Setting up a Program for Microbial Monitoring in the Pharmacy

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USP <797> APPLICABLE TO ALL PRACTICE SETTINGS WHERE STERILE PREPARATIONS ARE COMPOUNDED

- Hospitals
- Community pharmacies
- Home infusion services
- Ambulatory care services
- Physician offices
- Nursing homes

3 RISK LEVELS

- Low
- Medium
- High

  plus

- Immediate use exemption

Three Crucial Microbial Program Components

- Competency of personnel to compound aseptically
- Acceptability of environment and engineering controls
  - (hood[s], cleanroom/buffer zone, and anteroom)
- Acceptability of final product (high risk only)
  - sterility testing
  - endotoxin testing

HOSPITAL STAFF WHO COMPOUND

- Pharmacists
- Pharmacy Technicians
- Nurses
- Physicians

USP <797> IMMEDIATE USE EXEMPTION

- Emergency settings (e.g., ambulance, labor and delivery, emergency room)
- Operating Room
- Nursing units
- Satellite pharmacies

IF administration is begun within one hour and completed within 12 hours of preparation

ASEPTIC TECHNIQUE PROCESS VALIDATION

- On employment before compounding
- Annually (low or medium risk)
- Semi-annually (high risk)

HardyVAL™ CSP

low-risk level

Kit Contents Cat. no. HVL1

- 1 x 100ml Sterile Tryptic Soy Broth Vial
- 3 x 20ml Empty Sterile Vials
- 1 x Write-on Whirl-Pak® Bag
- 1 x Results Log Sheet

Procedure Summary (from USP <797>)

1. Aseptically transfer Tryptic Soy Broth to empty sterile vials using a sterile 10ml syringe.
2. Attach sterile adhesive seals.
3. Incubate at 25°C to 35°C.
4. Examine for turbidity at end of 14 days.

*Syringe(s), needle(s), and adhesive seals not included.

Whirl-Pak is a registered trademark of Nasco Industries, Inc.

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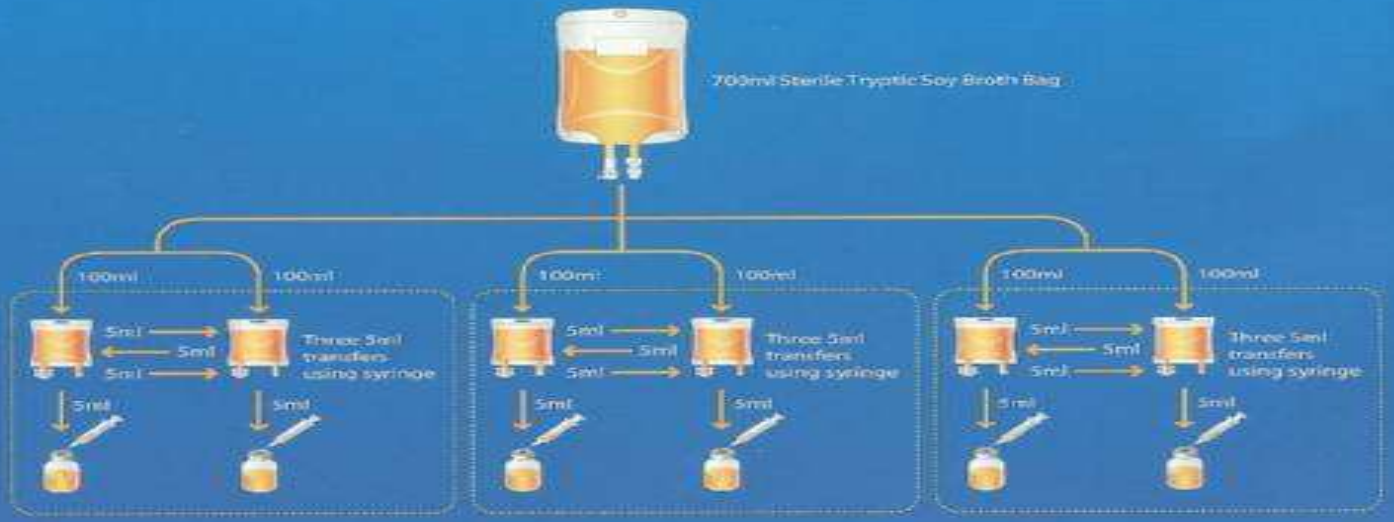
HardyVAL™ CSP
medium-risk level

Kit Contents Cat. no. HVM1

- 1 x 700ml Sterile Tryptic Soy Broth Bag
- 6 x 125ml Empty Sterile Bags
- 6 x 20ml Empty Sterile Vials
- 1 x Write-on Whirl-Pak® Bag
- 1 x Results Log Sheet

Procedure Summary (from USP <797>)

1. Aseptically transfer 100ml Sterile Tryptic Soy Broth to empty sterile bags using gravity tubing.
2. Transfer Tryptic Soy Broth between bags, using a sterile 10ml syringe.
3. Aseptically transfer 5ml Tryptic Soy Broth to small empty sterile vials.
4. Attach sterile adhesive seals.
5. Incubate at 25ºC to 35ºC.
6. Examine for turbidity at end of 14 days.



*Syringe(s), needle(s), and adhesive seals not included.

Whirl-Pak is a registered trademark of Nasco Industries, Inc.

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HardyVAL™ CSP

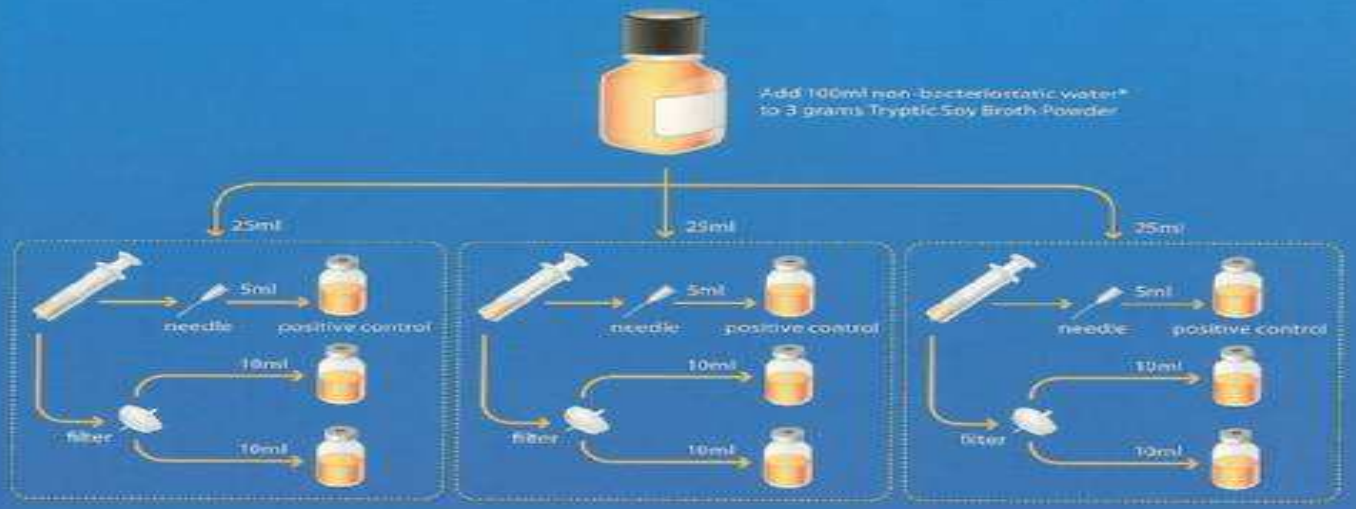
high-risk level

Kit Contents Cat. no. HVH1

1 x 3gm Tryptic Soy Broth Powder (non-sterile)
9 x 20ml Empty Sterile Vials
1 x Write-on Whirl-Pak® Bag
1 x Results Log Sheet

Procedure Summary (from USP <797>)

- Unscrew cap and add 100ml of water (non-bacteriostatic) to Tryptic Soy Broth powder.
- Screw on cap and mix.
- Transfer the appropriate amounts of Tryptic Soy Broth to empty sterile vials using a sterile 30ml syringe with and without a 0.2 micron filter.
- Attach sterile adhesive seals.
- Incubate at 25°C to 35°C.
- Examine for turbidity at end of 14 days.



*Syringe(s), needle(s), adhesive seals, non-bacteriostatic water, and filters not included.

Whirl-Pak is a registered trademark of Nasco Industries, Inc.

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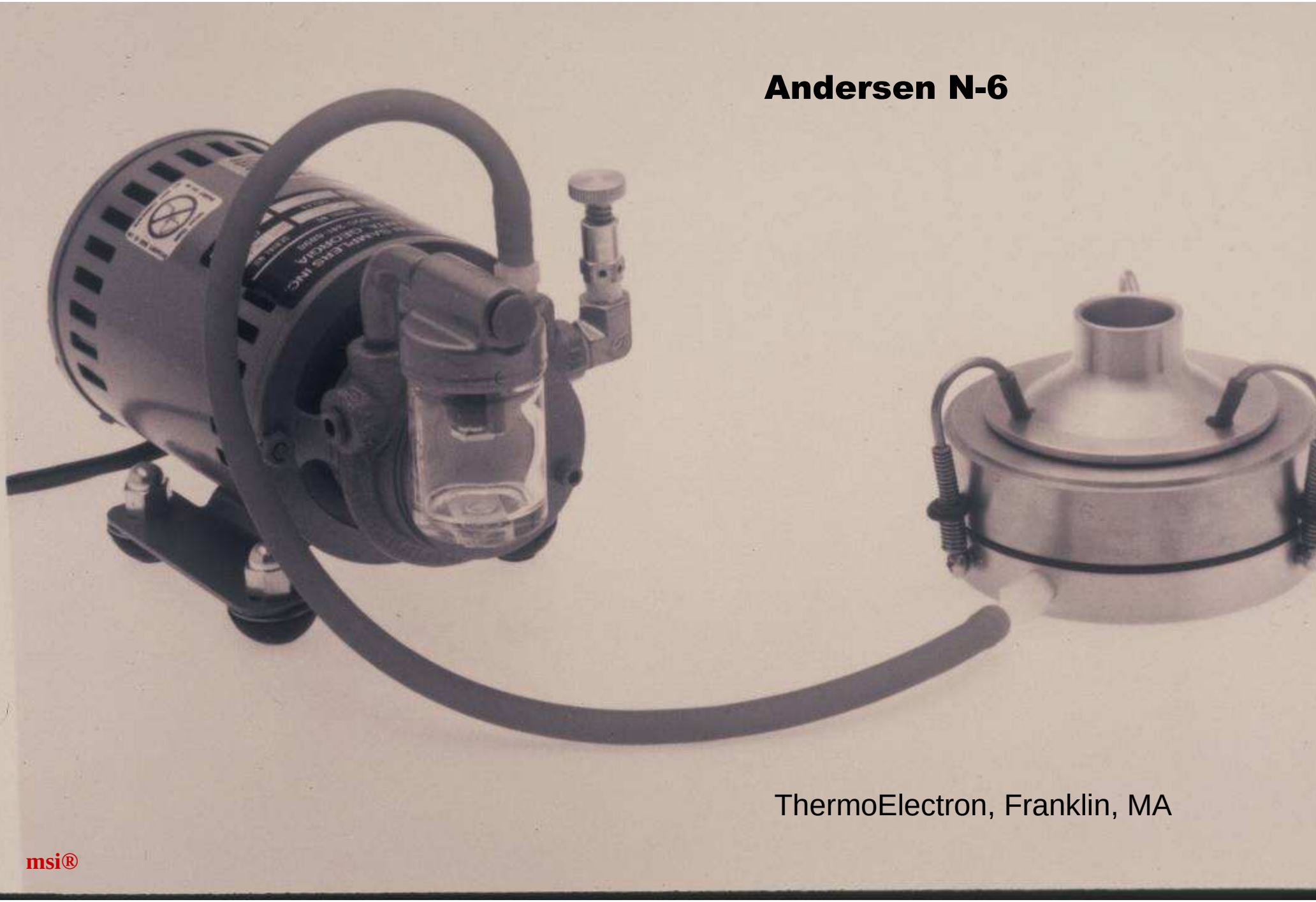
PURPOSE OF AN ENVIRONMENTAL MONITORING PROGRAM

- Should be able to detect adverse trends in microbial populations
- Should be able to use “forensic microbiology” to track problems in pharmacy

Baseline Surveillance

- How and What to Sample
  - Gravimetric (settling plates) vs electronic (volumetric) air sampling
- How and What to Sample
  - Active (occupied) vs passive (unoccupied) sampling
- How and What to Sample
  - How to choose an air sampler
    - Field calibration

Andersen N-6



ThermoElectron, Franklin, MA

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SKC Quick 30

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SKC, Inc., Eighty Four, PA

SAS Super 180

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SAS Bioscience International,
Rockville, MD

Dual Head Sampler

SAS Bioscience International, Rockville, MD

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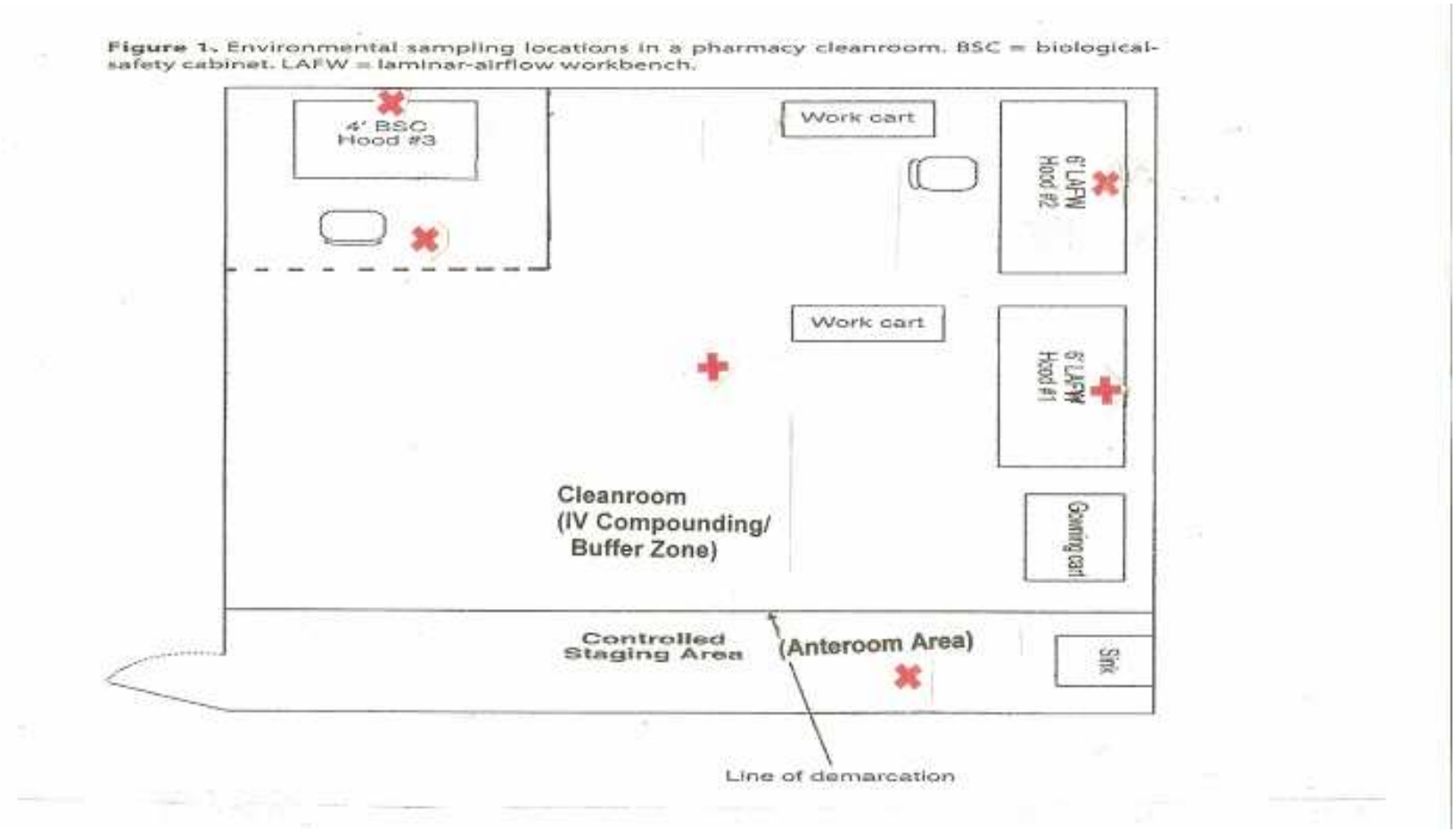
Baseline Surveillance, continued

- Where and When to Sample
  - Frequency and number of required air samples



Adapted from USP Chapter <797>

BASELINE SURVEILLANCE

- How to sample
  - Media and incubation temperatures to use
    - Bacteria:
      - TSA (tryptic soy agar) with polysorbate 80 and lecithin
        - ✓ Incubate at 35℃
    - Fungi:
      - MEA (malt extract agar)
        - ✓ Incubate at 28℃

MSI QUALITY CONTROL RECORD FOR COMMERCIAL MEDIA, REAGENTS AND STAINS

REVISION:

IDENTIFICATION

NAME	MALT EXTRACT AGAR PLATES			NUMBER
Lot number	**Source (circle one)**	**Date Received**	**Expiration Date**	**Storage Conditions**
	REMEL			2 - 8°C
	BBL			
	HARDY			

APPEARANCE (circle one in each category)

Package Damage	Medium color STRAW	Clarity CLEAR	Excess Moisture or drying	Visible Contamination	Checked Date BY
NO	YES	YES	NO	NO	
YES	NO	NO	YES	YES	

STERILITY TEST

Number of Units Tested	Temperature and Time of Incubation	Results (circle one)	Set Up Date BY
	28°C / 5 DAYS	Growth	
		No Growth	Checked Date BY

PERFORMANCE TEST

Test Organism	Stock Number	Expected Result	Observed Result	Set Up Date BY
Curvularia spp.		Good growth w/sporulation		
				Check Date BY

CORRECTIVE ACTION

Circle problems in red. Assign each a number and describe below.

FINAL ACTION

Release for Use	*REVIEWED* By	*COMMENTS*
Discard	Date	

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MSI QUALITY CONTROL RECORD FOR COMMERCIAL MEDIA, REAGENTS AND STAINS

Revised: 08/22/06

IDENTIFICATION

NAME	TSA W/POLY 80 & LECITHIN CONTACT PLATES				NUMBER
Lot number	Source (circle one)	Date Received	Expiration Date	Storage Conditions	952
	REMEL			2-8°C	
	BBL				
	HARDY				

APPEARANCE (circle one in each category)

Package Damage	Medium color STRAW	Clarity CLEAR	Excess Moisture or drying	Visible Contamination	Checked Date BY
NO	YES	YES	NO	NO	
YES	NO	NO	YES	YES	

STERILITY TEST

Number of Units Tested	Temperature and Time of Incubation	Results (circle one)	Set Up Date BY
	35°C + or -2°C/ 5 Days	Growth	
		No Growth	Checked Date BY

PERFORMANCE TEST

Test Organism	Stock Number	Expected Result	Observed Result	Set Up Date BY
Aspergillus niger	ATCC 1004	GG w/sporulation		
Staph. aureus	45	GG		Check Date BY
E. coli	17	GG		
C. albicans	6	GG		

CORRECTIVE ACTION

Circle problems in red. Assign each a number and describe below.

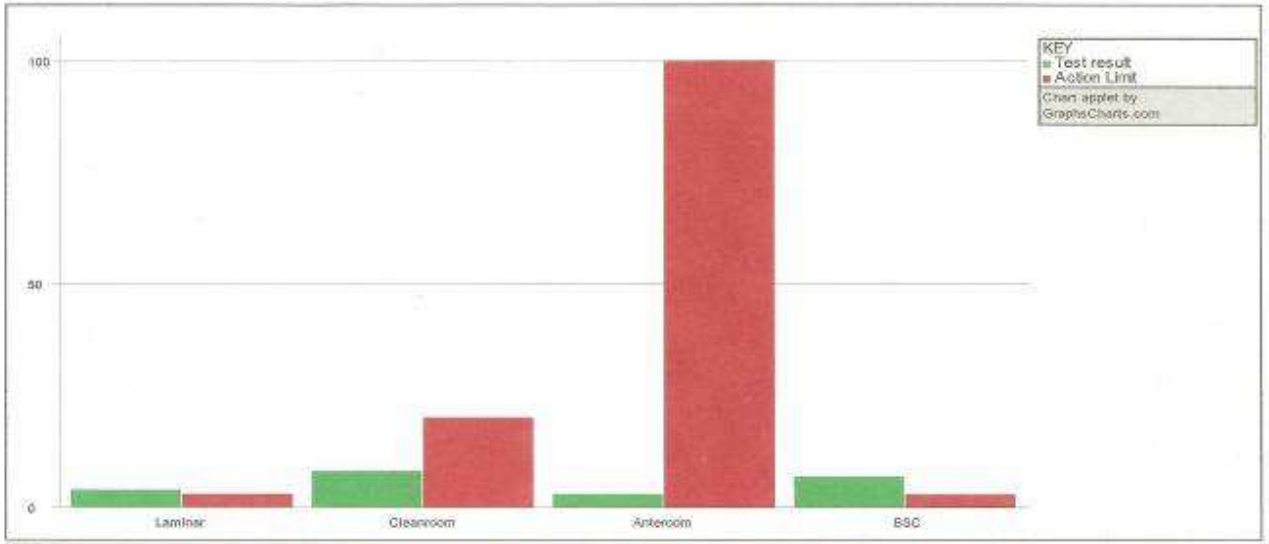
FINAL ACTION *REVIEWED* *COMMENTS*

Release for Use	By	
Discard	Date	

Baseline Surveillance

- Interpretation of data
  - Steps to take to develop a baseline

MSI Samples - Surveillance/Baseline *



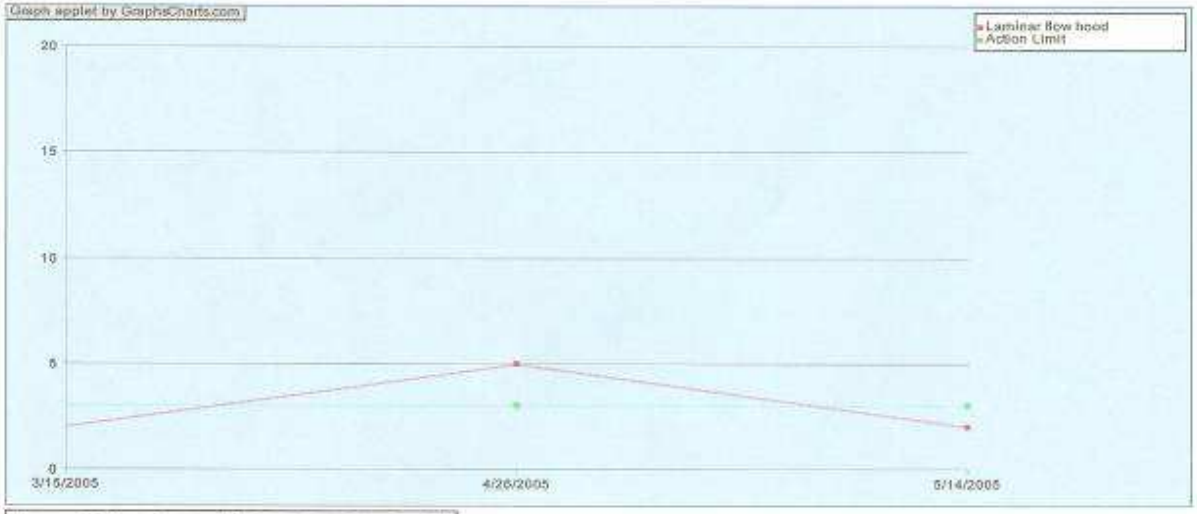
Collected	Laminar flow hood	Cleanroom	Anteroom	BSC
3/3/2005	4 cfu/m³	8 cfu/m³	3 cfu/m³	7 cfu/m³
	action limit >3	action limit >20	action limit >100	action limit >3

* Action Limits adapted from: USP <797> proposed revision, May, 2006.

Trending Data

- What should be trended?
  - Total counts (cfu/m^3)
  - Separate counts and specific types of microorganisms

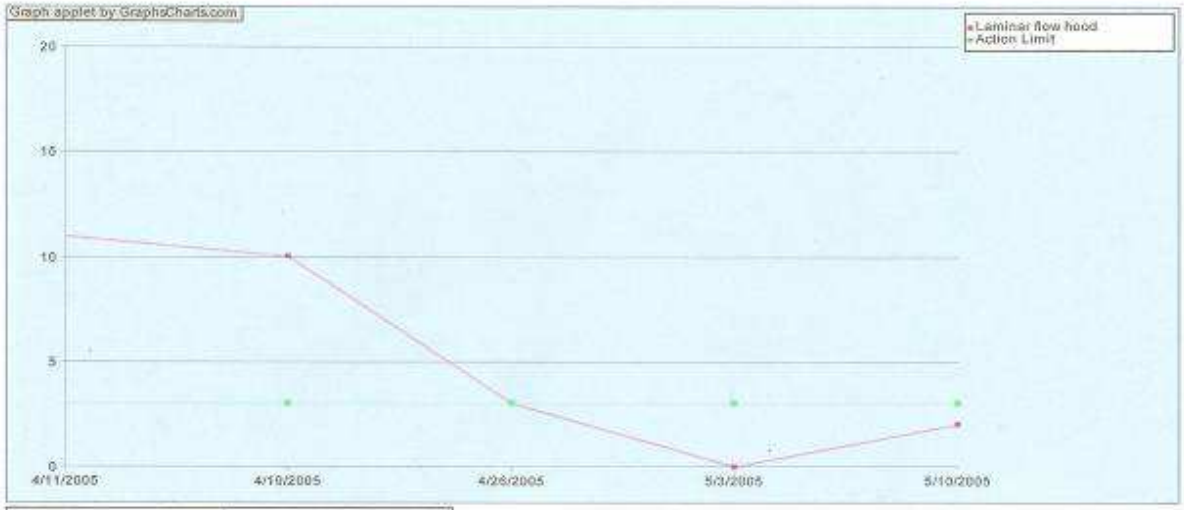
MSI Samples - Monthly Monitoring *



Collected	Laminar flow hood
3/15/2005	2 cfu/m³
4/26/2005	5 cfu/m³
5/14/2005	2 cfu/m³
	action limit >3

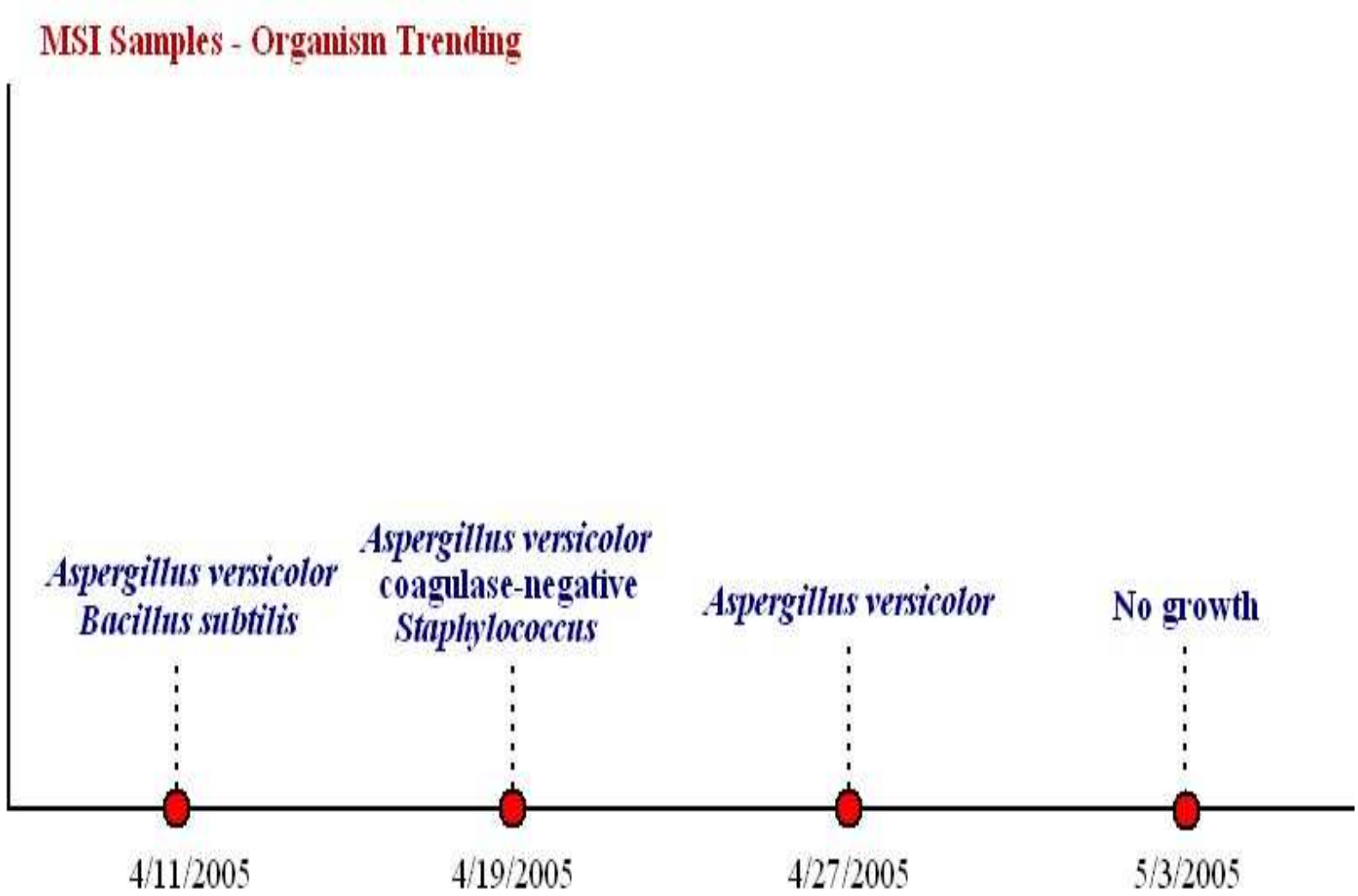
* Action Limit adapted from: USP <797> proposed revision, May, 2006.

MSI Samples - Weekly Monitoring *



Collected	Laminar flow hood
4/11/2005	11 cfu/m³
4/19/2005	10 cfu/m³
4/26/2005	3 cfu/m³
5/3/2005	0 cfu/m³
5/10/2005	2 cfu/m³
	action limit >3

* Action Limit adapted from: USP <797> proposed revision, May, 2006.


MSI Samples - Organism Trending
Aspergillus versicolor
Bacillus subtilis
Aspergillus versicolor
coagulase-negative
Staphylococcus
Aspergillus versicolor
No growth
4/11/2005
4/19/2005
4/27/2005
5/3/2005

POTENTIAL INTERVENTIONS: If Trending Increases in Bioburden are Seen or Environmental Monitoring is Unacceptable

- Retest areas exceeding alert limits
- Reassess cleaning procedures (Check records)
- Examine recent production activities for change or irregularities
- Reclean work area (3 cycles) using different cleaning agent
- Review other validation outcomes (end-product testing) for parallel increases in bioburden
- Retrain cleaning and compounding staff

STERILITY TESTING OF STERILE END-PRODUCTS (USP <71>)

- Direct inoculation (small volume)
- Membrane filtration (large volume)
- Special testing for beta-lactam antibiotics using beta-lactamases or cephalosporinases as appropriate

ENDOTOXIN TESTING OF STERILE END-PRODUCTS (USE <85>)

- For high risk only
- Allowable endotoxin limit (listed in separate USP monograph for each drug)

Morphine Official Monograph

- Contains not more than 17.0 USP Endotoxin Units per mg of morphine sulfate if labeled for intrathecal use
- Contains not more than 14.29 USP Endotoxin Units per mg of morphine sulfate if labeled for intravenous use

From: USP <797>, 2005; pp1315, 1316.

ENDOTOXIN TESTING OF STERILE END-PRODUCTS (USP <85>)

- Choosing a test method
  - Gel clot
  - Chromogenic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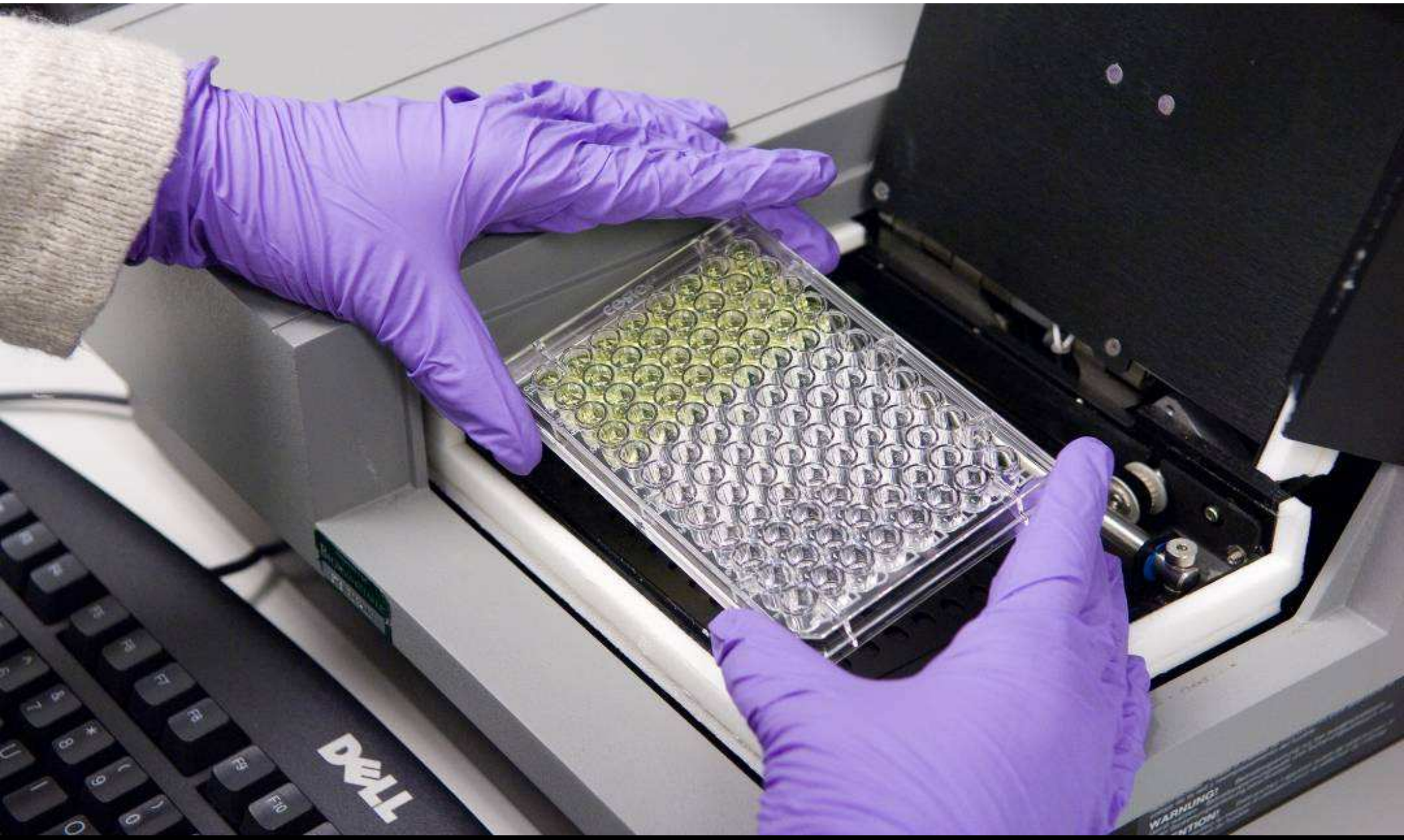
DELL
WARNING!

GOOD DOCUMENTATION IS KEY TO COMPLIANCE

- Refrigeration and freezer temperature logs
- Compounding room and storage room relative humidity and temperature logs
- Cleaning logs for LFHs, BSCs, CAIs
  - Cleanroom, anteroom and compounding equipment
- Equipment calibration logs

GOOD DOCUMENTATION IS KEY TO COMPLIANCE

- Filter change logs
  - Hoods
  - HVAC system for pharmacy
  - HVAC system for compounding area
- Employee written test re: aseptic technique
- Media-fill competency records

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