-NF 37: Pharmaceutical Compounding—Sterile Preparations (2019). United States Pharmacopeial Convention, Inc., Rockville, MD, US.

USP General Chapter <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests. USP 42-NF 37 (2008). United States Pharmacopeial Convention, Inc., Rockville, MD, US.

USP General Chapter <71> Sterility Tests USP 42-NF 37 (2008). United States Pharmacopeial Convention, Inc., Rockville, MD, US.

5 Nomenclature

The following are technical definitions and acronyms for terms used throughout this application guide:

Action Levels - The quantity of colony forming units (CFUs) at which the state of contamination control is lost, warranting investigation and mitigation of the cause.

Aseptic - A state of control, void of unwanted microbial contamination.

Aseptically Filled Media - Sterile media added to previously sterilized containers under aseptic conditions.

Chain of Custody (COC) - See Lab Sample Submission Documentation.

Colony Forming Unit (CFU) - A measure of the number of the microorganisms present on a sampling device after incubation to estimate the total viable microbial inhabitance of an area sampled.

CSP - Compounded Sterile Preparation.

Data Expression - The appropriate unit of measurement used when reporting results for documentation.

Detection Level (Limit of Detection, Analytical Sensitivity) - The lowest quantity or concentration that can be reliably recovered with a given analytical method.

Documentation - Retrievable record of information that provides evidence required by regulatory standards.

Don - To put on garbing materials.

Exceeded Level - The resulting number of CFU recovered from a sample media device that is above the established action level.

Facility Designated Individual – A person or persons responsible for overseeing the site that is being tested.

Fingertips - The pads of each of the four fingers and the thumb, not the proximal tips.

Genus Level Identification - A correlation of a microorganism based on taxonomic rank of genus, more specific than family but less specific than species. Example: Staphylococcus is a genus that includes some species that are generally harmless and some antibiotic-resistant strains.

Growth Promotion - A study where an unexposed sampling device is inoculated with specific microorganisms in specific quantities and compared to an expected number of colony forming units after incubation. This is normally performed by the manufacturer for the certificate of analysis. See USP <61>.

Irradiated - A method of sterilization through controlled exposure to gamma wave radiation. This is commonly used for sterilizing microbial growth media.

Lab Sample Submission Documentation - A form used to relay the necessary data and requirements of an environmental monitoring session from the sample collector to the lab. It may also be used to track possession and relinquishment of samples.

Media – A combination of water, nutrients and a solidifying agent (for solid growth media) used to grow microorganisms. Different nutrients and chemicals are added to allow for the growth of different microorganisms. Neutralizers for disinfectants are added to gloved fingertip sampling media.

PEC - Primary Engineering Control - A device or zone that provides an ISO Class 5 air quality environment for sterile compounding.

PPE - Personal Protective Equipment.

RABS - Restricted-Access Barrier System - An enclosure that provides HEPA-filtered ISO Class 5 unidirectional air that allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contamination, and that generally are not to be opened during operations.

Sampling Device - Any item designed to collect a representation of contamination in or on an area, capable of supporting growth of microorganisms during incubation.

Sanitize - To reduce the number of microorganisms including fungi, viruses, and bacteria on inanimate surfaces.

SOP - Standard Operating Procedure.

Speciation - A characterization of a microorganism to a more specific taxonomic rank of species compared to genus. Example: *Staphylococcus epidermidis*, where Staphylococcus is the genus name and epidermidis is the species name.

TSA - Tryptic Soy Agar.

USP - United States Pharmacopeia.

Viable - The ability to multiply, spawn, grow or to otherwise exhibit properties indicative of a living organism.

6 Materials and Equipment

TSA with neutralizers (e.g., lecithin and polysorbate 80)

Sterile compounding facility-supplied cleaning materials and PPE for non-hazardous and hazardous cleanrooms and SCAs including appropriately sized gowns/smocks/bunny suits, sterile gloves, face masks, head cover, shoe covers and beard cover if applicable.

Incubators

7 Precautions/Safety

Items required for gloved fingertip testing should enter the sterile compounding facility as per the facility's SOPs.

Garb according to the sterile compounding facility's SOPs.

All materials required for testing must be cleaned according to the sterile compounding facility's material transfer process SOP.

8 Procedures

8.1 General Considerations

USP <797> and <825> only require the testing of sterile gloves. However, additional testing of garb donned may be appropriate, depending on the sterile compounding operation. If the sterile compounding facility uses sterile garb, such as a gown, coverall, hood, or sleeves, additional garbing competency samples may be considered such as on forearms, chest, waistline, or a location on the hood (cheek or forehead). USP <797> and <825> do not have action levels for these additional garbing competency samples as they are not required and would need to be determined by the sterile compounding facility.

8.2 Training

Prior to being evaluated for hand hygiene and garbing, personnel should be appropriately trained (e.g., didactic audio/visual education, hands-on training, simulation challenges, review of SOPs, etc.) and pass a competency test to demonstrate an understanding of their responsibility in a compounding area to minimize contamination.

8.3 Media Considerations

Each lot of media requires a certificate of analysis that documents the results of the quality control testing performed which includes growth promotion, pH, and sterilization. This growth promotion testing is completed by the manufacturer. It is in addition to and prior to the quality control testing that may be performed at the microbiological lab if required or requested.

Media must be stored according to the manufacturer's instructions. If the media is exposed to temperatures outside the manufacturer's specified range, it must be visually evaluated before use and discarded if showing signs of dryness or contamination. For many media manufacturers, media may be used for the collection of gloved fingertip samples up to and including the expiration date. For additional information reference the media's instructions for use.

Media should be at least double bagged and should be irradiated to ensure testing is performed with a sterile product. The double bags allow for layers of packaging to be shed as the media is transferred into the controlled environment. Media is available from manufacturers in two ways:

terminally sterilized media (such as being irradiated after production), and aseptically filled media. Media that is aseptically filled has a significant risk of being contaminated prior to use and is not recommended.

Media used for gloved fingertip testing must be a general-purpose media, such as Tryptic Soy Agar (TSA) and must incorporate neutralizers such as lecithin and polysorbate 80. TSA is suitable for the recovery of both bacterial and fungal organisms whereas the lecithin and polysorbate 80 can neutralize a wide range of chemicals used for cleaning the controlled areas. Gloved fingertip samples only need to be collected with TSA plus neutralizers. This is referred to as the single plate method, where one plate of TSA is used to collect a sample at a specified location.

USP <797> does not specify the size of plate to use. Ideally the plate is large enough for each fingertip from one hand to be rolled over the surface without any overlap. By not overlapping the fingertips, it is possible to identify which fingertip had contamination and provide a means for remedial training in the event the action level is exceeded. Petri dish size plates (~100 mm) should be considered as they have sufficient space to roll each fingertip over the agar surface. Contact plates (~55 mm) are an option but it is more difficult. Paddles may not be large enough to fit all fingers on one paddle, resulting in more than one paddle being used per hand to get a good rolling motion over the surface.

8.4 Testing Technique

Do not spray gloved hands with 70% sterile isopropyl alcohol or any other cleaning agent immediately before being tested. Using a separate sampling device for each hand, compounding personnel must gently roll fingertip then thumb pads on the surface of the agar (plate, paddle or slide), without overlapping. Pressure during the testing must not split or damage the media. Carefully replace lid or cover using aseptic technique and seal with parafilm or an approved cleanroom tape.

8.5 Testing Frequency

8.5.1 Initial Gloved Fingertip Testing

Initial evaluation of garbing with gloved fingertip testing is performed a minimum of 3 consecutive times. Gloved fingertip testing is done after 3 complete garbing and hand hygiene procedures. Sterile compounding facilities may decide to perform additional testing based on operations.

8.5.2 Ongoing Gloved Fingertip Testing

After successful completion of the initial gloved fingertip evaluation, subsequent gloved fingertip testing is required. Reference the current versions of applicable USP compounding chapters for testing frequency requirements. Subsequent testing is recommended to be performed every 6 months post media fill.

Sterile compounding facilities may consider performing gloved fingertip testing more frequently to ensure compounding personnel remain vigilant in maintaining good aseptic technique (e.g., random testing of each compounding staff member). This eliminates testing bias that comes with a scheduled test.

8.6 Labeling Samples

Label samples on the base of the plate. The lid of the plate should not be labeled because it may be removed or separated from the sample. Label each fingertip sampling device with a personnel identifier: right or left hand, date of testing, and any additional relevant identifiers. Ensure sample labeling correlates with the required documentation.

8.7 Testing Procedures

8.7.1 Initial Gloved Fingertip Procedure for a Cleanroom Suite

Initial gloved fingertip testing must be performed immediately after donning garb including sterile gloves preferably in the room where gloving is performed.

Sample as directed in section 8.4 of this CAG.

8.7.2 Initial Gloved Fingertip Procedure for a RABS

Initial gloved fingertip testing is to take place directly after donning facility approved garb, including sterile gloves, which are donned inside the RABS and over the gauntlet gloves.

Compounding personnel must place sampling devices in the transfer chamber and bring sampling devices into the main chamber prior to placing sterile gloves over gauntlet gloves.

Compounding personnel don sterile gloves over gauntlet gloves in a manner that does not contaminate them.

Opening of sampling devices may require operator intervention. Sample as directed in section 8.4 of this CAG.

8.7.3 Ongoing Gloved Fingertip Procedure for a Cleanroom Suite

Aseptically transfer sampling devices to the PEC and collect samples as indicated in section 8.4 of this CAG after completing a media-fill test or compounding a sterile preparation.

8.7.4 Ongoing Gloved Fingertip Procedure for a RABS

Aseptically transfer sampling devices to the PEC and collect samples are indicated in 8.4 after completing a media-fill test or compounding a sterile preparation.

8.8 Sample Documentation

If submitting to a contract lab for incubation, the lab will require documentation to establish a chain of custody. Laboratories may differ slightly in the information they require to process samples.

If incubating in-house, capture the required information as defined in organizational SOPs or as delineated in section 8.13 of this CAG.

8.9 Transporting Samples

After testing is complete, samples are kept cool but not frozen prior to arriving at the lab. If shipping samples to a lab, ship them with an overnight carrier. There should be a limited amount of time between when the samples are taken and when they arrive at the lab for analysis; samples should arrive at the lab the day after testing.

Samples must be packaged in a manner that prevents them from being contaminated during transport. Procedures for shipping should be discussed with the lab receiving the samples as each lab may have specific requirements. Plates are stacked together so lids do not come off during transport. Place all samples in a sealed plastic bag. When shipping or transporting to the lab, securely pack the shipping container with padding such as bubble wrap or filler material to prevent damage to samples.

The lab should initiate the testing process the same day of receipt. Any delay in the shipment or testing of the samples must be documented and justified. In the event of samples being stored or delayed in shipment for an extended amount of time, discuss each situation with the lab and determine if retesting should be performed.

8.10 Controls

When using a third-party lab, negative and positive controls should be submitted for each lot of media used during the testing session and these controls must stay with the actual test samples through the testing process and shipping. In the event controls are not submitted with the samples, it is not acceptable to send plates of the same lot separately to the lab for testing. Each lab may have specific requirements for controls.

Negative controls are plates and media containers that have not been opened and are incubated along with the samples. Media is suitable if there is no growth of organisms. Negative controls that have growth of organisms at the end of the incubation period should be investigated to determine whether a retest of all sample locations utilizing that lot of media should be performed.

Positive controls are unopened media devices that will be inoculated with microbes by the lab (a list of appropriate microorganisms can be found in USP <61>) for growth or no growth result to ensure the media can still support growth after transport to the lab. Positive control testing is not the equivalent to the growth promotion studies outlined in USP <61>, which may be used by the manufacturer for the certificate of analysis testing.

8.11 Sample Incubation and Enumeration

NOTE: In-house incubation and enumeration of sample colonies may be performed. Prior to initiating an in-house incubation program, sterile compounding facilities fully evaluate their ability to properly incubate and evaluate results. Outsourcing to a qualified lab with validated procedures and equipment may by more suitable.

At a minimum, follow the current USP <797> incubation requirements. The following are recommended incubation parameters:

After gloved fingertip testing is complete, sampling devices should be inverted and placed in a calibrated incubator.

Incubate the sampling device at a temperature of 30°C to 35°C for no less than 48 hours and then at 20°C to 25°C for no less than 5 additional days.

After incubation of sampling device at 30°C to 35°C the number of CFU per hand/device is recorded prior to placing in incubator at 20°C to 25°C.

After incubation is completed at 20°C to 25°C samples should be removed from incubator and the number of CFU per hand/device is recorded.

Determine if the number of CFUs have exceeded the action level delineated in USP <797> by counting the total number of CFUs on both hands. Specialized training is required to ensure proficiency in the differentiation of separate CFUs and bacteria from fungi.

Consider performing identifications to at least the genus level on recovered CFUs. This information can be used to identify adverse trends before out of compliance results are received.

8.12 Data Expression

Report fingertip sample data as the CFU total for both hands reported as one number.

The total count for both hands is reported and action levels are applied as required by the current version of USP <797> and <825>

If no colonies are recovered, the results are reported as less than the detection level. For example, zero CFU recovered on a set of fingertip samples is reported as “<1 CFU/both hands.”

8.13 Documentation

The information listed below must be captured and is needed to summarize the testing.

- Facility name, address and room location identification
- Name of person evaluated
- Name of evaluator
- Evaluation date and time
- Media type, manufacturer, lot numbers and expiration dates
- Media certificate of analysis
- Purpose of testing (initial, ongoing)
- Action levels
- Processing lab name and address or indicate samples were incubated by the sterile compounding facility
- Date samples were received by the lab (not needed if samples were incubated by the sterile compounding facility)
- Identification of who reads and documents the results
- Total microbial count in the appropriate units for gloved fingertip samples
- Incubation temperatures, dates, and times
- Results of the positive and negative control testing performed by the lab
- Sample Status (at, below or exceeded action level)
- Deviation (e.g. testing procedure, handling, cleanroom behavior, incubation)
- Signature of sterile compounding facility management or designee and date of review
- Actions taken in the event of an exceeded action level, if applicable

8.14 Data Analysis

Any gloved fingertip sample that is above the action level requires additional investigation.

Table 1:Gloved Fingertip Sampling Action Levels (USP 797, 2008)

Gloved Fingertip Testing	Action Levels (total number of CFUs on both hands)
Initial gloved fingertip testing	≥1
Gloved fingertip testing post media-fill testing	>3

8.15 Review of Results

Report test results for all gloved fingertip testing to the Facility Designated Individual(s) as soon as possible after test results are known. Designated facility personnel are responsible for reviewing sample results and the required documentation as listed in the section 8.13 titled “Documentation”. In the event of an exceeded level for initial gloved fingertip testing, there must be three consecutive successful tests. These should not occur all at one time, but should be collected the next three consecutive times the individual performs the hand hygiene and garbing process.

8.16 Investigation and Remediation of Exceeded Action Level

An exceeded action level may require additional training prior to retesting. Each organization must identify in their SOPs how they will handle personnel who have exceeded the action levels for testing. Until personnel qualification evaluation testing is performed with satisfactory results a compounder may not perform sterile compounding.

Recurring exceeded action levels among multiple compounding staff should warrant review of the training program, SOPs, PPE, hand hygiene materials, cleaning agents, facilities, equipment, media devices (e.g. lot #s) and viable air and surface results. Identification of growth to at least the genus level on fingertip samples can prove useful in a root cause analysis.

9 Addresses and Contacts

Controlled Environment Test Association (CETA)
701 Exposition Place, Suite 206, Raleigh, NC 27615 US
Phone: 919-792-6339
Email:info@cetainternational.org
Website: www.cetainternational.org

Department of Health and Human Services
Food and Drug Administration (FDA)
10903 New Hampshire Avenue, Silver Spring, MD 20993-0002
Phone: 1 888-463-6332
Website: www.fda.gov

Institute of Environmental Sciences and Technology (IEST)
1827 Walden Office Square, Suite 400, Schaumburg, IL 60173 US
Phone: (847) 981-0100
Email: information@iest.org
Website: www.iest.org

International Organization For Standardization (ISO)
Chemin de Blandonnet 8, CP 401
1214 Vernier, Geneva, CH
Phone: +41-22-7490111
E-mail: central@iso.org

United States Pharmacopeia (USP)
12601 Twinbrook Parkway, Rockville, MD 20852 US
Phone: 800-227-8772
Email: compoundingsl@usp.org
Website: www.usp.org