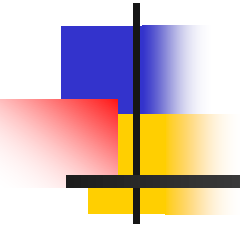


# Cleaning & Sanitization Concepts



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# Cleaning and Sanitization Concepts

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## ■ **Cleaning**

- The process of removing dirt, oil, stains and/or impurities from a surface
- Can remove microbes and particulates from a surface by the physical cleaning action
- There is no significant chemical kill of organisms



# Cleaning and Sanitization Concepts

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- **Cleaning**

- Cleaning is the most important step to successful sanitization
- Residues and buildup can interfere with sanitization if not removed



# Cleaning and Sanitization Concepts

---

- **Cleaning**

- Cleaning agents are consists of some type of surfactants
  - ❖ Anionic surfactants provide good cleaning ability
  - ❖ Alkaline or acidic formulas available



# Cleaning and Sanitization Concepts

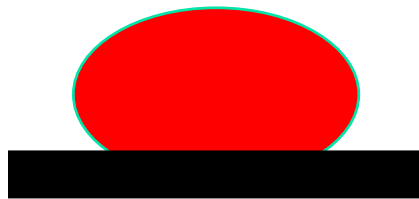
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## ■ **Cleaning**

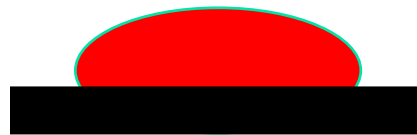
- Surfactants act as a detergent
  - ❖ Enable the solution to displace particulate matter
  - ❖ Penetrate soil and oil
  - ❖ Has a oily consistency

# Cleaning and Sanitization Concepts

- Influence of Surfactants on Wetting
  - Ability to displace particles
  - Penetrate soil and surface irregularities



**No Surfactants**



**Surfactant A**

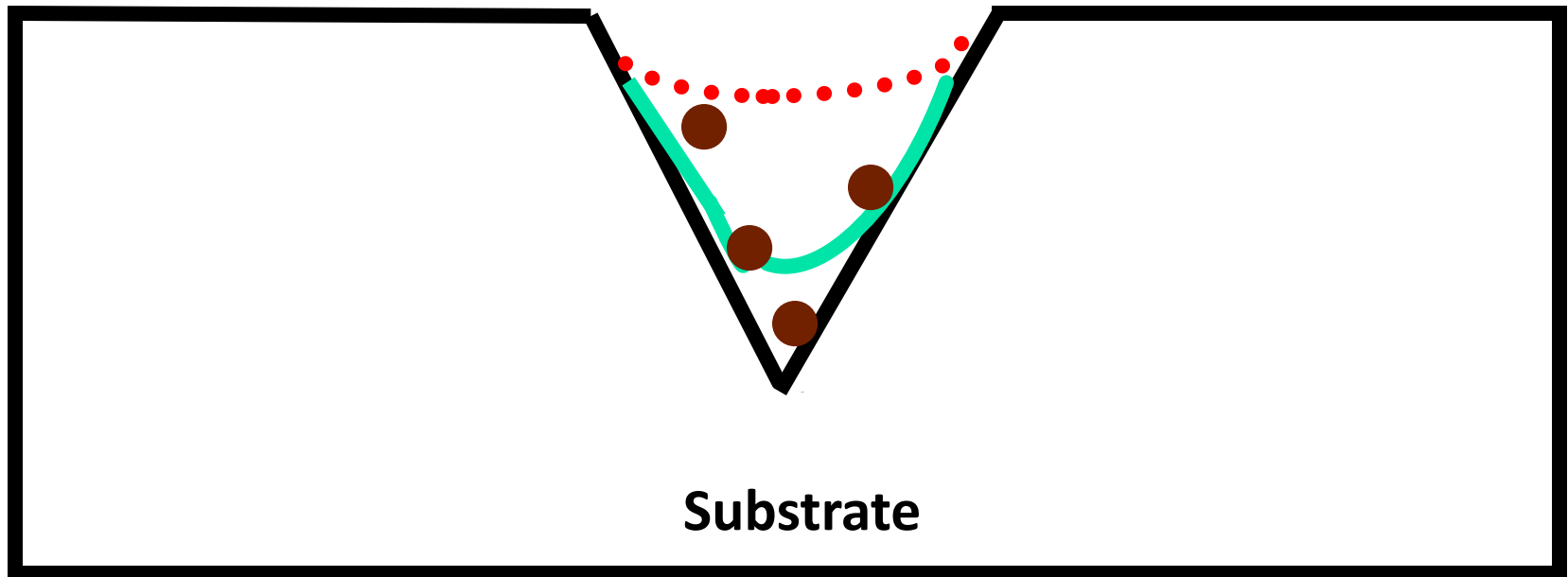


**Surfactant B**

# Cleaning and Sanitization Concepts

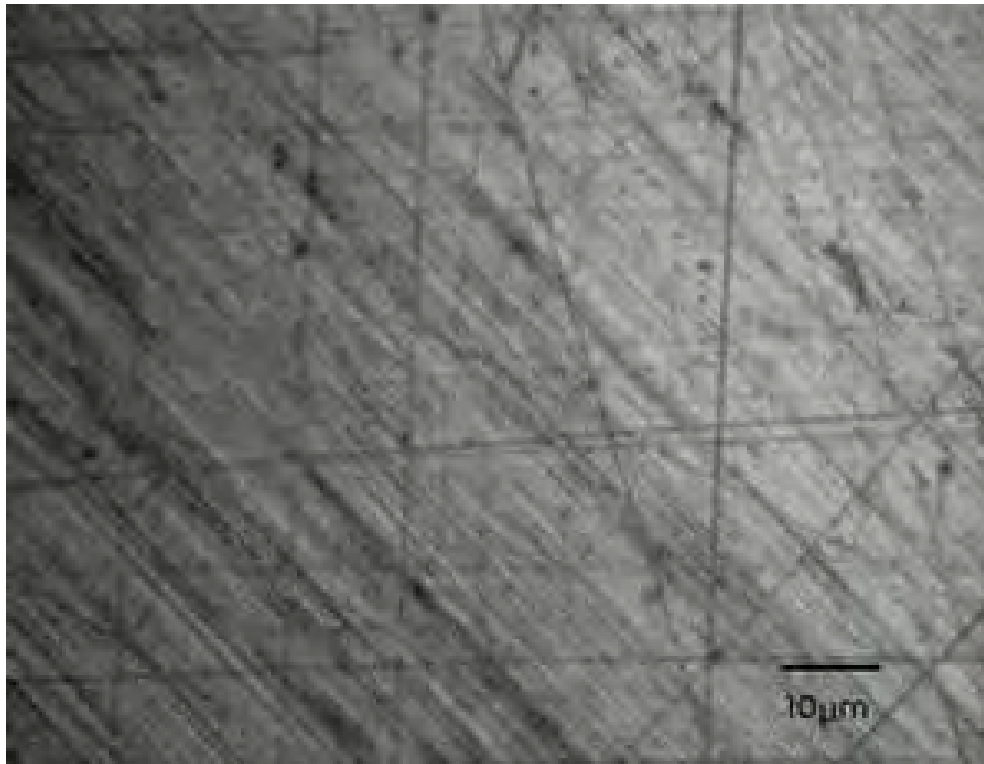
Water

With surfactant



# Cleaning and Sanitization Concepts

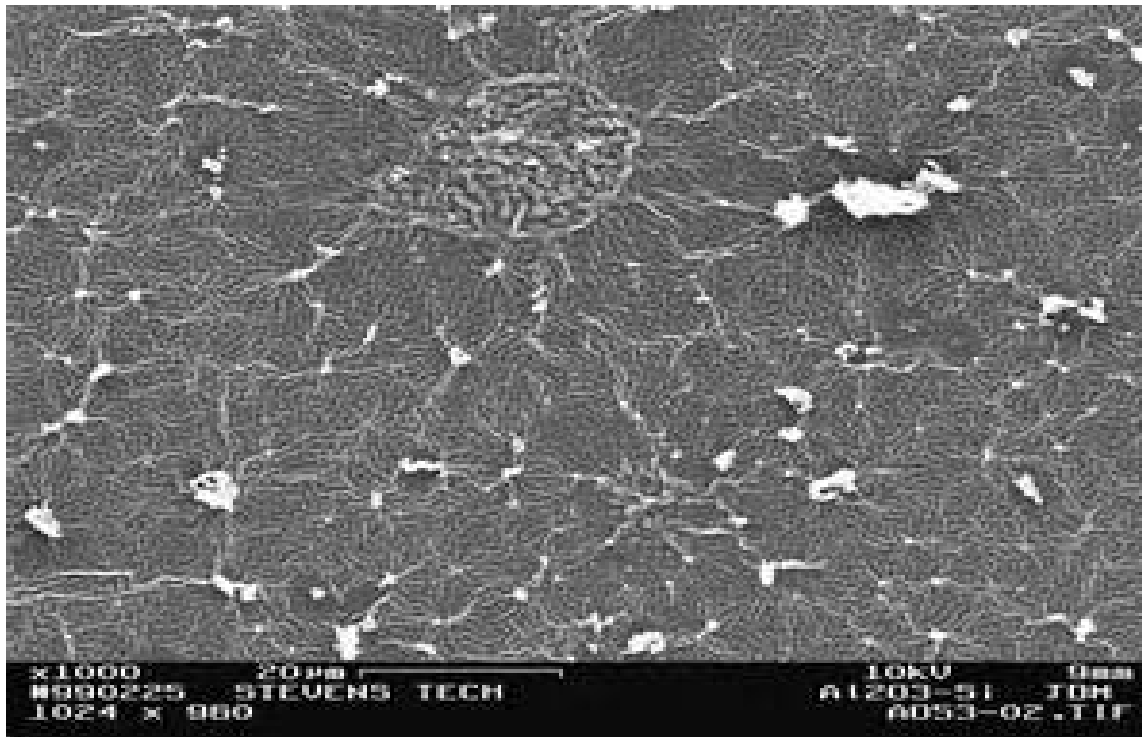
- **Aluminum Surface**





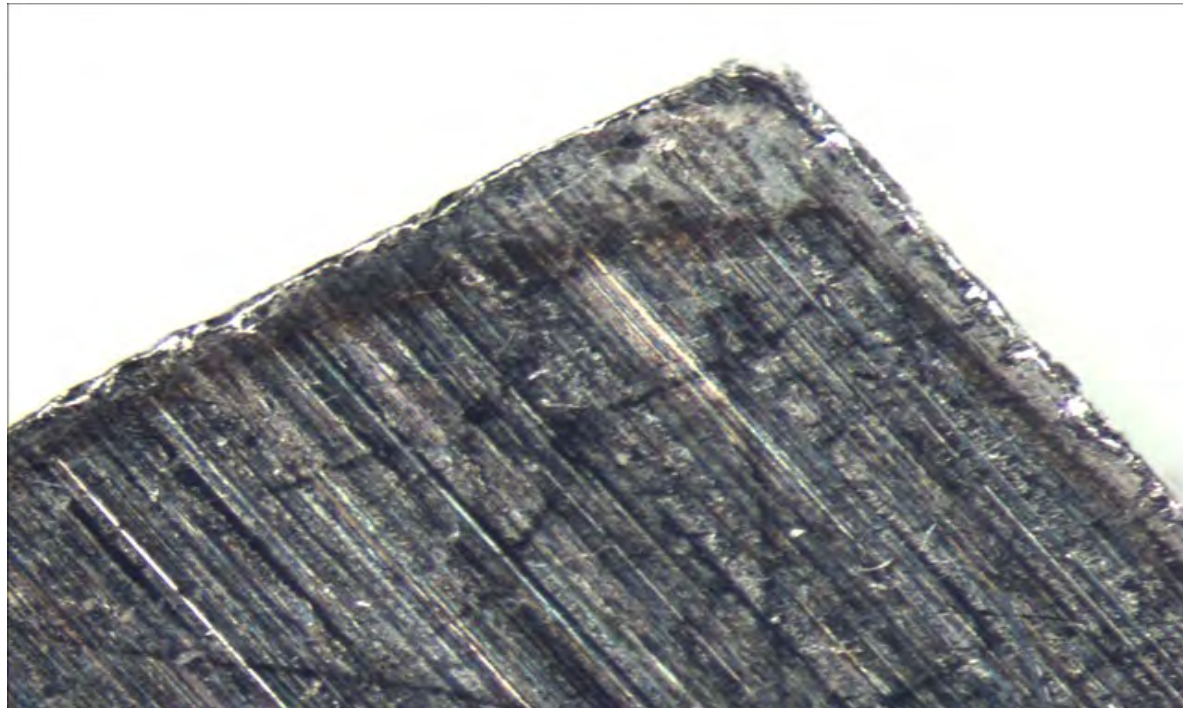
# Cleaning and Sanitization Concepts

- **Aluminum Surface SEM 1000X**



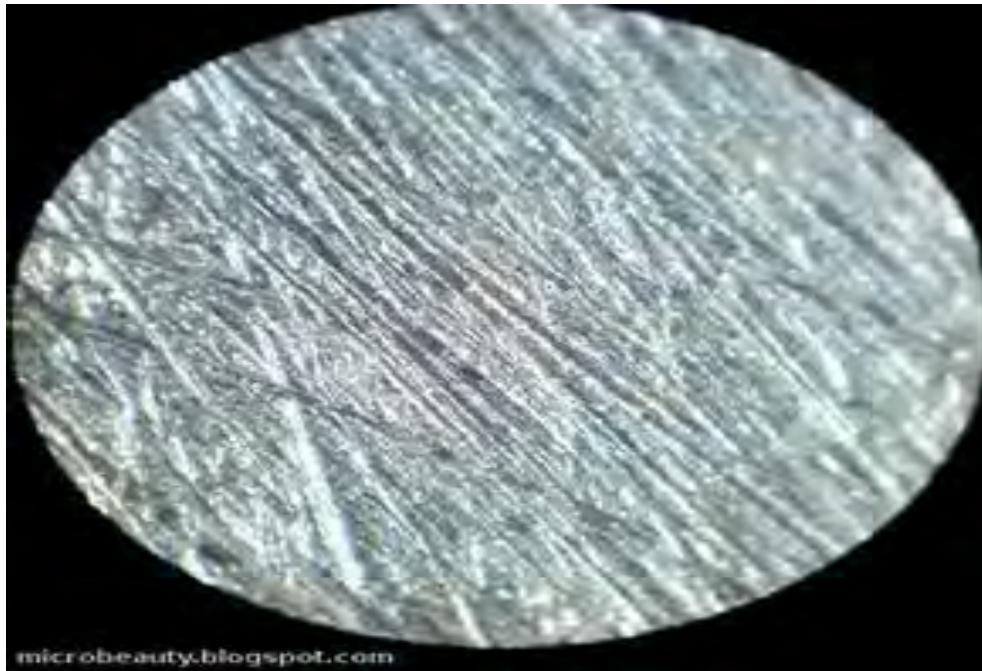
# Cleaning and Sanitization Concepts

- **Stainless Steel 250X**



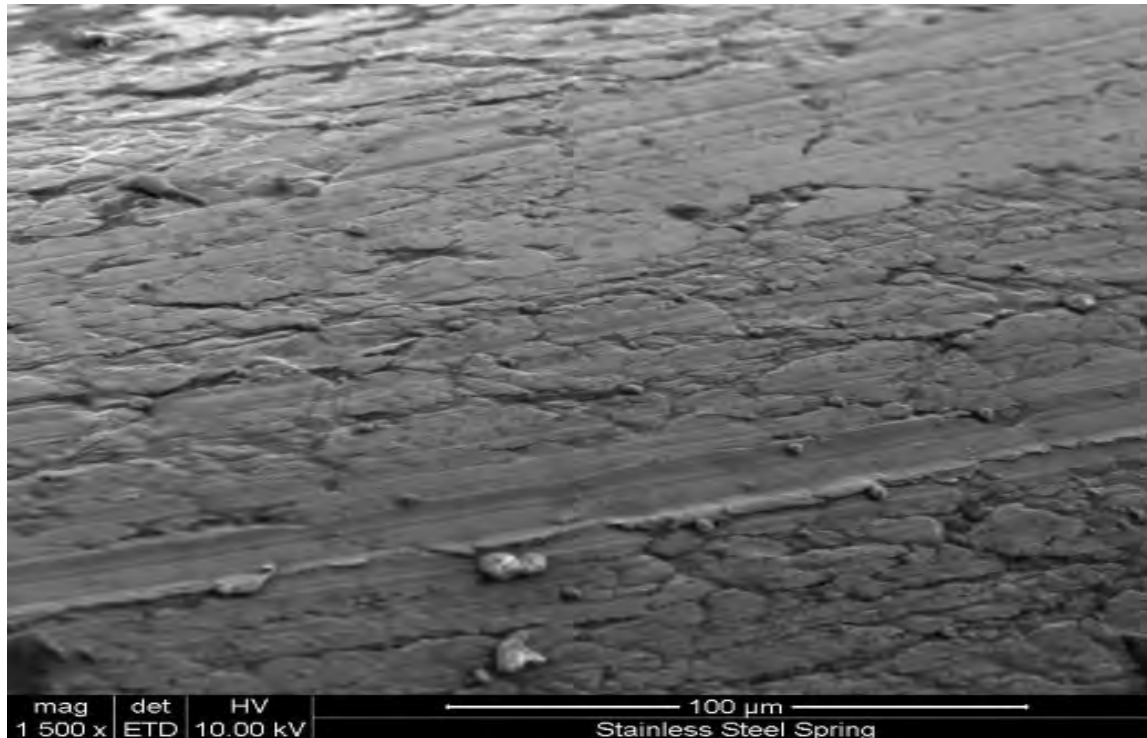
# Cleaning and Sanitization Concepts

- **Stainless Steel 1000X**



# Cleaning and Sanitization Concepts

- **Polished Stainless Steel 1500X**



# Cleaning and Sanitization Concepts

- **Stainless Steel SEM 6000X**



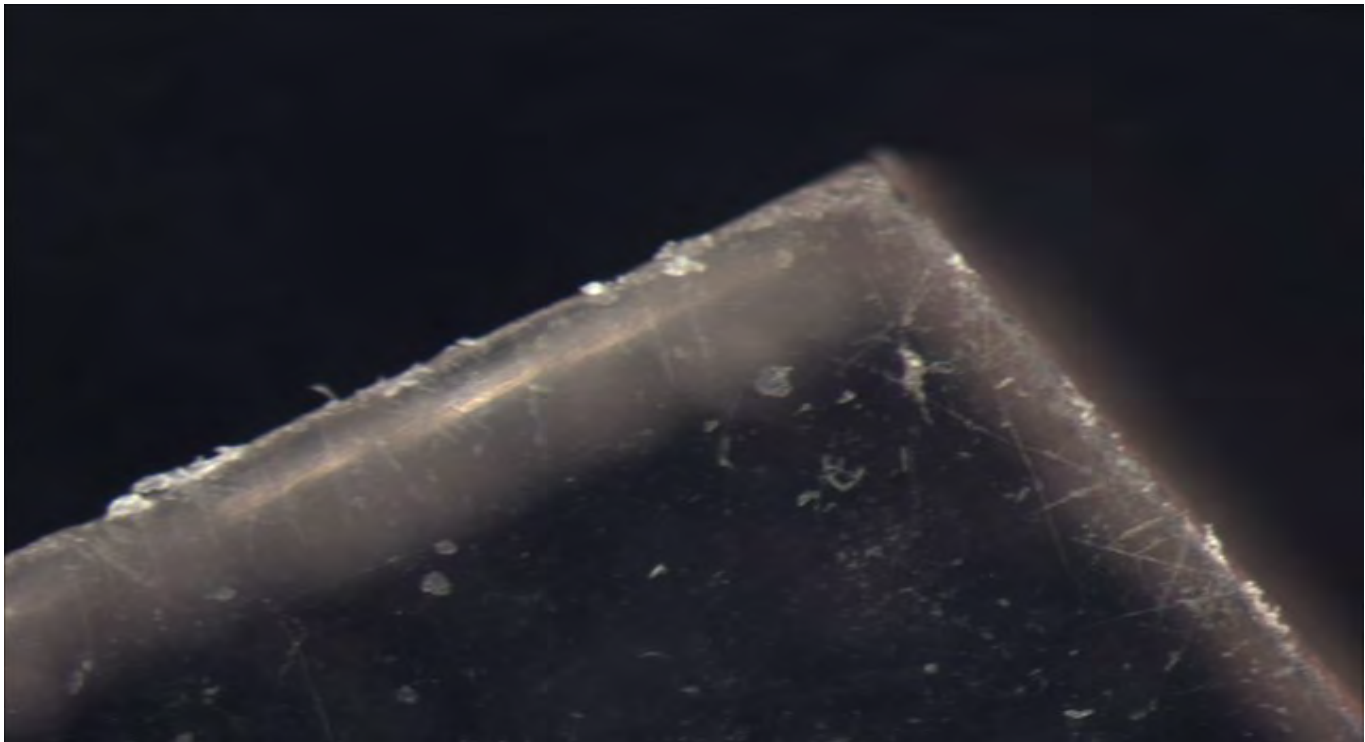
# Cleaning and Sanitization Concepts

- **Vinyl Surface**



# Cleaning and Sanitization Concepts

- **Curtain**

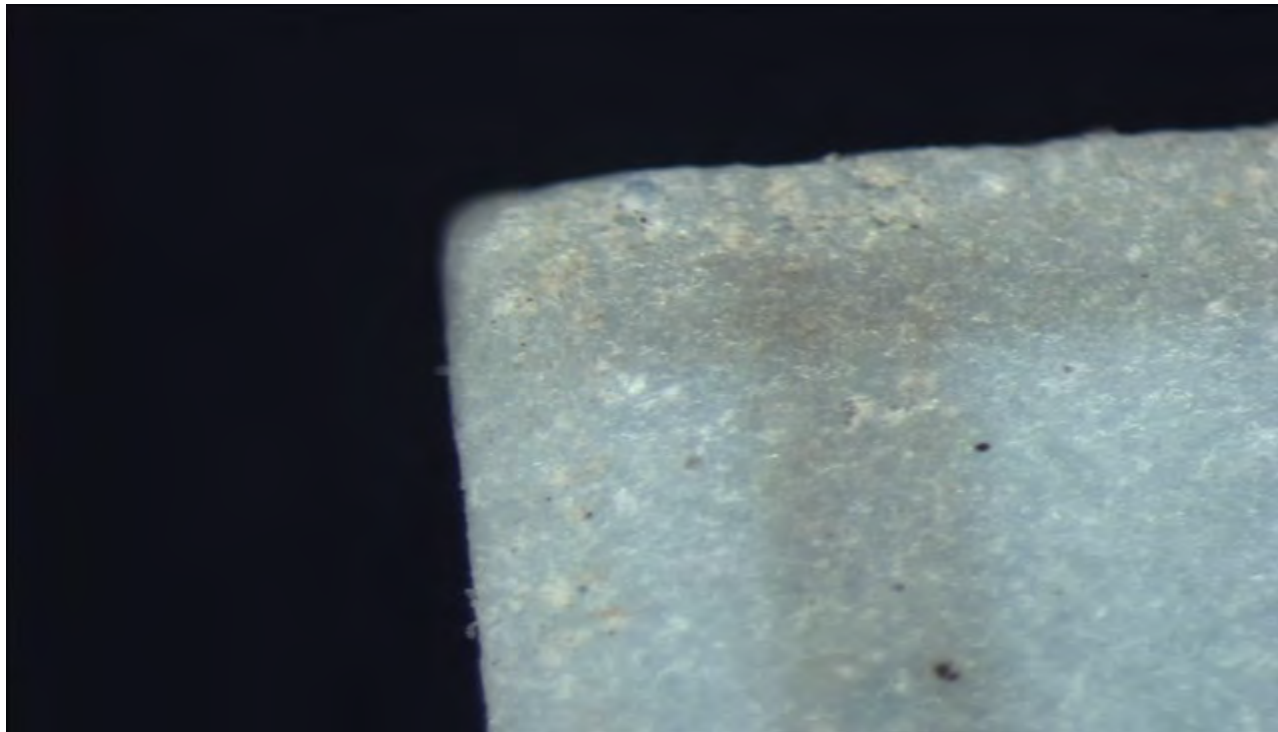






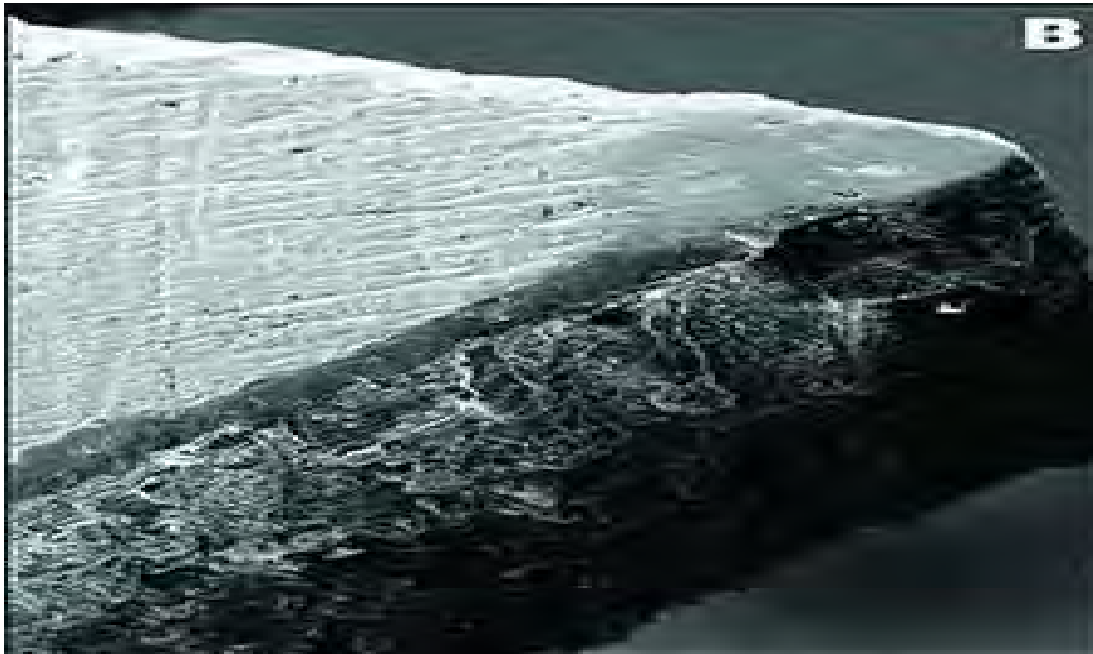
# Cleaning and Sanitization Concepts

- **Tank Wheel**



# Cleaning and Sanitization Concepts

- **Epoxy Floor**



# Cleaning and Sanitization Concepts

- **Kydex Wall Material**





# Cleaning and Sanitization Concepts

---

## ■ Sanitizer EPA Requirement

- Proper use results in bacteria reduction of >99.9%, but does not eliminate all bacteria present
- Target organisms
  - Escherichia coli
  - Staphylococcus aureus
  - Salmonella typhi



# Cleaning and Sanitization Concepts

---

- **Disinfect EPA Requirement**

- Proper use results in 100% kill of vegetative bacteria, target viruses and target fungi
- Target organisms
  - *Salmonella cholerasuis*
  - *Staphylococcus aureus*
  - *Pseudomonas aeruginosa*



# Cleaning and Sanitization Concepts

---

- **Sporicide/Cold Sterilant**

- Proper use results in 100% kill of microorganisms including bacterial and fungal spores
- Target organisms
  - *Bacillus subtilis*
  - *Clostridium sporogenes*



# Cleaning and Sanitization Concepts

---

- **Sterilize**

- Proper use results in 100% kill of all microorganisms, including bacterial spores
- Always requires pre-cleaning



# Cleaning and Sanitization Concepts

---

- **The term cleaning is often used interchangeably with sanitization an/or disinfection, but they are drastically different**
- **There is no significant difference between sanitization & disinfection for the purpose of this discussion. They are often used interchangeably**





# Cleaning and Sanitization Concepts

---

- **Categorize the solutions as follows**
  - Cleaners
  - Cleaner/Sanitizer
  - Sanitizer
  - Sporicide



# Cleaning and Sanitization Concepts

---

- **Identify the surfaces to be cleaned and/or sanitized. Determine if the solution will negatively effect the surface**
  - Discoloration of the material
  - Corrosion and/or pitting
  - Deteriorate of the surface over time
  - Incompatibilities which can cause surfaces to become sticky



# Cleaning and Sanitization Concepts

---

- **Determine the type of cleaner and or sanitizer required based on the following**
  - Type and number of organisms present
  - Amount of organic mater present
  - Types of surfaces to be sanitized
  - Classification of the area
  - Product incompatibility



# Cleaning and Sanitization Concepts

---

- **Determine the type of cleaner and or sanitizer required based on the following:**
  - Prepare in-house or purchase
  - Concentrate or ready to use
  - Cost per gallon
  - Sterile filtration required



# Cleaning and Sanitization Concepts

---

## ■ **Disinfectant Effectiveness**

- Bioburden load
- Pre-cleaning of surface may be required
- High or Low pH
- Surface irregularities
- Quality of water used to prepare



# Cleaning and Sanitization Concepts

---

## **PREPARATION OF DISINFECTANTS**

### **■ Water**

- WFI for aseptic filling/processing areas
- PW for non-critical areas

### **■ Concentrate or Ready to Use**

- Sterile or non-sterile
- Cost effective



# Cleaning and Sanitization Concepts

---

## ■ **Disinfectant Effectiveness**

- Concentration of the solution
- Accuracy of the measuring devices used to make the disinfectants
- Temperature of the concentrate and water
- Ability of solution to penetrate cell wall



# Cleaning and Sanitization Concepts

---

## **PREPARATION OF DISINFECTANTS**

### **■ Measuring devices**

- Don't use markings on buckets or carboys
- Use graduated cylinders
- For concentrated single dose units, is there a need to rinse container to deliver the entire content



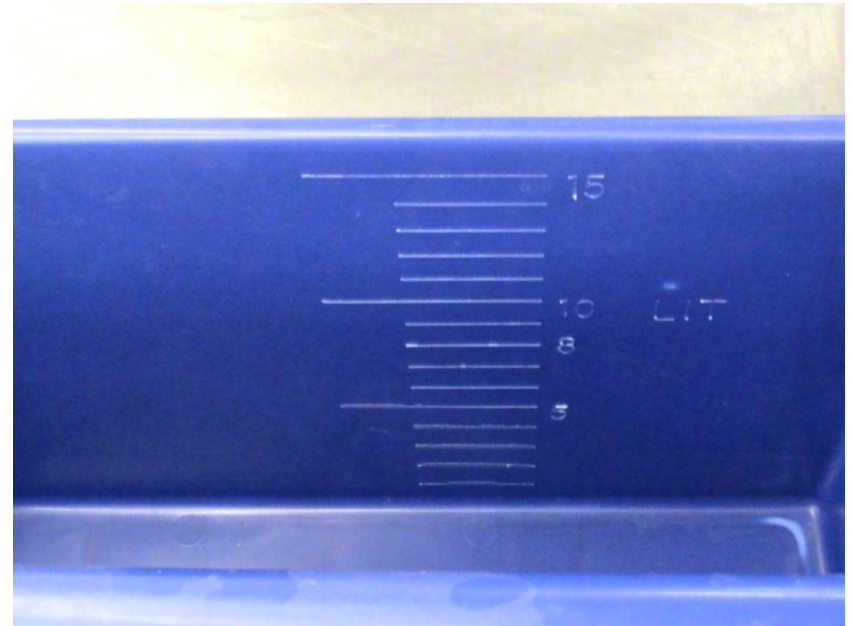
# Cleaning and Sanitization Concepts

## VARIOUS MEASURING DEVICES



# Cleaning and Sanitization Concepts

## MEASURING DEVICES





# Cleaning and Sanitization Concepts

---

## PREPARATION OF DISINFECTANTS

### ■ **Mixing solutions**

- In general, the concentrate is added to the correct volume of water
- If WFI is poured into a bucket containing the concentrate, the solution tends to foam.



# Cleaning and Sanitization Concepts

---

## PREPARATION OF DISINFECTANTS

### ■ Sterile filtration

- Required for aseptic processing areas
  - ❖ Sterile filter directly into the area through a pass through for large volumes
  - ❖ Filter into sterile spray/squirt bottles
- Not required for non-critical areas such as Grade-A/B Areas



# Cleaning and Sanitization Concepts

---

## ■ Disinfectant Effectiveness

### ➤ Contact time

- ❖ Time required for solution to reduce the target organisms by 3-logs
- ❖ This is a wet contact time
- ❖ Air exchanges in clean room makes it difficult to maintain
- ❖ Many solutions evaporate quickly
- ❖ Determined by disinfectant efficacy testing



# Cleaning and Sanitization Concepts

---

## ■ **Disinfectant Effectiveness**

- Disinfectant efficacy testing
  - ❖ Representative surfaces found in a clean room
    - ✓ Floor, Dycem, walls, curtains, filling equipment, cart wheels and stainless steel
  - ❖ Evaluate all solutions used as a sanitizer or sporicidal agent
  - ❖ Not required for cleaning solutions



# Cleaning and Sanitization Concepts

---

## ■ **Disinfectant Effectiveness**

- Disinfectant efficacy testing
  - ❖ Representative micro-organisms
    - ✓ Gram Positive and Negative
    - ✓ Bacillus and Mold
    - ✓ Yeast
    - ✓ Environmental isolates recovered from the filling areas



# Cleaning and Sanitization Concepts

---

## ■ **Disinfectant Effectiveness**

- Disinfectant efficacy testing
  - ❖ Define contact time. Most producers of sanitizers/sporicidal agents recommend 10 minutes
  - ❖ Suggest using a 5 minutes
  - ❖ The surfaces in the clean room may not remain wet for 10 minutes due to the high air exchanges





# Cleaning and Sanitization Concepts

---

## Component

- Water
- Antimicrobials
- Oxidants
- Bases
- Acids

## Disinfectant Functions

Solvent

Kill, reduce microbes

Oxidize, kill microbes

Alkalinity source

Acidity source



# Cleaning and Sanitization Concepts

---

## Component

- Surfactants
- Chelan's

## Disinfectant Functions

Wetting/Detergent

Bind calcium/iron and stabilize oxidants



# Cleaning and Sanitization Concepts

---

## **CLEANING AGENT**

- **Only cleans**

- Provides no chemical killing action
- Leaves a residue
- Contact time not required
- Just like dish washing soap

# Cleaning and Sanitization Concepts

## CLEANING AGENT





# Cleaning and Sanitization Concepts

---

## **CLEANER/SANITIZERS**

- **Phenols with a High or Low pH**
  - Broad spectrum but not sporicidal
  - Leaves a residue
  - Moderate evaporation rate
  - Surfactants provides good cleaning
  - Activity affected by incompatible nonionic detergents and other chemicals



# Cleaning and Sanitization Concepts

---

## **CLEANER/SANITIZERS**

### **■ Phenols with a High or Low pH**

- Absorbed into the skin with potential health risks
- Kill by precipitating proteins within the cell and also disrupts cell membrane functions
- LpH and Vesphene



# Cleaning and Sanitization Concepts

---

## **CLEANER/SANITIZERS**

### **■ Quaternary Ammonium**

- Broad spectrum but not sporicidal
- Leaves a residue
- Moderate evaporation rate
- Surfactants provides good cleaning
- Activity affected by incompatible chemical agents



# Cleaning and Sanitization Concepts

---

## **CLEANER/SANITIZERS**

### **■ Quaternary Ammonium**

- Kill by disrupting cell membrane permeability
- Decon-Quat





# Cleaning and Sanitization Concepts

---

## **CLEANER/SANITIZERS**

### **■ Glutaraldehyde/Formaldehyde**

- Broad spectrum
- Leaves a residue with compatibility issues
- Moderate evaporation rate
- Can be considered a sporicidal agent at high concentrations or extended contact times



# Cleaning and Sanitization Concepts

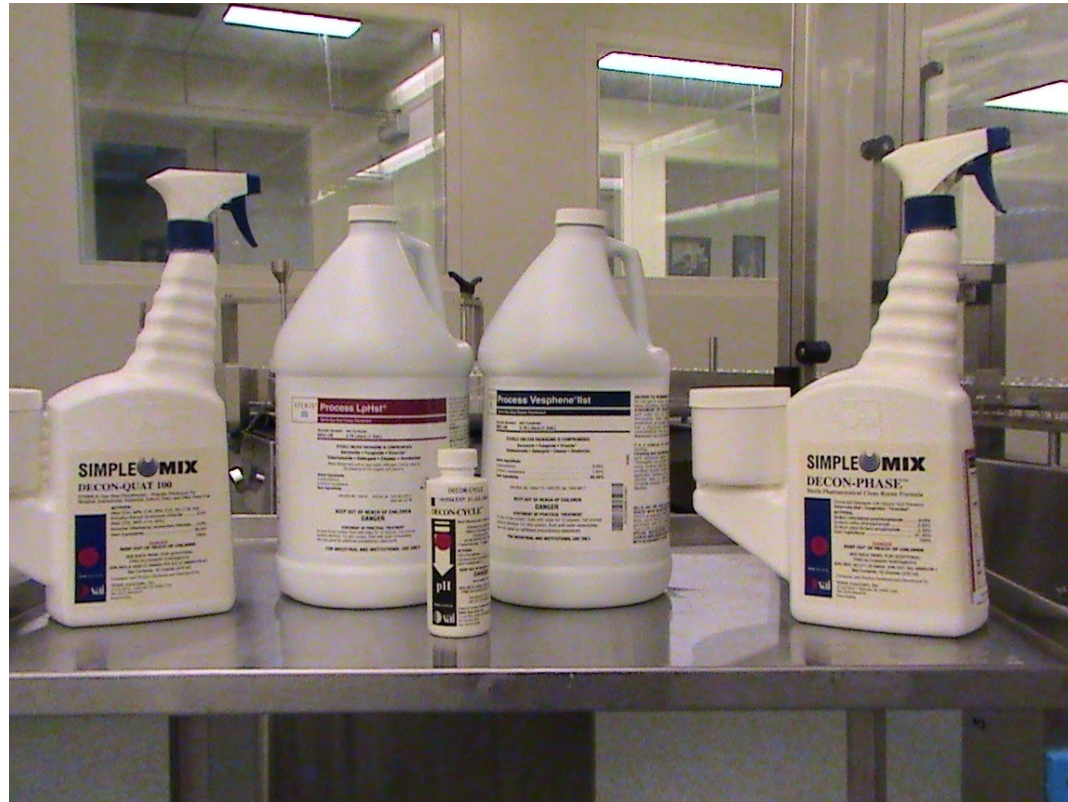
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## **CLEANER/SANITIZERS**

- **Glutaraldehyde/Formaldehyde**
  - Provides limited cleaning
  - Cost of this solution is a significant consideration
  - Health risks

# Cleaning and Sanitization Concepts

## COMMON CLEANER/SANITIZERS





# Cleaning and Sanitization Concepts

---

## **SANITIZATION ONLY**

- **Isopropyl Alcohol at 70%**
  - Broad spectrum
  - Does not leave a residue
  - Evaporates quickly
  - Limited contact time



# Cleaning and Sanitization Concepts

---

## **SANITIZATION ONLY**

- **Isopropyl Alcohol at 70%**

- Not sporicidal
- Pre cleaning required
- Flammable
- Sterile pressurized canisters/Spray bottles
- Extracts lipids from cell membrane to kill



# Cleaning and Sanitization Concepts

---

## **SANITIZATION ONLY**

- **Hydrogen Peroxide at 3 – 6%**
  - Broad spectrum
  - Does not leave a residue
  - Non corrosive
  - Short expiration date



# Cleaning and Sanitization Concepts

---

## **SANITIZATION ONLY**

- **Hydrogen Peroxide at 3 – 6%**
  - Moderate evaporation rate
  - Provides no chemical cleaning ability
  - Pre cleaning required
  - Minimal sporicidal activity at this concentration

# Cleaning and Sanitization Concepts

## COMMON SANITIZERS ONLY







# Cleaning and Sanitization Concepts

---

## **SPORICIDAL AGENTS**

- **Hydrogen Peroxide at >30% (VHP)**
  - Broad spectrum
  - Does not leave a residue
  - Moderate evaporation rate
  - Provides no chemical cleaning ability
  - Sporicidal



# Cleaning and Sanitization Concepts

---

## **SPORICIDAL AGENTS**

- **Sodium Hypochlorite  $\geq 0.52\%$** 
  - Broad spectrum
  - Leaves a residue
  - Moderate evaporation rate
  - High level of disinfectant efficacy
  - Pre-cleaning required



# Cleaning and Sanitization Concepts

---

## **SPORICIDAL AGENTS**

- **Sodium Hypochlorite  $\geq 0.52\%$** 
  - Sporicidal at  $> 200$  ppm
  - Corrosive to soft metals and stainless steel
  - Temperature and light sensitive
  - Safety concern
    - ❖ Generation of chlorine gas
    - ❖ Contact with eyes and/or skin



# Cleaning and Sanitization Concepts

---

## **SPORICIDAL AGENTS**

- **Peracetic acid/Hydrogen peroxide**
  - Broad spectrum and sporicidal
  - Leaves a residue
  - Moderate evaporation rate
  - Pre-cleaning required



# Cleaning and Sanitization Concepts

---

## **SPORICIDAL AGENTS**

- **Peracetic acid/Hydrogen peroxide**
  - Corrosive to soft metal
  - Temperature sensitive
  - Pungent vinegar like odor
  - Spore-Klenz
  - Decon Spore

# Cleaning and Sanitization Concepts

## COMMON SPORICIDAL AGENTS





# Cleaning and Sanitization Concepts

---

## **CONTAINERS FOR DISINFECTANTS**

### **■ Sterile spray/Squeeze bottles**

- Aspirates room air into the master solution
- Possibility of contaminating the solution
- Non-sporicidal agents should expire in 24 hours
- Sporicidal agents are self sanitizing and could have a longer expiration date if validated



# Cleaning and Sanitization Concepts

---

## **CONTAINERS FOR DISINFECTANTS**

### **■ Sterile Aerosol Cans**

- Does not aspirate room air into the master solution
- No contamination of the solution
- Define expiration date based on validation data



# Cleaning and Sanitization Concepts

## CONTAINERS FOR DISINFECTANTS



# Cleaning and Sanitization Concepts

**WHATS WRONG WITH THIS PICTURE?**





# Cleaning and Sanitization Concepts

---

## **ROTATION OF DISINFECTANTS**

- **Resistance**
- **Rotation**
- **Built Immunity**



# Cleaning and Sanitization Concepts

---

## **ROTATION OF DISINFECTANTS**

- Resistance has many of meanings:
  - Webster's: “To withstand the force or effect”
  - Medical: A drug product (usually an antibiotic) not being effective in destroying an organism in the human body.



# Cleaning and Sanitization Concepts

---

- Resistance has many of meanings:
  - Pharmaceutical & Biotechnology: Used to describe an organism not being destroyed by a certain type of planned destructive force.
  - In “**THEORY**” that an organism can develop or build an immunity to a chemical agent.



# Cleaning and Sanitization Concepts

---

- **For the Pharmaceutical Industry, Resistance does not mean**
  - Developing an immunity to a disinfectant
  - The changing of an organism's susceptibility to a chemical germicide.
- **Resistance means**
  - An organism that is not destroyed by a chemical agent in the population tested



# Cleaning and Sanitization Concepts

---

## ■ Built Immunity

- Natural selection is a slow process
- Requires high populations of cells
- Constant selective pressure
- Building an immunity to a disinfectant has never been documented in the clean room
- It is a theory



# Cleaning and Sanitization Concepts

---

- **The CDC Oct. 28, 1997**

- Antibiotic resistant microorganisms are susceptible to chemical germicides.
- The mechanisms by which chemical germicides and antibiotics work are completely different
- There does not seem to be a relationship between antibiotic resistance and chemical germicide effectiveness"





# Cleaning and Sanitization Concepts

---

## ■ **USP 1072 on Disinfectants**

- The microbial resistance is less likely, as disinfectants are stronger agents than antibiotics
- Are applied in high concentrations against low populations of microorganisms, so the selective pressure for the development of resistance is less profound.



# Cleaning and Sanitization Concepts

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- **FDA Aseptic Processing 2004**
  - No reference about rotation of disinfectant
  - The suitability, efficacy, and limitations of disinfecting agents should be assessed
  - The effectiveness disinfectants should be measured by their ability to ensure that potential contaminants are adequately removed from surfaces.
  - Rotation of disinfectants are not required



# Cleaning and Sanitization Concepts

---

- **Recommend Rotation of Disinfectants**
  - A build up of residual will not occur
  - Organisms not killed by the first disinfectant may be killed by a second disinfecting agent.



# Cleaning and Sanitization Concepts

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## **TIME CONSTRAINTS**

- **Cleaning of an aseptic area room is to be completed within a defined period of time**
- **Routinely performed on the third shift**
- **Preparation date and times must be on all containers used in cleaning/sanitization**



# Cleaning and Sanitization Concepts

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## **STORAGE CONDITIONS**

- **UV sensitive**
- **Temperature sensitive**
- **Stability data required for expiration dating**



# Cleaning and Sanitization Concepts

---

## **APPLICATION METHODS**

- **Apply sanitizer to a sterile low particulate cloth and apply**
- **Spray directly on to surface and wipe with low particulate cloth**
- **Method should be based on configuration of item being sanitized**



# Cleaning and Sanitization Concepts

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## **APPLICATION METHODS**

- **Define maximum area to be sanitized prior to adding additional solution**
  - Surfaces approximately 4 ft<sup>2</sup>
  - Wet mop approximately 25 ft<sup>2</sup>
- **Spray/Constant Flow system**
- **Single, double or triple bucket method**

# Cleaning and Sanitization Concepts

## APPLICATION METHODS





# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



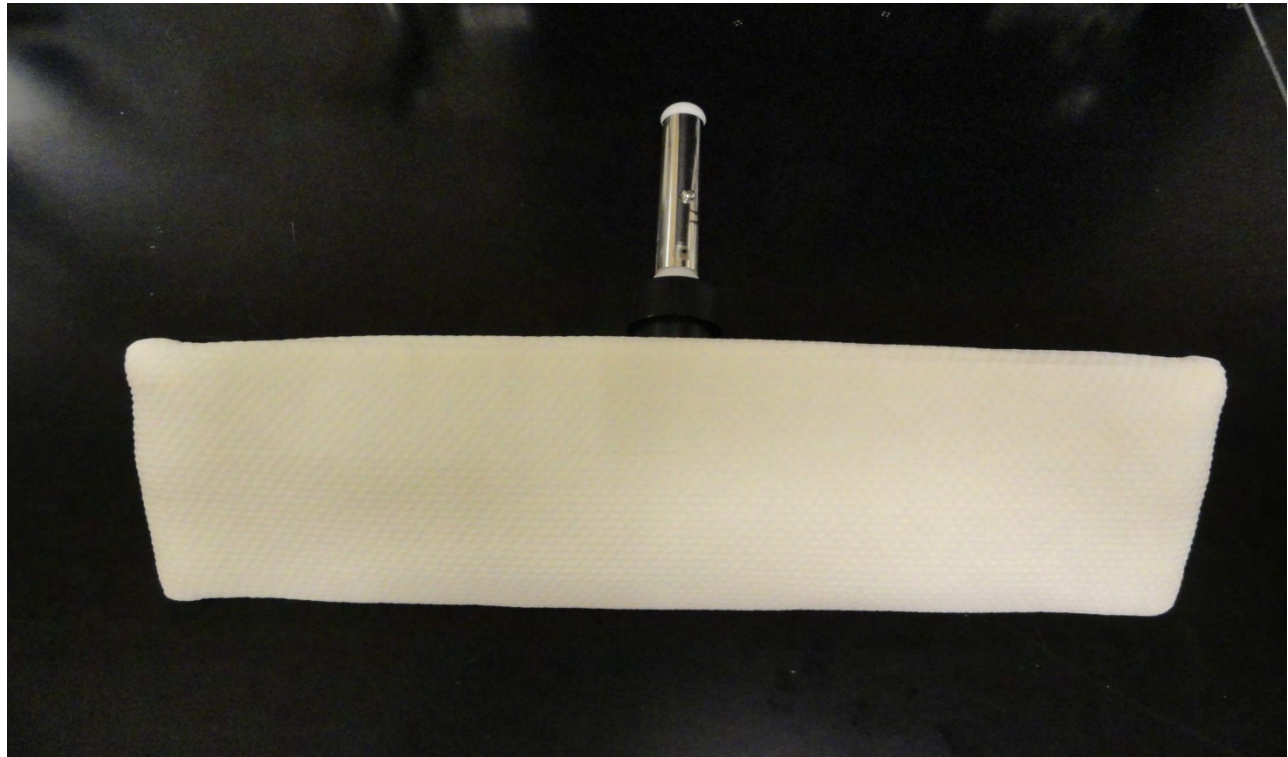
# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

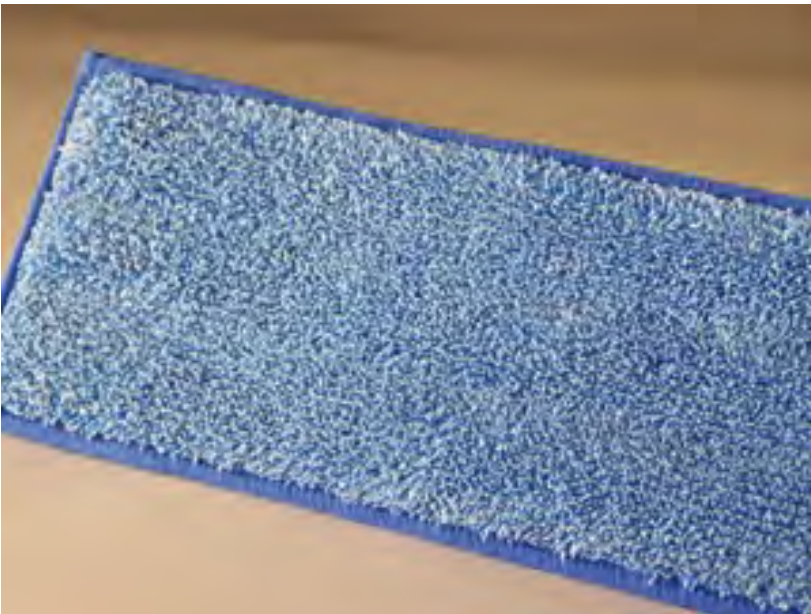
## APPLICATION METHODS





# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## APPLICATION METHODS



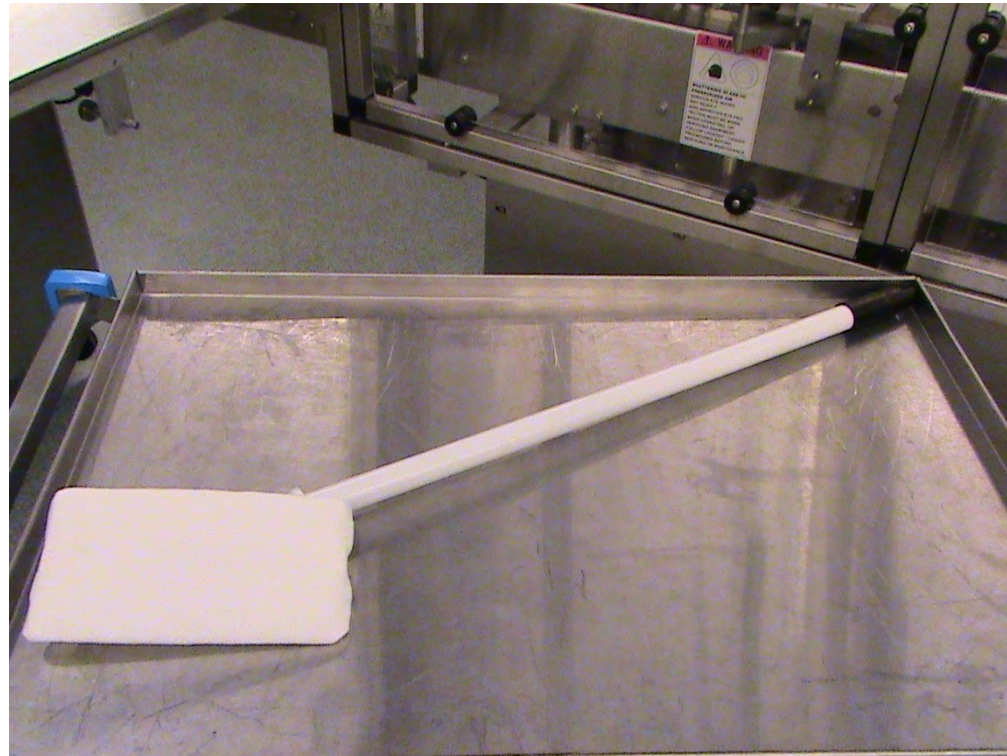
# Cleaning and Sanitization Concepts

## APPLICATION METHODS



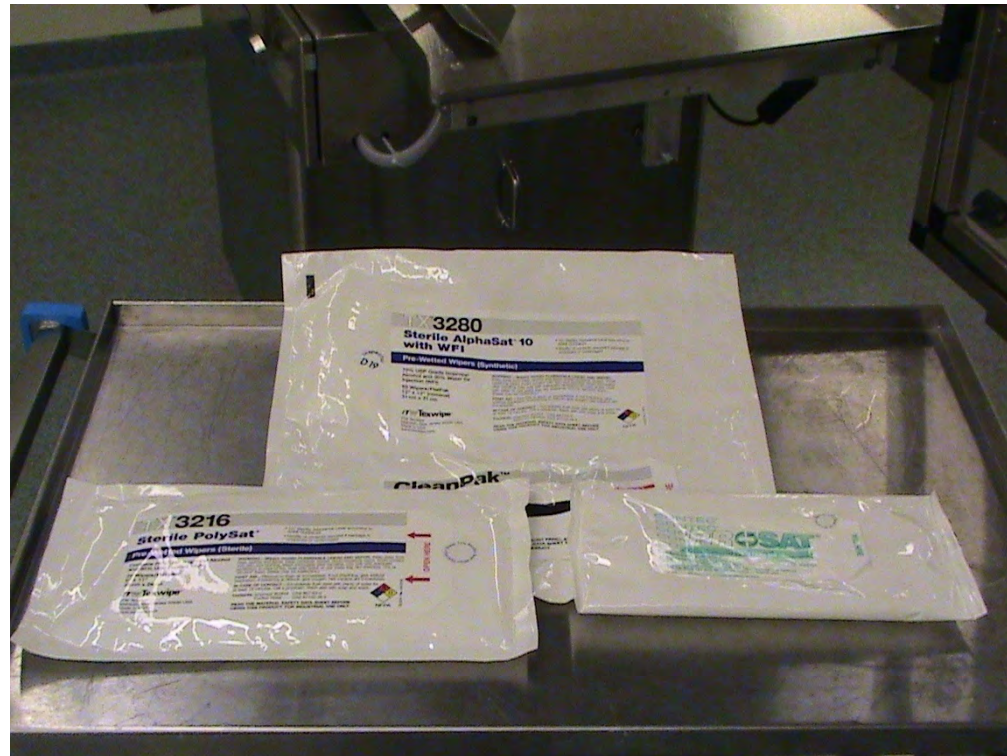
# Cleaning and Sanitization Concepts

## APPLICATION METHODS



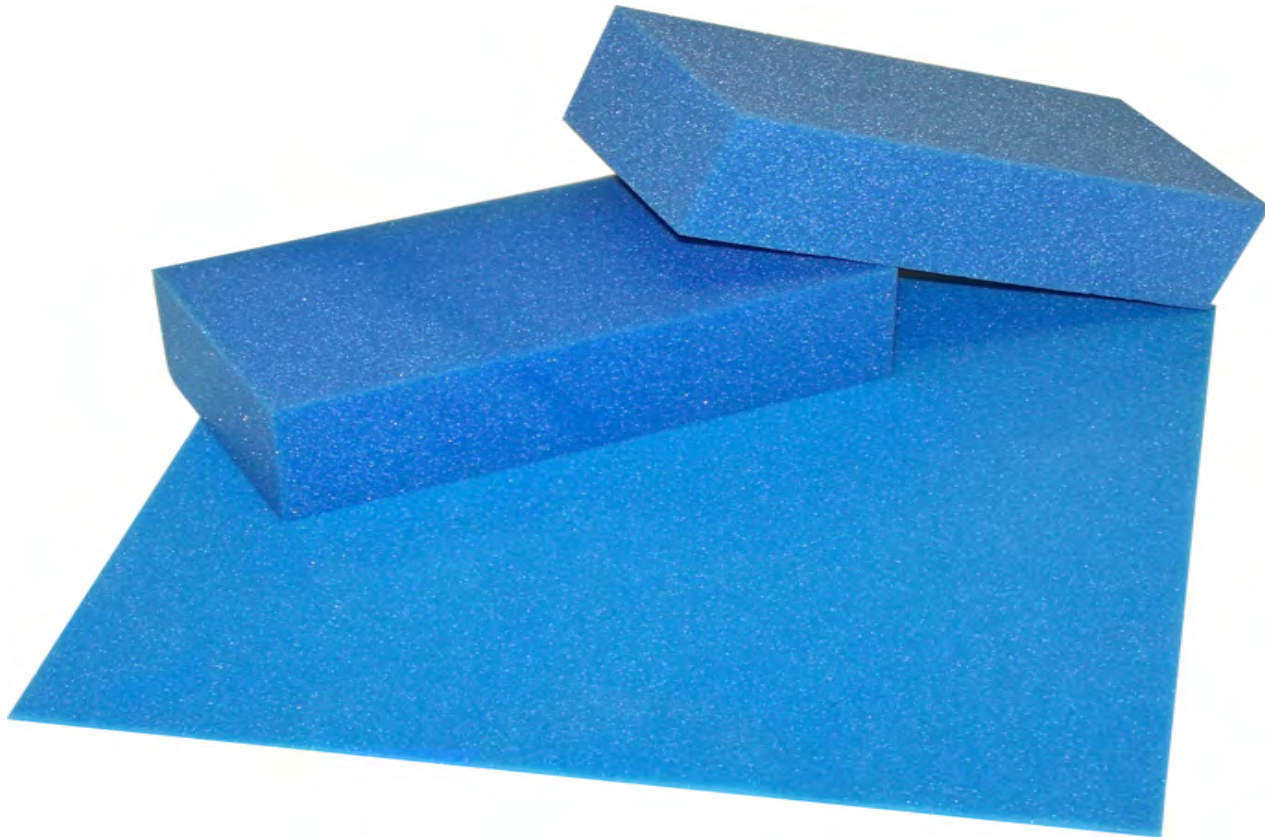
# Cleaning and Sanitization Concepts

## APPLICATION METHODS



# Cleaning and Sanitization Concepts

## **APPLICATION METHODS**



# Cleaning and Sanitization Concepts

## APPLICATION METHODS





# Cleaning and Sanitization Concepts

## APPLICATION METHODS





# Cleaning and Sanitization Concepts

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## **PASS-THROUGH APPLICATIONS**

- **May be able to remove outer packaging as apposed to sanitization**
- **Use the appropriate sanitizer based on the application**
- **For critical areas, a combination of a sporicidal and sterile alcohol should be used**



# Cleaning and Sanitization Concepts

---

## **PASS-THROUGH APPLICATIONS**

- **SOP should be flexible enough to allow wiping or spraying based on the commodity**
- **Applying sufficient disinfectant is extremely important**
- **Contact time is essential for proper kill**



# Cleaning and Sanitization Concepts

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## **FACILITY RESTART PROCEDURES**

- **Clean the facility with approved cleaner**
- **Clean/Sanitize the facility**
- **Application of a sporicidal agent**



# Cleaning and Sanitization Concepts

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## **FACILITY RESTART PROCEDURES**

### **■ Final Sanitization/Wipe down**

- Critical surfaces: Wipe with 70% sterile alcohol
- Ceiling, Walls and Floors: Broad spectrum sanitizer



# Cleaning and Sanitization Concepts

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## **Residual Disinfectant**

- **After sanitization, there is residual solution remaining on surfaces**
  - Ceilings
  - Wall
  - Floors
  - Equipment



# Cleaning and Sanitization Concepts

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## **Residual Disinfectant**

- **For ceilings, walls and floors, this is typically not an issue**
  - Personnel should not be touching these surfaces with their gloved hands
  - These are non product contacting surfaces
  - Airflow from these areas must not enter the critical processing areas



# Cleaning and Sanitization Concepts

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## Residual Disinfectant

- HEPA filter grates are usually not sanitized on a routine basis with anything other than alcohol or hydrogen peroxide
- In most cases, the residual will not interfere with particulate testing
  - ❖ If a particle probe is placed on the wall, this can effect results





# Cleaning and Sanitization Concepts

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## Residual Disinfectant

- **Some companies use WFI as a wipe down of the ceiling walls and floors**
  - This removes the majority of residual on these surfaces
  - Not required by any regulatory agency
  - No significant value added



# Cleaning and Sanitization Concepts

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## **Residual Disinfectant**

- Requires a significant amount of time to the process
- Requires sterilization of additional buckets, mops and handles
- WFI must be sterile filtered or autoclaved
- Containers must be surface sanitized upon entry into the room



# Cleaning and Sanitization Concepts

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## **Residual Disinfectant**

- Critical areas and product contacting surfaces
- Must be wiped with sterile WFI or better yet sterile alcohol or hydrogen peroxide
- This will remove any residual residue from the surface
- Must be considered a wipe down unless the required contact time is met

# Cleaning and Sanitization Concepts

## Residual Decon-Clean



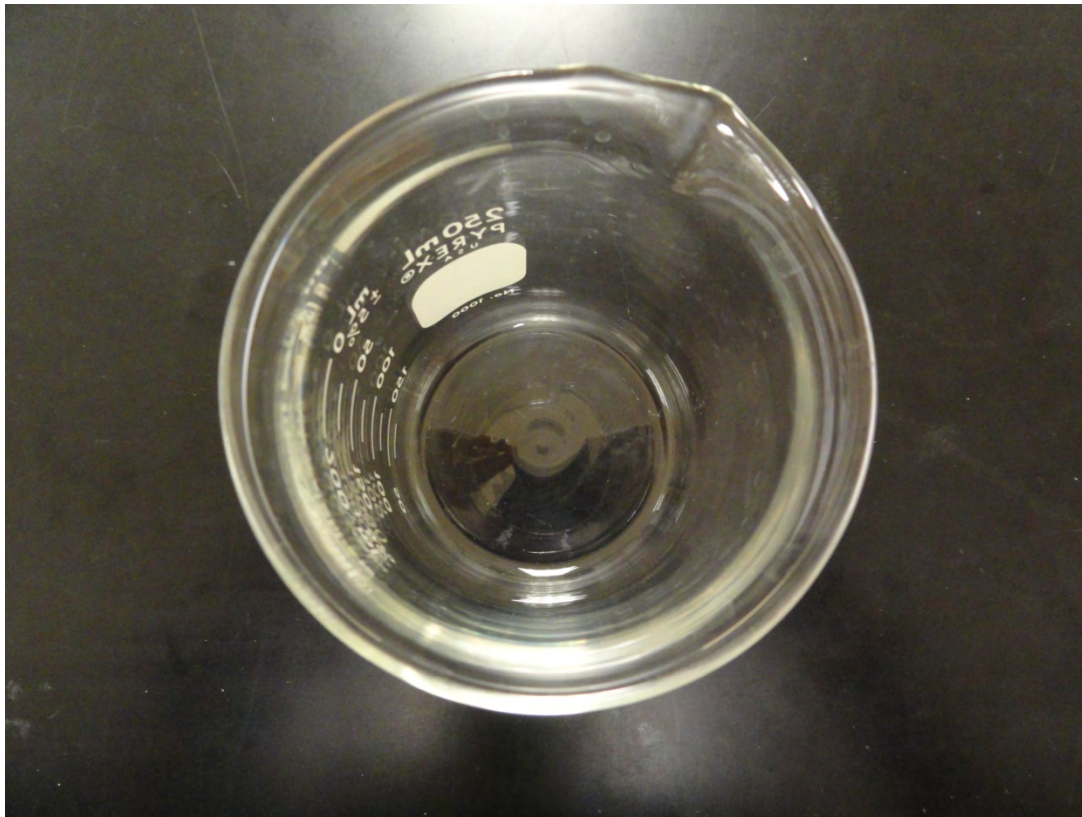
# Cleaning and Sanitization Concepts

## Residual Decon-Clean



# Cleaning and Sanitization Concepts

## Residual Disinfectant Alcohol



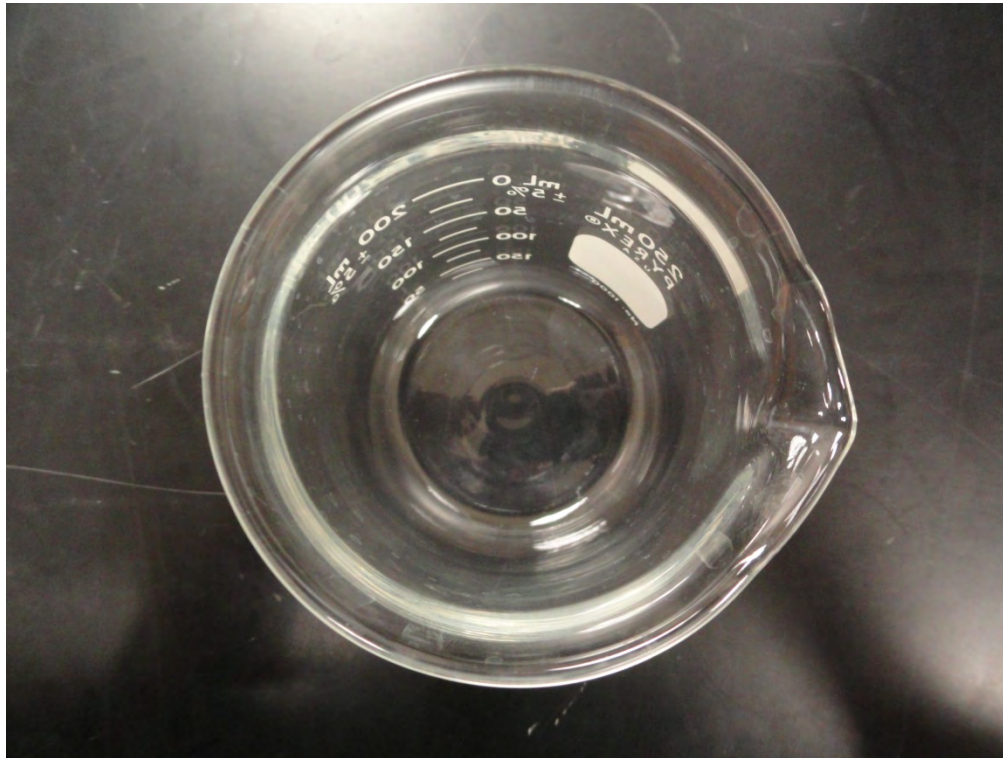
# Cleaning and Sanitization Concepts

## Residual Disinfectant Alcohol



# Cleaning and Sanitization Concepts

## Residual Hydrogen Peroxide





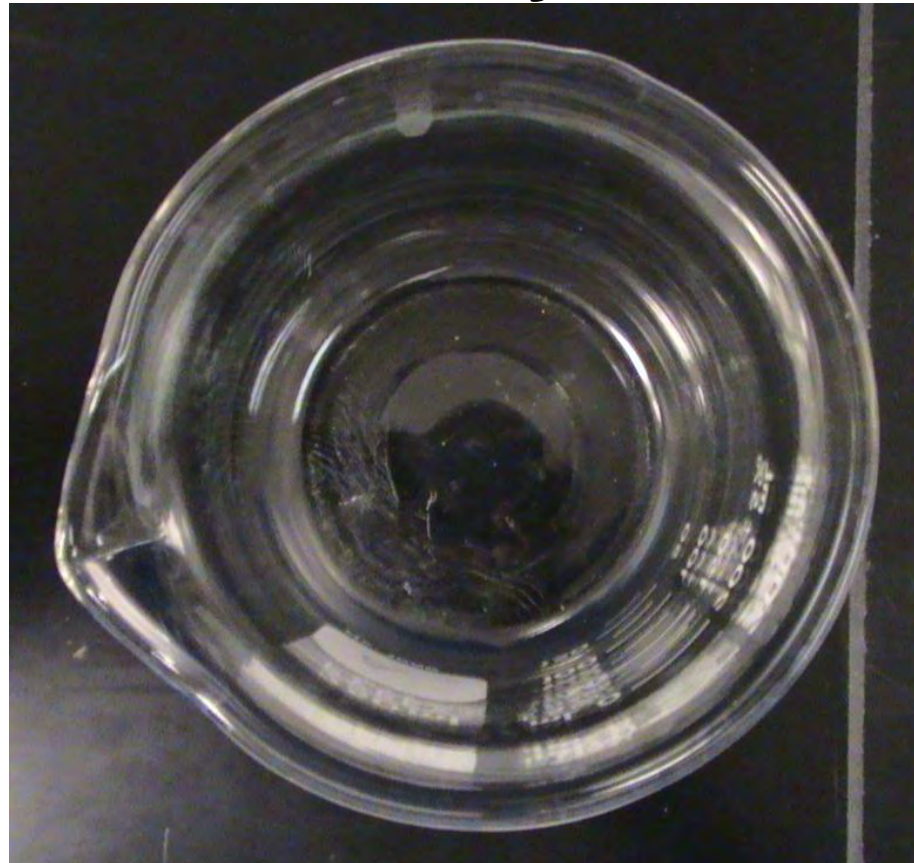
# Cleaning and Sanitization Concepts

## Residual Hydrogen Peroxide



# Cleaning and Sanitization Concepts

## Residual Quaternary Ammonium



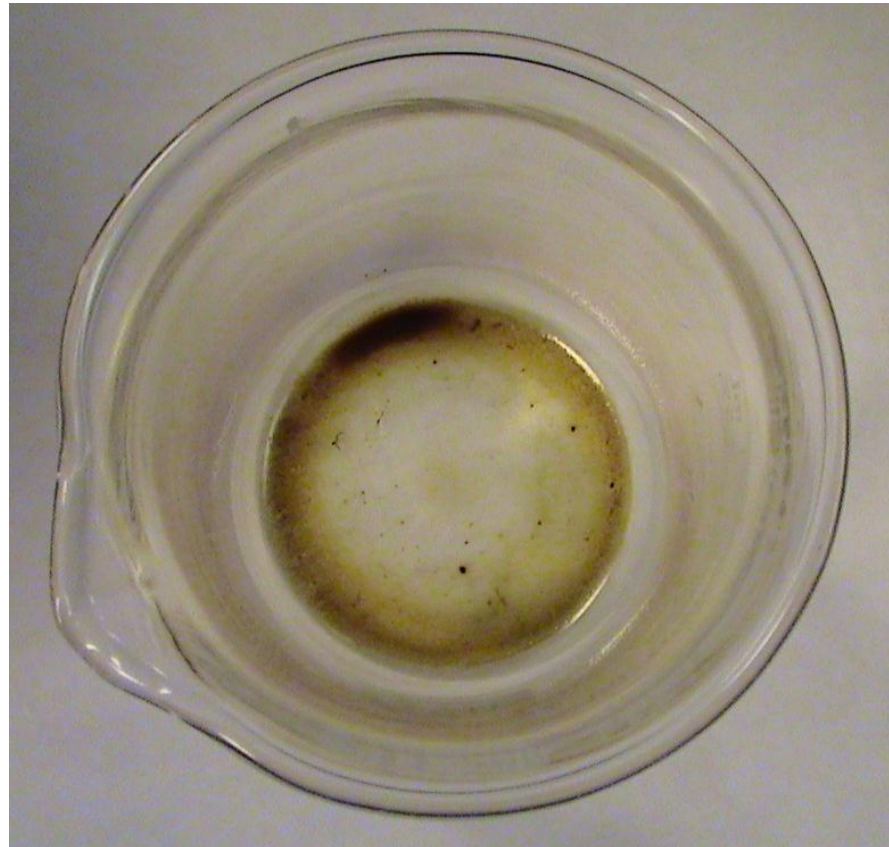
# Cleaning and Sanitization Concepts

## Residual Quaternary Ammonium



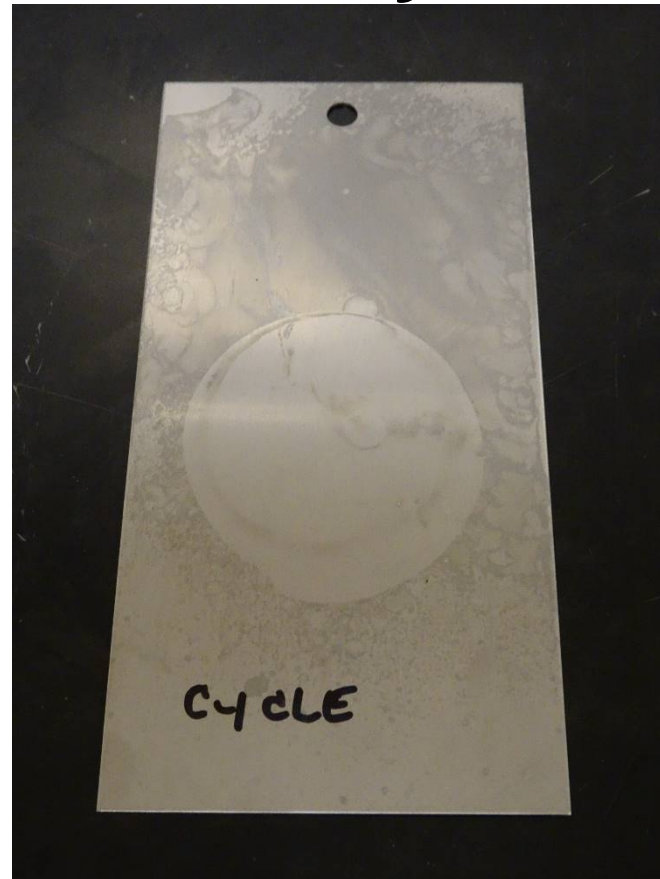
# Cleaning and Sanitization Concepts

## Residual Decon-Cycle



# Cleaning and Sanitization Concepts

## Residual Decon-Cycle



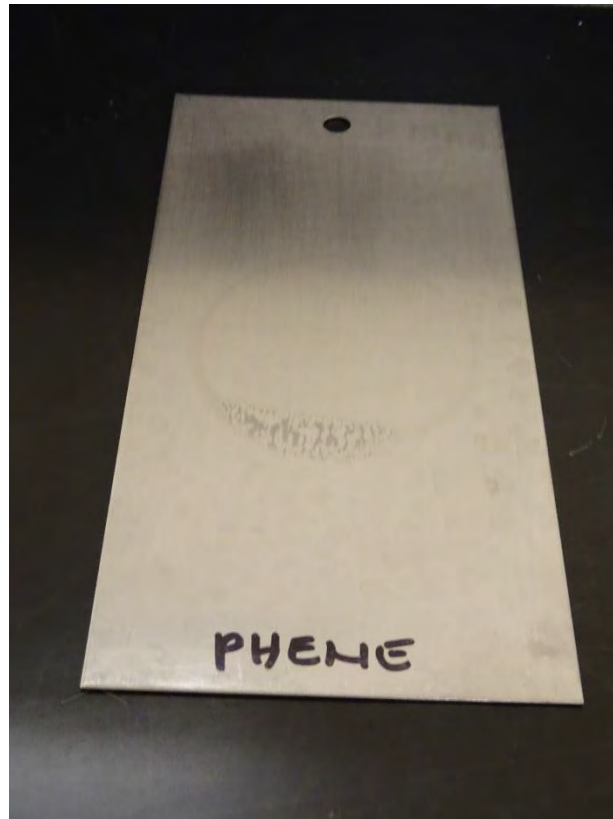
# Cleaning and Sanitization Concepts

## Residual Decon-Phene



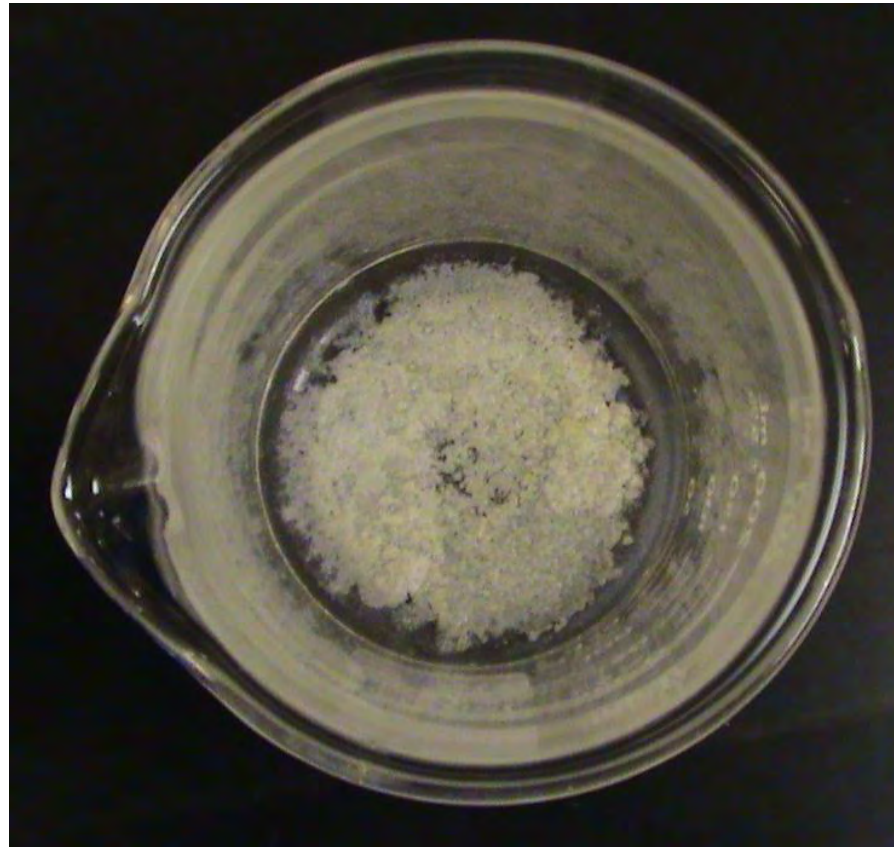
# Cleaning and Sanitization Concepts

## Residual Decon-Phene



# Cleaning and Sanitization Concepts

## Residual Conflict





# Cleaning and Sanitization Concepts

## Residual Conflict



# Cleaning and Sanitization Concepts

## Residual Decon-Spore



# Cleaning and Sanitization Concepts

## Residual Decon-Spore



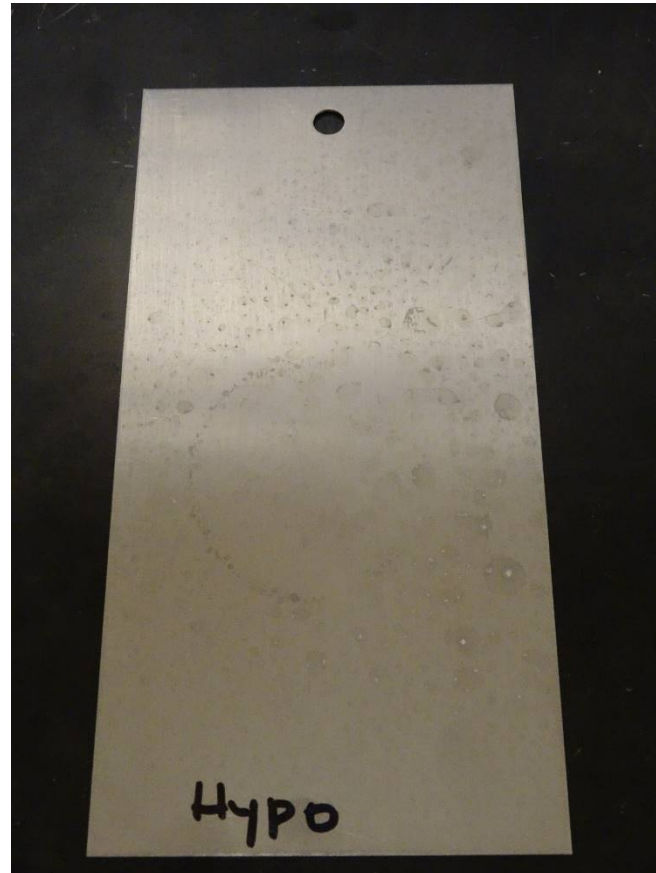
# Cleaning and Sanitization Concepts

## Residual Hypo-Chloride



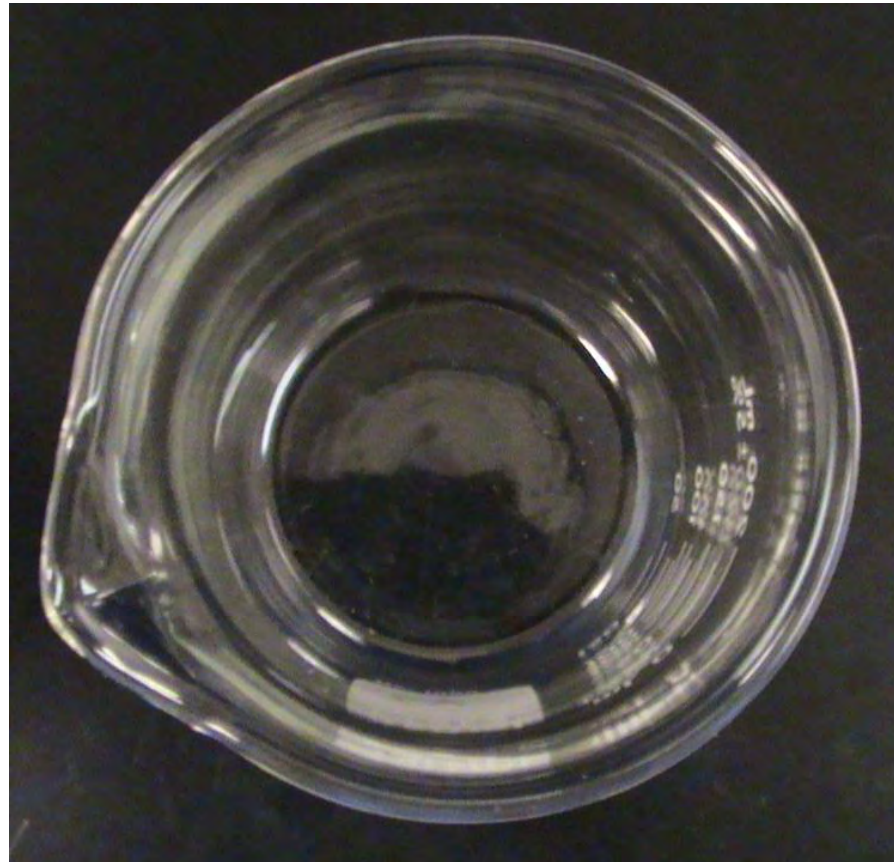
# Cleaning and Sanitization Concepts

## Residual Hypo-Chloride



# Cleaning and Sanitization Concepts

## Residual Lysol

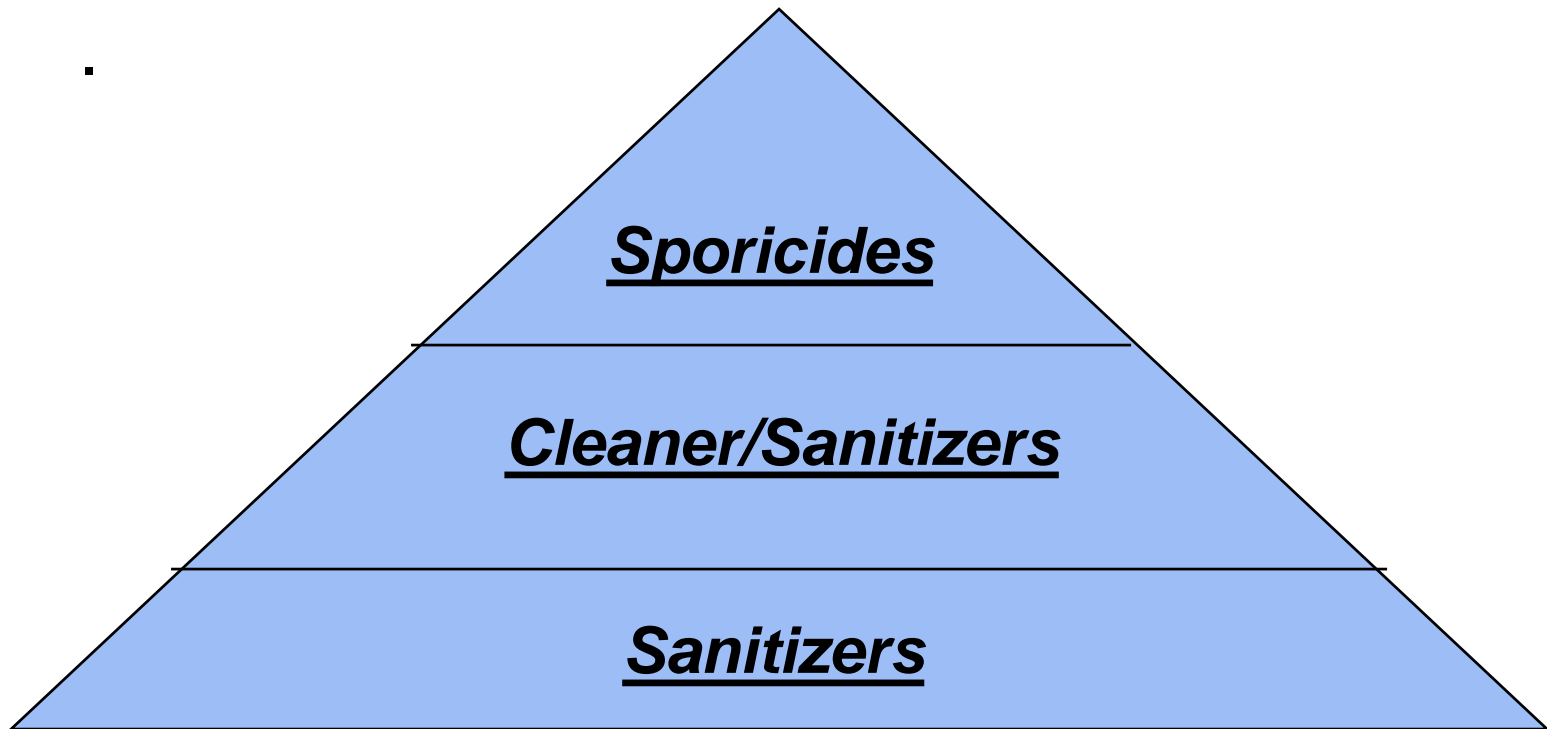


# Cleaning and Sanitization Concepts

## Residual Lysol



# Cleaning and Sanitization Concepts







# Cleaning and Sanitization Concepts

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## **ALTERNATIVE METHODS**

- **Chlorine Dioxide Gas (Isolators)**
- **Fumigation/Fogging**
- **Full immersion**



# Cleaning and Sanitization Concepts

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## ■ Takeaway Message

- Define cleaning and sanitizing solution as follows and used properly
  - ❖ Cleaner
  - ❖ Cleaner/Sanitizer
  - ❖ Sanitizer
  - ❖ Sporicide



# Cleaning and Sanitization Concepts

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## ■ Takeaway Message

- Evaluate preparation method of solutions
- Ensure proper application method and techniques are used
- Confirm wet contact time
- Assess disinfectant efficacy testing protocol