

# Understanding the Environmental Sampling Requirements of USP 797

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Eric S. Kastango, MBA, RPh, FASHP  
President-Clinical IQ, LLC  
Florham Park, NJ 07932



# Disclaimer

"Although I am a member of the USP Sterile Compounding Expert Committee, I am speaking today in my individual capacity and not as a member of the Committee or as a USP representative.

The views and opinions presented are entirely my own. They do not necessarily reflect the views of USP, nor should they be construed as an official explanation or interpretation of <797>."

# Program Objectives



- Discuss the elements of USP chapter 797 and its history
- Define the 797 requirements of environmental sampling
- Discuss the facility-related and personnel elements of environmental sampling

# USP <797>: Pharmaceutical Compounding-Sterile Preparations

- The intent of the chapter is “to prevent patient harm and fatality from microbial contamination (nonsterility), excessive bacterial endotoxins, large content errors in the strength of correct ingredients, and incorrect ingredients in CSPs.”
- Chapter formerly known as <1206>: Sterile Drugs for Home Use
- Effective January 1, 2004
- Revised and effective June 1, 2008

# History of Compliance



- Past national surveys have repeatedly shown that hospital pharmacies routinely do not comply with published guidelines for compounding sterile preparations.
- In the most recent national survey evaluating compliance with “ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products,” it was found that only 5.2% of pharmacies were fully compliant with garb attire requirements for compounding risk level 1 preparations.
- Only 4.7% of hospital pharmacies were fully compliant with documentation procedures for high risk level preparations.

# History of Compliance

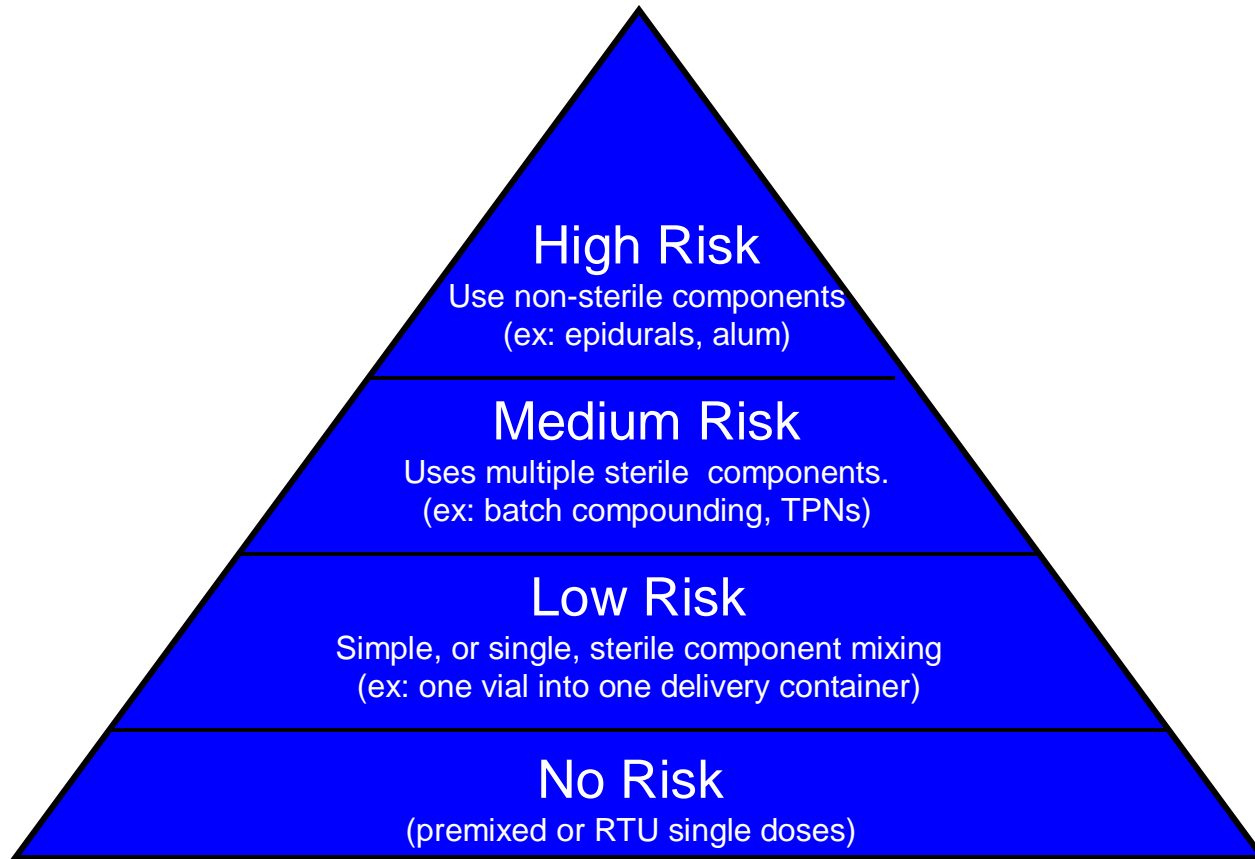


Voluntary standards do not work as effectively as mandatory regulations

“You get more with a kind word and a gun, than just a kind word”

Al Capone

# Underlying USP <797> Philosophy: A risk based approach to CSPs



# USP <797> Elements

- There are three broad areas that contribute to meeting the objectives of USP <797>

<b>Contamination Control</b>	<b>Training and Documentation</b>	<b>CSP Checks and Tests</b>
<ul style="list-style-type: none"><li>• Address particulate sources – people, products, process</li><li>• Create a “clean” environment where aseptic compounding will take place</li></ul>	<ul style="list-style-type: none"><li>• Compounding personnel are skilled, educated and trained</li><li>• Operator testing for proficiency</li><li>• Written policies, procedures</li><li>• Document training</li></ul>	<ul style="list-style-type: none"><li>• Reduce occurrence of contamination</li><li>• Verify the process produced correct CSPs</li><li>• Use the same process each time</li><li>• If contamination or error happens, detect it and take action</li></ul>

# Drivers of Compliance



- State Boards of Pharmacy

- What does your state BOP requirement?

- [http://www.clinicaliq.com/component/option,com\\_google\\_maps/Itemid,111/](http://www.clinicaliq.com/component/option,com_google_maps/Itemid,111/)

- TJC

- Do not survey to USP standards BUT there are several features of the USP chapter in TJC standards

- Will require compliance if State Board of Pharmacy does

- FDA

- Unlikely unless patient injury or death occurs

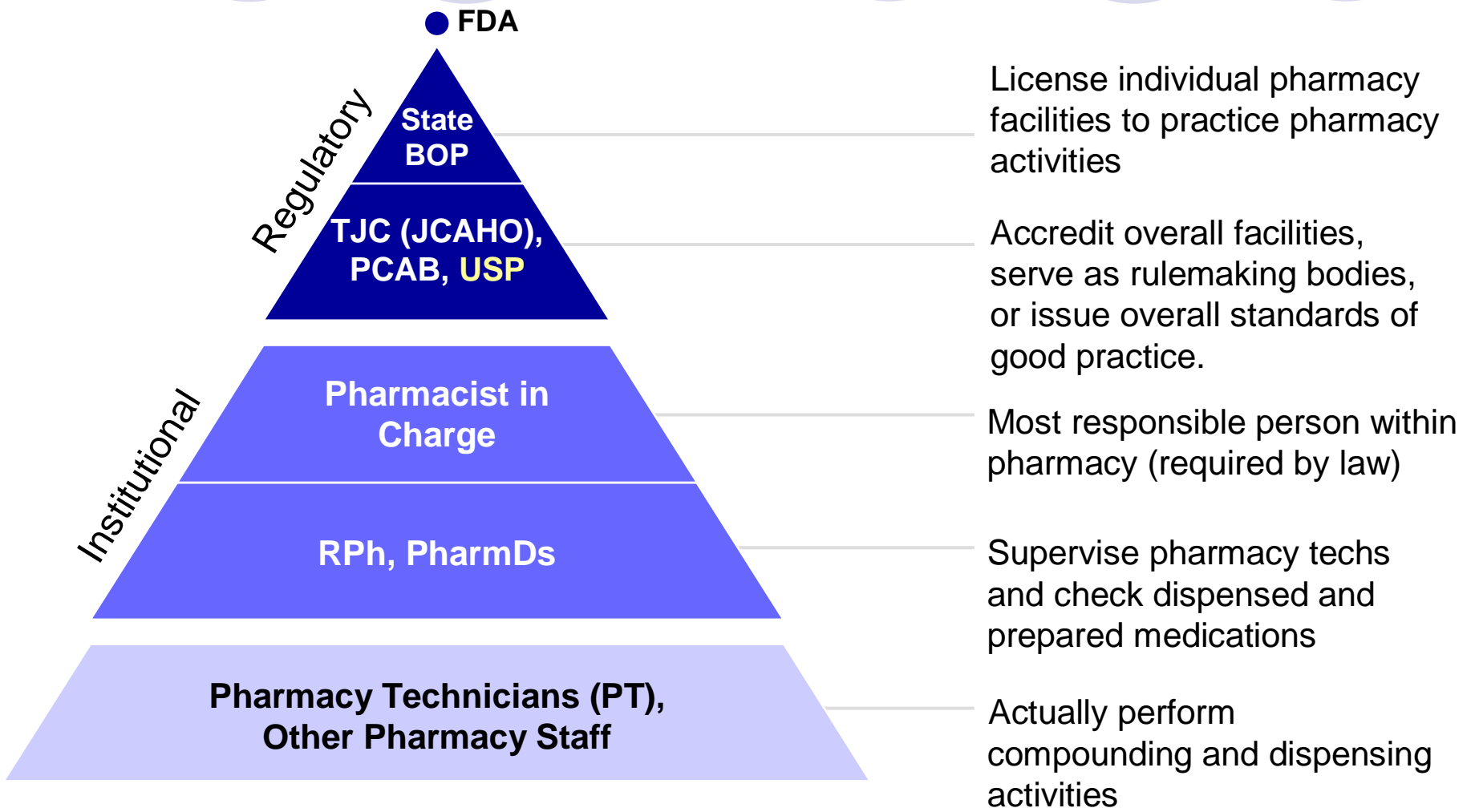
- Indefensible position in the event of civil actions

- Considered a community standard

- Reimbursement denial due to Infections

- CMS (Federal Medicare Program)

# Who governs compounding & dispensing activities?



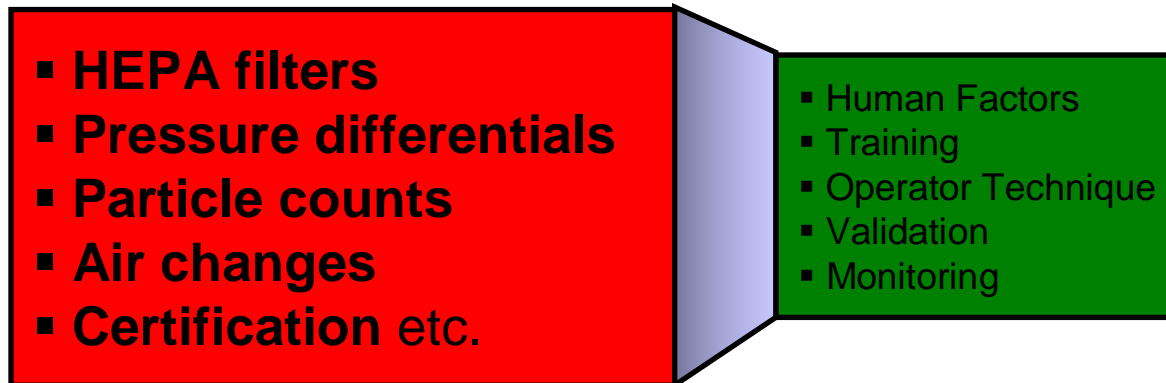
# The Joint Commission (TJC)

- Formerly known as JCAHO (Jay-Co)
- Requires annual assessment of MM 8.10 (Medication Management standard).
  - The organization evaluates its medication management system to identify risk points along with corresponding improvements
- Must consider updated technologies and successful practices (e.g., USP 797)
  - Will be cited for failing to considering successful practices

# Environment vs. Personnel

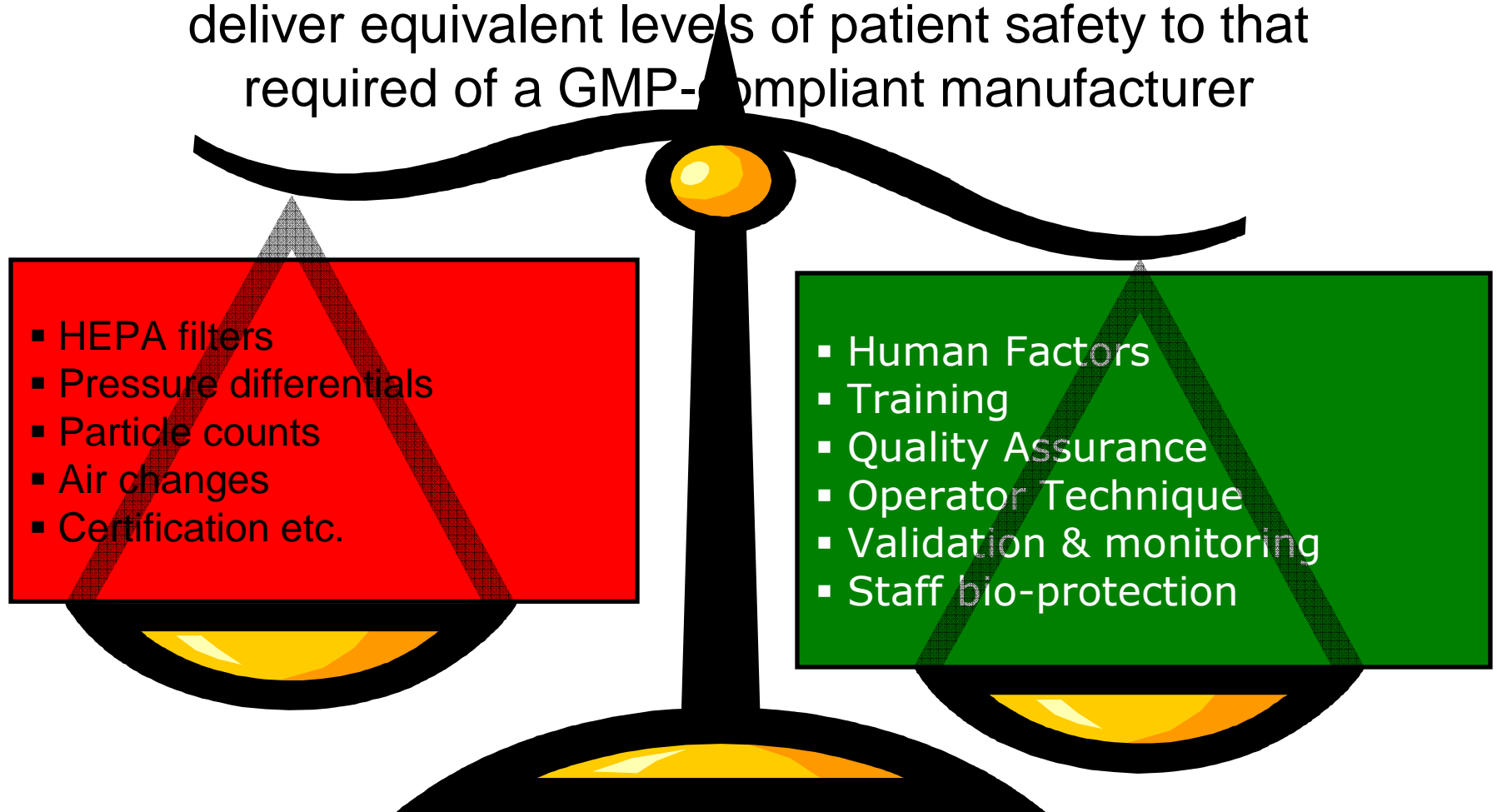
## Trends:

- Codes and Guidelines give undue weighting to engineering controls establishing air quality
- Relative lack of emphasis on other factors that we believe can prove to be of equal or greater importance in the safety of sterile compounding



# Environment vs. Personnel

and that make it practical for pharmacies to deliver equivalent levels of patient safety to that required of a GMP-compliant manufacturer





# Environment vs. Personnel

*“ The most important variable affecting microbial contamination of admixtures was the aseptic technique of personnel, not the environment in which the drugs were compounded. ”*

Thomas M, Sanborn M, Couldry R. *I.V. admixture contamination rates: Traditional practice site versus a class 1000 cleanroom.* Am J Health-Syst Pharm 2005;62:2386-92.

# Compounding Personnel



1954, Charles Schultz  
Copyright, United Feature Syndicate, Inc.

- A human person in a cleanroom is considered a broad spectrum particle generator enclosed by inefficient mechanical filters which may also be sources of particles
- The human body harbors an average of 150-200 different classes of bacteria
- Hands have an average of 100,000 organisms / sq mm
- The body sheds 5 grams of skin fragments each day along with shedding 1 layer of skin every 5 days (size range 10 to 300 micron – 1000<sup>th</sup> of a mm)
- “Our greatest asset and also our biggest liability!”

# Sources of Microbial Contamination in Aseptic Processing\*

Source	Ranks	
	1986	2001
<b>Personnel</b>	<b>1</b>	<b>1</b>
Human error	2	2
Aseptic assembly	4	3
Non-routine activity	3	4
Mechanical failure	5	5
Airborne contaminants	7	6
Improper sanitization	6	7
Surface contaminants	7	7
0.2 µm filter failure	8	8
HEPA failure	9	9

\*Agalloco J, Akers J, Madsen R. *Aseptic Processing: A Review of Current Industry Practice*. Pharmaceutical Technology. 2004; 28(10, Oct):128.

# Inherent Particles Present in Cleanrooms

<b>Activity</b>	<b>Particles <math>\geq 0.3 \mu\text{m}</math></b>
Person emits during garmenting process	3,000,000/min
Cleanest skin (hands)	10,000,000/ft <sup>2</sup>
Employee street clothes	10,000,000 – 30,000,000/ft <sup>2</sup>
Floor and bench surfaces	> 10,000,000/ft <sup>2</sup>
Garments supplied by cleanroom laundry	1,000,000/ft <sup>2</sup>

# Employee hand hygiene and garbing

- Unacceptable practices



# Employee hand hygiene and garbing

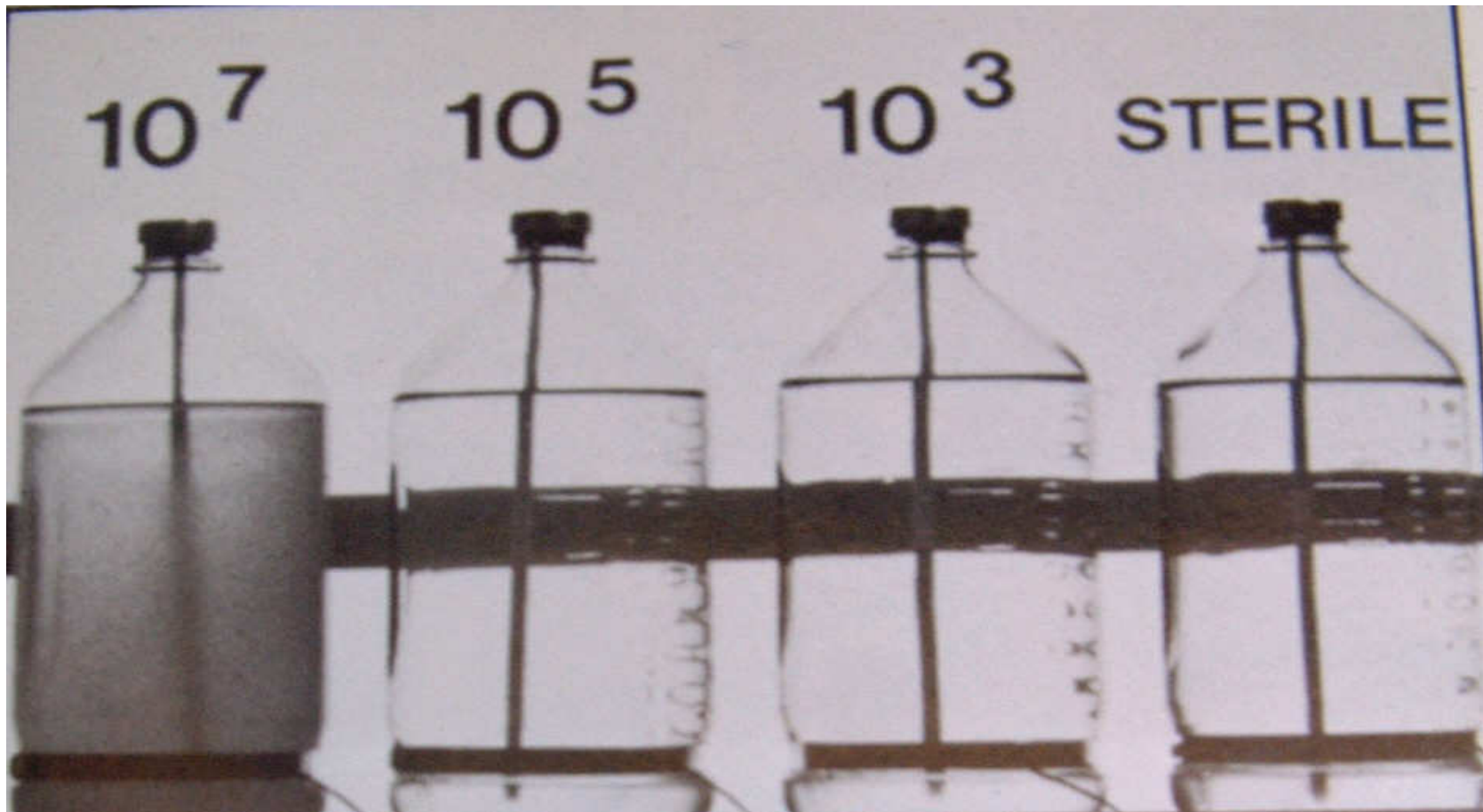
- Unacceptable practices



# Garbing requirements

<b>Garb requirement</b>	<b>Immediate-use</b>	<b>Low Risk (12 hr)</b>	<b>Med Risk</b>	<b>High Risk</b>
Makeup/Jewelry restrictions	N	Y	Y	Y
Hand hygiene	Y	Y	Y	Y
Hair/facial cover	N	Y	Y	Y
Shoe covers	N	Y	Y	Y
Low-shed gown	N	Y	Y	Y
Sterile Gloves	N	Y	Y	Y
Masks	N	Y	Y	Y

# Non-Visibility of Microbial Contamination



Numbers of Bacteria per mL in 1L bottles

Millipore Corp. *Hospital Pharmacy Filtration Guide* (Cat. No. MP801)

Bedford, MA; 1980:3

# Environmental Sampling



## Environmental Sampling Task

- Dilemma:
  - One of the most contentious section of USP Chapter <797>
  - Since 1970's, the US Centers for Disease Control (CDC) has not advocated routine viable environmental monitoring
  - The US Food and Drug Administration requires sterile processing operations to perform daily monitoring of viable air, surface and personnel glove fingertip samples

# Environmental Sampling/Testing

## Viable Microbial Environmental Sampling/Testing (EST)

None

Daily



**US Centers for  
Disease Control &  
Prevention**

**US Food and Drug  
Administration**

# Environmental Sampling/Testing

## Viable Microbial Environmental Sampling/Testing (EST)

Targeted

USP 797

Daily



US Centers for  
Disease Control &  
Prevention

US Food and Drug  
Administration

# Environmental Sampling



- Designed to demonstrate that the primary and secondary engineering controls, disinfecting procedures, and work practices result in a suitable environment for aseptic compounding
- Utilizes several approaches to assess and evaluate:
  - Total particle counts
  - Air viable organism cfu
  - Surface viable organism cfu
  - Finger touch plates

# Environmental Sampling/Testing

Newly revised chapter ties viable and nonviable testing to certain conditions as a minimum standard for compliance. This approach was in response to the recommendations made by the IC Advisory Panel, which had members from the CDC, APIC, SHEA, ASM, and a hospital based pharmacist.<sup>1</sup>

<sup>1</sup> Arjun Srinivasan, Judene Bartley, William Rutala, Alice Weissfeld, and Kathleen Gura  
Keith St. John was Chair of this Advisory Panel, appointed by CEO of USP, Roger Williams, MD

# Environmental sampling/testing conditions:

- As part of the commissioning and certification of new facilities and equipment.
- Following any servicing of facilities and equipment.
- As part of the re-certification of facilities and equipment (i.e., every 6 months).

# Environmental sampling/testing conditions –continued:

- In response to identified problems with end products or staff technique
- In response to issues with CSPs, observed compounding personnel work practices, or patient-related infections (where the CSP is being considered as a potential source of the infection.)

# Environmental Sampling/Testing

- EST section has been separated into a facility-related performance metric and a personnel –related performance metric
- Facility-related Environmental Sampling
  - Viable particle air sampling via volumetric method (impaction) to occur at least every 6 months, *linked with re-certification activities*
- Personnel-related Environmental Sampling
  - Personnel fingertip sampling during initial training, with media fills - utilized as a *competency assessment tool*
  - Surface sampling for viable microorganisms to assess the effectiveness of disinfection – *another competency assessment*

# Viabile Air Sampling



- Collection method via electric volumetric sampler (impaction preferred method)
- Gravimetric methods (e.g., plates or paddles) are not permitted
- Growth media used: Trypticase Soy Agar and Malt Extract Agar
- Sampling plan developed and based on a risk assessment of compounding activities
- Sampling locations to include:
  - Each ISO Class 5 Engineering Control
  - Area in ISO Class 7 and 8 and segregated areas and around ISO Class 5 area at greatest risk (e.g., pass-thru, labeling, staging, gowning areas)

# Volumetric Air Sampling Equipment



Merck MAS100



Biotest RCS



BioScience SAS180



Biotest RCS Isolator

# Viability Air Sampling



- Sampling plan to include:
  - Method of collection (e.g., Impaction sampling)
  - Frequency of testing
  - Volume of air sampled (400-1000L)
  - Time of day and activity of compounding
  - CFUs action levels
- Minimum frequency of testing
  - Initial facility commissioning
  - At least every six months during recertification of facility and engineering controls of all sterile compounding areas

Reference: USP <1116>: Microbiological Evaluation of Clean Rooms and Other Controlled Environments

# Environmental Monitoring

- Viable Air Sampling
  - Gravimetric vs. Volumetric Sampling



Courtesy of MSI, Inc. Houston, TX ([www.microbiologyspecialists.com](http://www.microbiologyspecialists.com))

# Environmental Sampling: Employee-centric Activities



- The risk of contaminating a CSP prepared under low-risk level and medium-risk level conditions is highly dependent on:
  - Proper hand hygiene and garbing practices,
  - Compounding personnel aseptic technique, and
  - Presence of surface contamination
  - Assumes all work is performed in a certified and properly functioning ISO Class 5

# Environmental Sampling: Employee-centric Activities



- Compounding personnel shall:
  - Complete didactic training,
  - Pass written competence assessments,
  - Undergo skill assessment using observational audit tools (see Appendices III–V)
    - Garbing and Gloving Competency Evaluation
    - Aseptic Manipulation Competency Evaluation
    - Cleaning And Disinfecting Competency Evaluation
  - Successfully complete aseptic media fill testing

# Environmental Sampling/Testing



- Glove fingertip sampling occurs annually for Low and Medium Risk and semi-annually for High Risk Level to assess staff competency of maintaining aseptic practices
- Surface sampling used to evaluate the effectiveness of cleaning/disinfecting procedures and work practices and occurs annually for Low and Medium Risk and semi-annually for High Risk Level sterile compounding

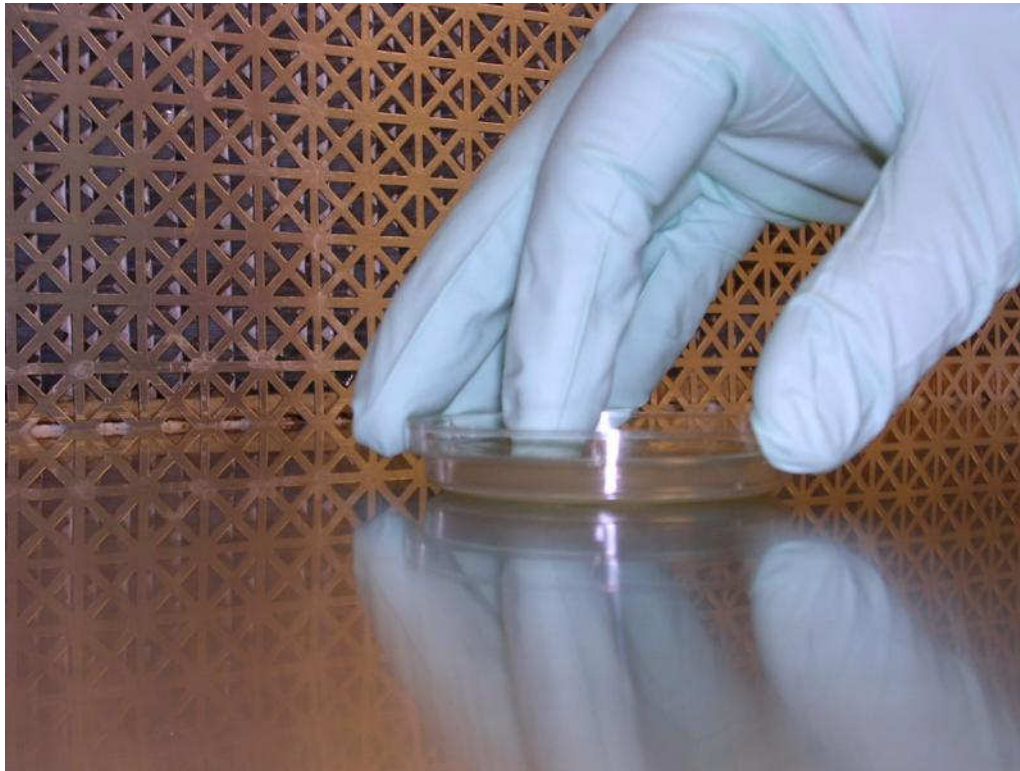
# Environmental Sampling: Surface

- Surface Cleaning and Disinfection Sampling and Assessment
  - Surface sampling is an important component of the maintenance of a suitable microbially controlled environment
    - Transfer of microbial contamination from improperly disinfected work surfaces via inadvertent touch contact by compounding personnel can be a potential source of contamination of CSPs
  - It is useful for evaluating facility and work surface cleaning and disinfecting procedures and employee competency in work practices such as disinfection of component/vial surface cleaning.

# Environmental Sampling: Surface

- Surface Cleaning and Disinfection Sampling and Assessment
  - Sampling of all ISO classified areas will occur on a periodic basis at the end of compounding
  - Contact plates (plate size 24-30 cm<sup>2</sup>)
  - Swabs (defined template)
  - Plates to have a neutralizing agents (lecithin and polysorbate 80)

# Environmental Sampling: Surface



# Environmental Sampling: Cleaning

- Cleaning And Disinfecting Competency Evaluation
  - Compounding personnel and other personnel responsible for cleaning shall be visually observed during:
    - Performance of cleaning and disinfecting procedures
    - During initial personnel training on cleaning procedures
    - During changes in cleaning staff,
    - At the completion of any media-fill test procedure
  - Visual observation documented on Sample Form (Appendix V)



# Final summary comments....

- The revised Chapter <797> places much more emphasis on individual training and evaluation of those who compound sterile preparations, and SHEA, APIC, CDC, and ASM representatives on the USP IC Advisory Panel agreed with the link of performance measures with education and training. [This section is now entitled *Viable and Nonviable Environmental Sampling (ES) Testing*.]
- New checklists were added to the appendices to further incorporate process measurements into the overall quality control program. The checklists help to provide an overview of the chapter as well.
- Due to input from Dr. Bill Rutala, Appendix II of Chapter <797> includes a table of common disinfectants used in healthcare for inanimate surfaces, along with their microbiocidal activity.
- SHEA, APIC, CDC, and ASM representatives on the USP IC Advisory Panel view this as opening the door to new options for disinfection in pharmacies beyond exclusively using 70% isopropyl alcohol.

# Patient Safety remains Priority #1!

- Patient Safety is a partnership involving multiple disciplines and is not achieved in “isolation.”
- It takes all of us working together to achieve the goal of “zero tolerance” for preventable healthcare-associated infections, whether at the patient’s bedside or in the pharmacy.



# Any Questions ?

Access to USP <797> FAQs:

<http://www.usp.org/audiences/pharmacist/797FAQs.html>

Information on State Board of Pharmacy's  
requirements regarding USP<797>:

[http://www.clinicaliq.com/component/option,com\\_google\\_maps/Itemid,111/](http://www.clinicaliq.com/component/option,com_google_maps/Itemid,111/)

My contact information:

**Eric S. Kastango**

eric.kastango@clinicaliq.com

Phone number: (973) 765-9393