Infection Prevention for Pharmacy Compounding

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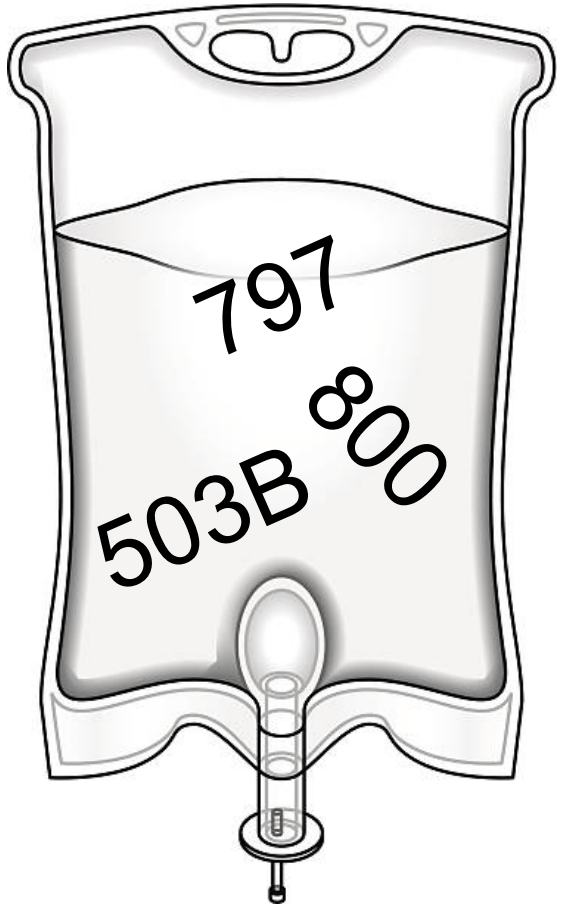
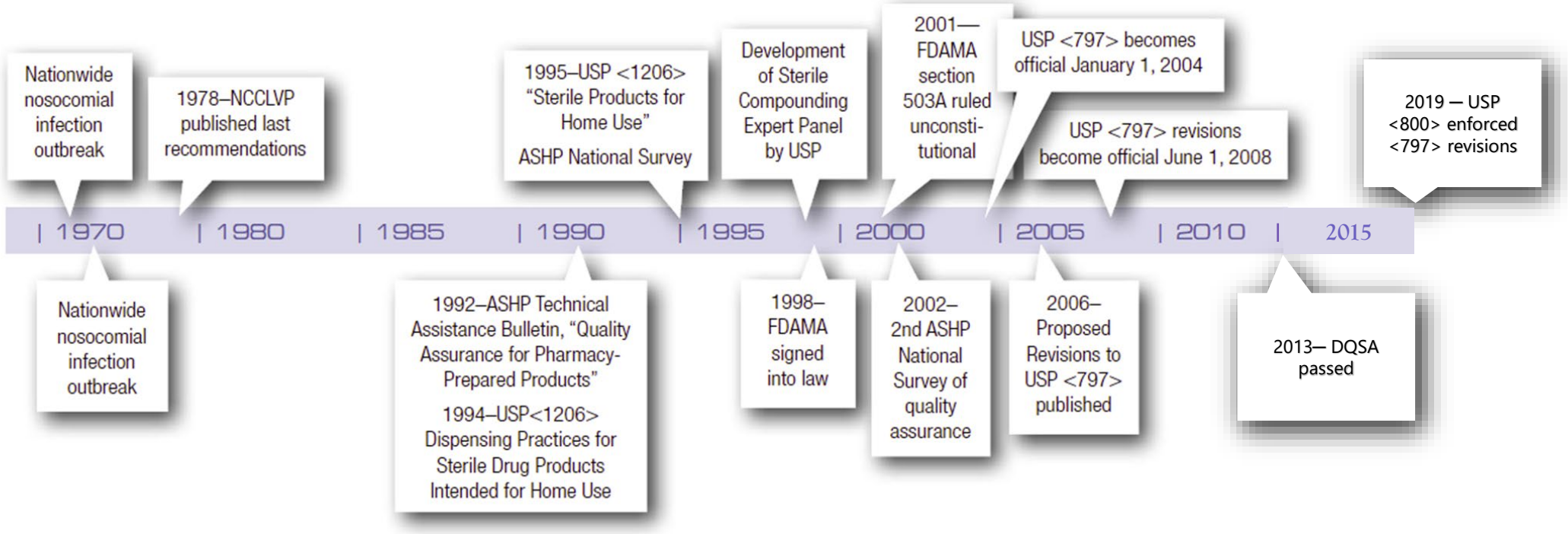
Infection Prevention Starts with Regulation



Compounding Regulation has a Rich History

FIGURE 1

Evolution of Sterile Compounding Standards



http://www.ashp.org/DocLibrary/BestPractices/PrepGdlCSP.aspx

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Regulation Informed by Compounding Misadventures

Year	State	Description
2002	Michigan	Pharmacy preparing injectable methylPREDNISolone and baclofen recalled the products because of contamination with Penicillium mold, Methylobacterium, and/or Mycobacterium chelonae
2003	Missouri	Ba… ba… wi…
2004	Texas, New York, Michigan, Missouri	36… re… sy…
2005	New Jersey, California	Up… co… co…
2005	Minnesota	2 … op… an…
2005	California	St… be…
2005	Maryland	10… co…
2006	Nevada	1 … su…
2006	Ohio	1 … ch… so…
2007	Washington, Oregon	2, … co… 0.…
2009	Florida	21 horses died after receiving a compounded vitamin supplement containing vitamin B, potassium, magnesium, and selenium (product not approved in the US).
2010	Illinois	1 child died after receiving more than 60 times the amount of sodium chloride prescribed due to a compounding error in a hospital pharmacy
…	…	…neration developed …AVASTIN …nt lost vision, another
…	…	…ition solutions were …compounding using … in a compounding
…	…	…fter use of the …receiving injections of …rom the same
…	…	…ingitis after receiving …d by a compounding …ilum (a brown-black
…	…	…ntain mold by a …nding pharmacy was
…	…	…n were recalled after …tions.
…	…	…ving a contaminated
…	…	…ad of fosphenytoin
…	…	…Hospira all issues …on in compounded
2015	Nationwide	The NIH suspends 46 clinical trials after discovering defects in the drug manufacturing process

Federal and State Regulators Guide Practice

FDA

USP

BOP

TJC

Law or Opinion? Differences are Present in Definitions

BOP

- Taking two or more ingredients and combining them into a dosage form of a drug, exclusive of compounding by a drug manufacturer, distributor, or packer

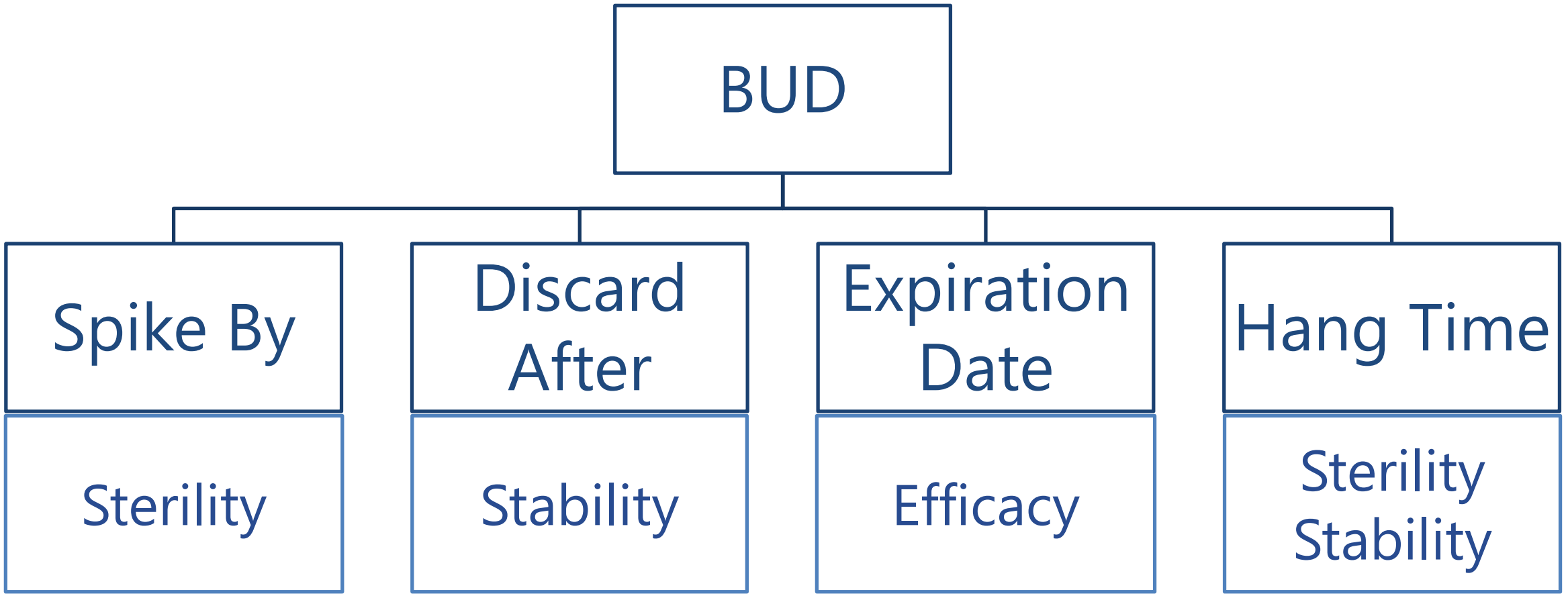
FDA

- Combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient
- Compounding does not include mixing, reconstituting, or similar performed in accordance with approved labeling

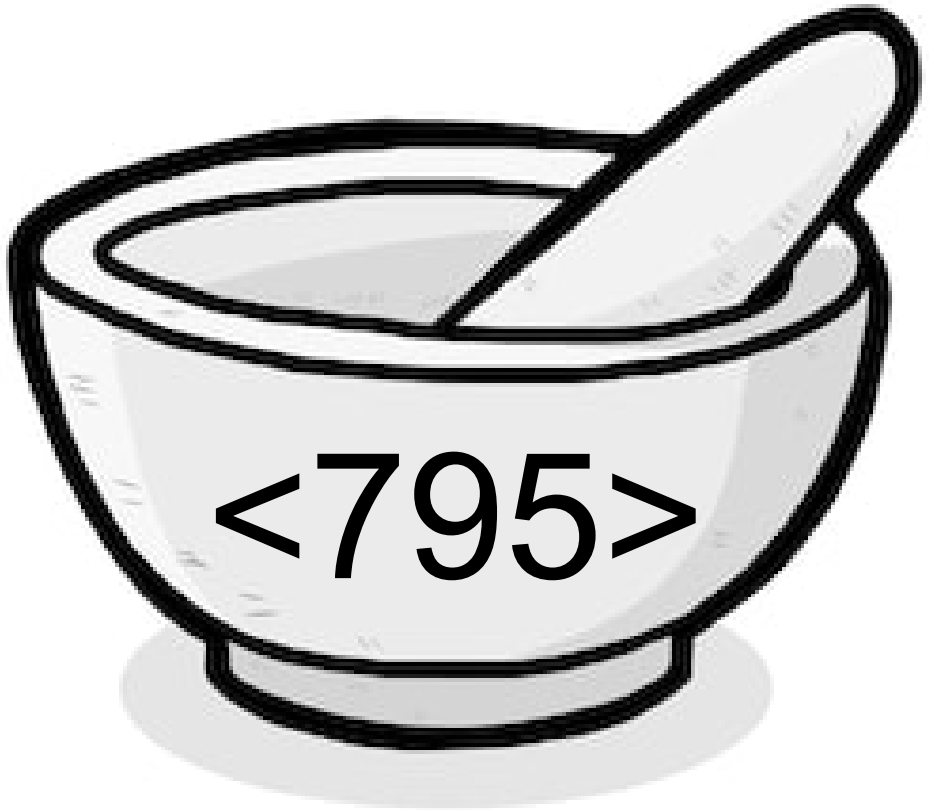
USP

- The preparation, mixing, assembling, alternating, packaging, and labeling of a drug or drug-delivery device
- Specifically includes: Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients

Beyond Use Dates (BUD) Mitigates Infection Risks



Beyond Use Dating Matters for Nonsterile Compounds



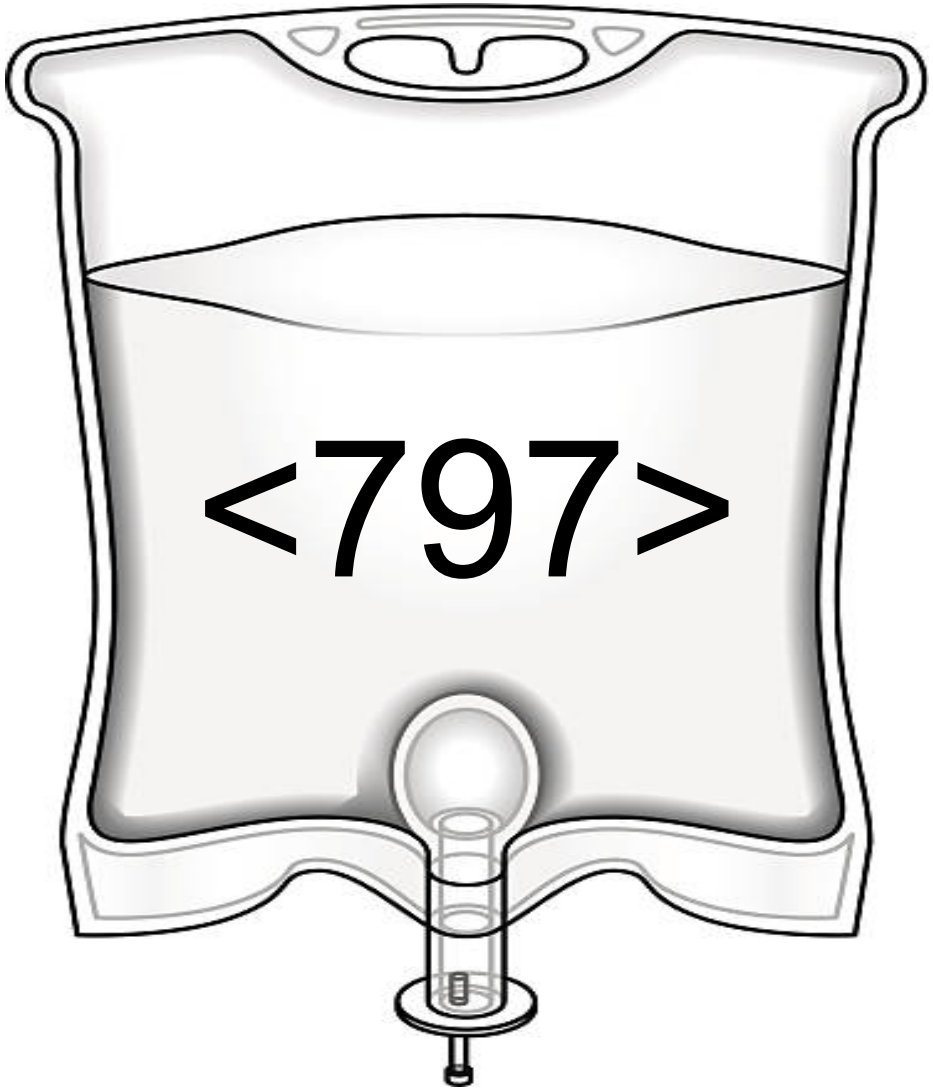
Nonsterile BUD based on Water

Categories	BUD
Non-aqueous formulations	No later than the expiration of the earliest API or 6 months, whichever is earlier
Water containing oral formulation	No later than 14 days when refrigerated
Water containing Topical/Dermal and Mucosal Liquid and Semisolid Formulation	No later than 30 days

Note: no BUD should never be longer than any ingredient's expiration.

Stability data that is longer can override these limits, however microbial growth should be considered.

Sterile Compounding Requires Controls



Contamination is Present During Compounding

Sterility - Trissel 2003[1] and 2005[2]

Estimated microbial contamination for Low and Medium-risk CSPs

Risk Level	Number of CSPs	Contamination Rate
Low	**1058**	**0.1%**
Medium	**539**	**5.8%**

*Even worse rate for staff who regularly compounded, IV pharmacists

1. Am J Health Syst Pharm. 2003; 60:1853-55
2. Am J Health Syst Pharm. 2005; 62:285-288.

Vial Type Can Also Impact Infection Risk

Single Use Vials

- ISO 5 air: 6 hours
- Worse than ISO 5 air: 1 hour

Multi Use Vials

Any air: 28 days

Or manufacturers specification

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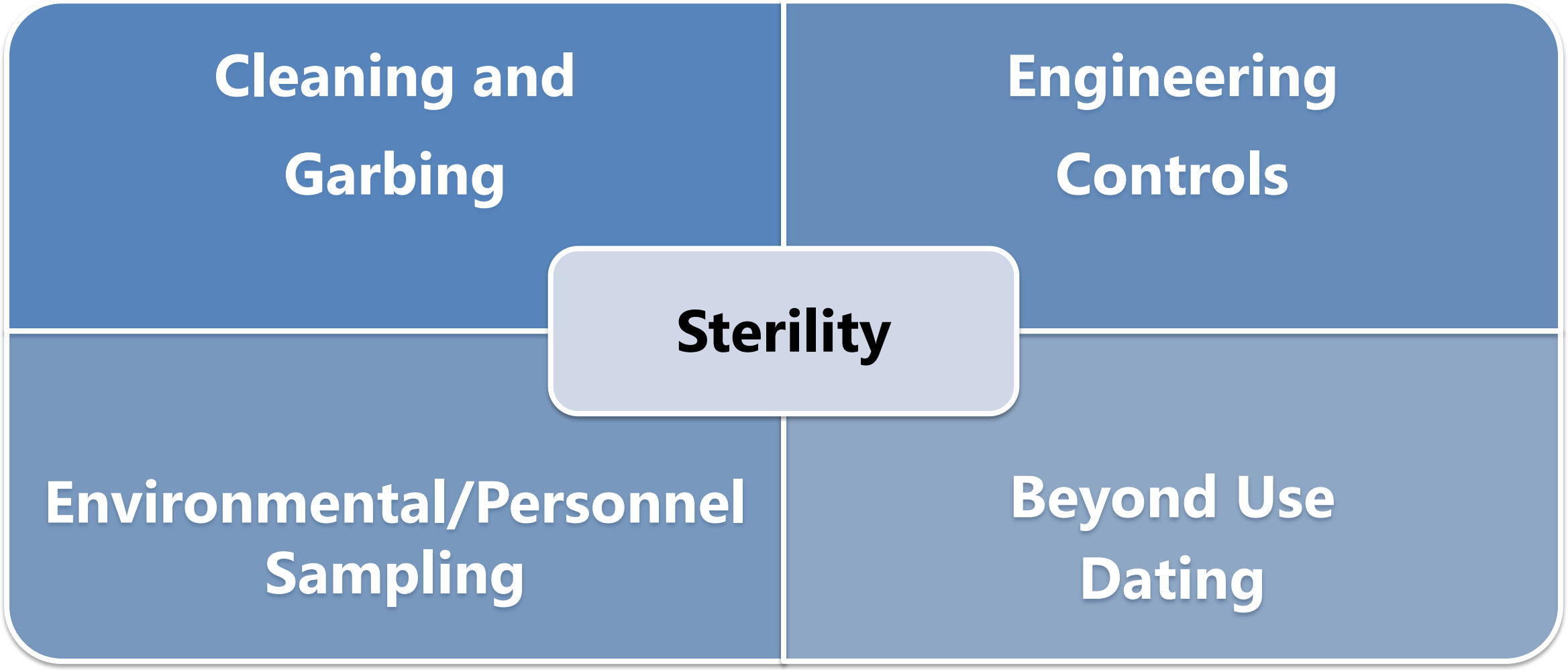
Many Variables Impact Sterile Compounding



Hygiene and Garbing Prevent Particle Shedding

Department of Pharmacy

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Follow CSP Policy Before Entering:

1. Remove all Jewelry
2. Put on Hair and Face Covers
3. Put on shoe covers
4. Wash Hands and Forearms to Elbows
5. Put on Non-shedding Approved Gown / Coat
6. BEFORE working in hood and as needed Re-sanitize Hands
7. Put on Gloves
8. Sanitize Gloves

Regular Cleaning Prevents Microbial Growth

SPA Day Shift Daily Cleaning FF Table: Sterile Products Area (IV Room)

Description:
Due at: 10/17/2019 15:15
Started at: 10/17/2019 08:25
Completed at: 10/17/2019 08:25

Task	
At the start of shift and prior to compounding, clean ALL sides/edges of First Fill table with germicidal detergent and/or isopropyl alcohol.	☑
At the start of shift and prior to compounding, clean seat and backrest surfaces of First Fill chair with germicidal detergent and/or isopropyl alcohol.	☑
At the start of shift and prior to compounding, clean ALL wall areas having direct contact (back & sides) of the First Fill table with germicidal detergent and/or isopropyl alcohol.	☑
Before beginning compounding, between each batch, and at the end of the shift, clean First Fill table surface with germicidal detergent and/or isopropyl alcohol.	☑
At the start of shift and prior to compounding, clean ALL outside surfaces of First Fill Cart with germicidal detergent and/or isopropyl alcohol.	☑

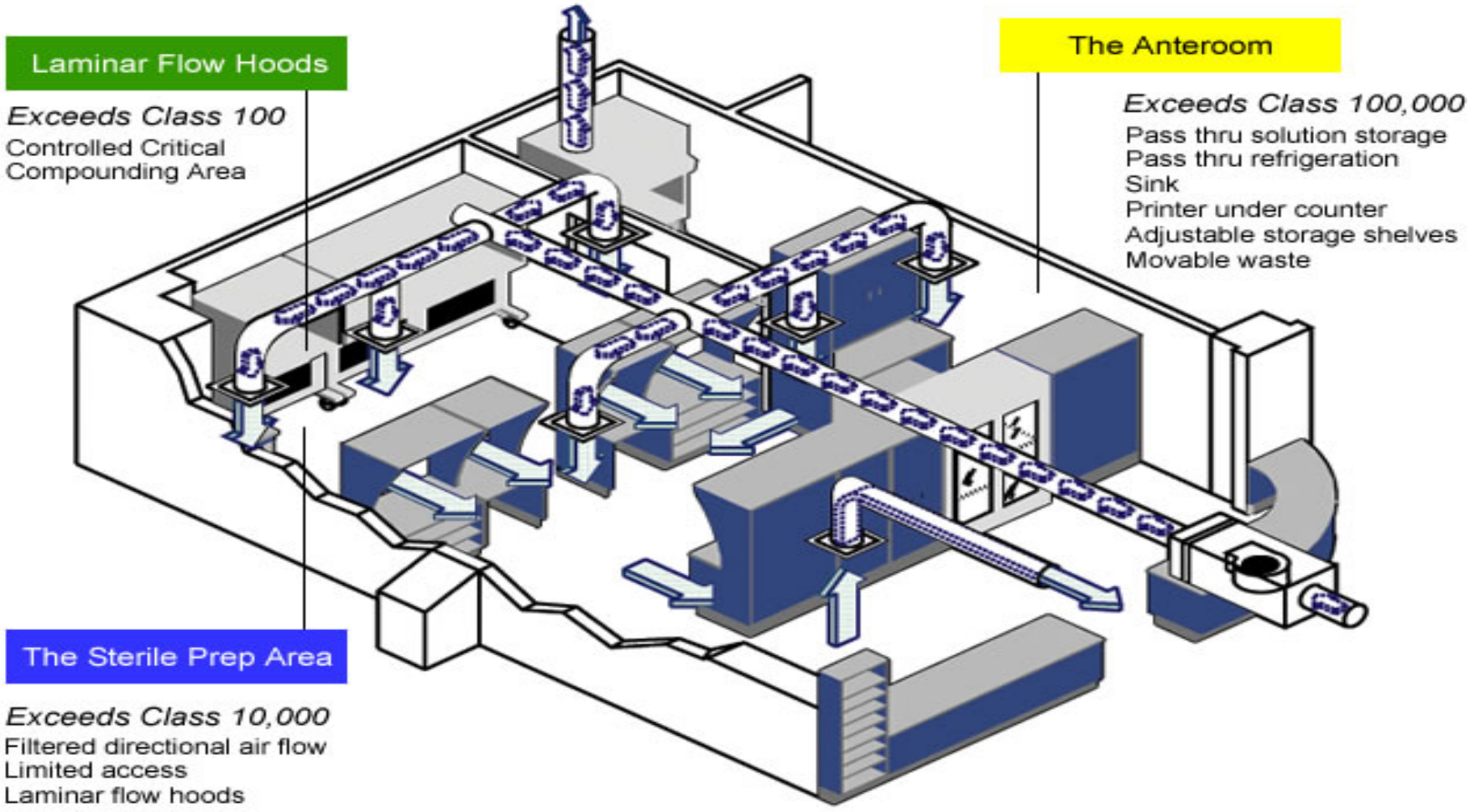
Engineering Controls Limit Particle Distribution

Cleanroom Particle Count Classifications

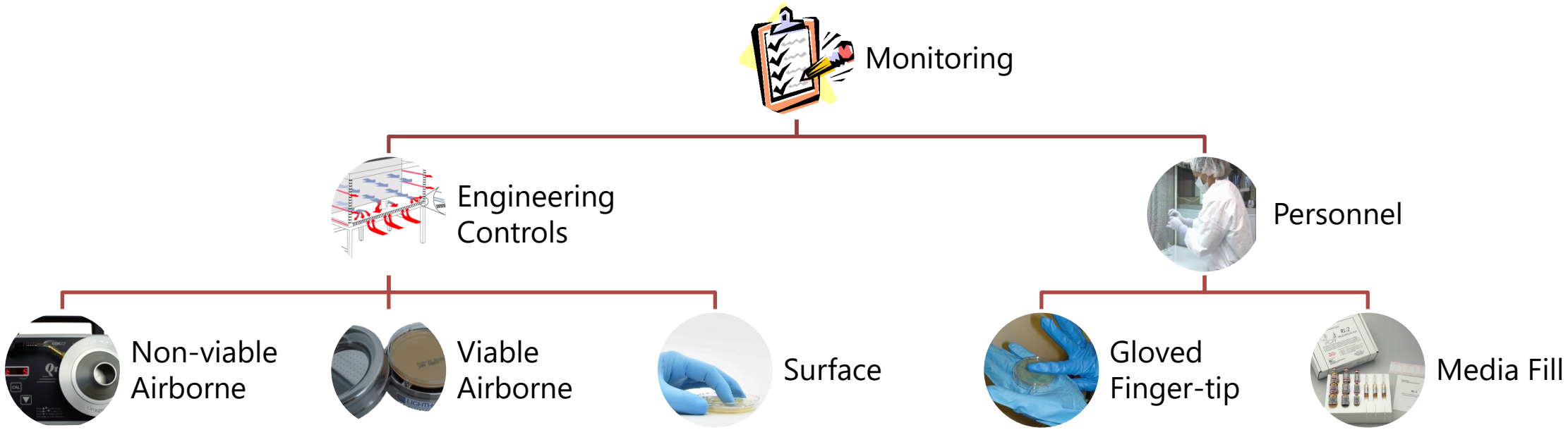
ISO 14644-1[a]	FS 209E[b]	Maximum Particle Concentration (0.5 micrometers)	
		Particles/m^3	Particles/ft^3
1			
2		4	
3	1	35	1
4	10	352	10
5 PEC/LAFW	100	3520	100
6	1000	35,200	1000
7 Buffer Room	10,000	352,000	10,000
8 Ante Room	100,000		100,000
9			1,000,000

[a]International Organization of Standardization
[b]Federal Standards

Engineering Controls Limit Particle Distribution



Environmental/Personnel Sampling is Critical



Sterile Compounding BUDs Based on Risk

Risk Level	Description	Room Temp	Fridge	Frozen
Immediate Use	Aseptic preparation in any air quality, exemption to facilitate administration	1 hour	N/A	N/A
Low – SCA	Low risk compounding occurring in a ISO 5 PEC without a cleanroom	12 hours	N/A	N/A
Low	Three or less sterile ingredients in a cleanroom using all sterile containers	48 hours	14 days	45 days
Medium	Multiple patients or administrations, 4+ sterile starting ingredients in cleanroom	30 hours	9 days	45 days
High	Nonsterile ingredients, exposure to worse than ISO 5 air, nonsterile devices	24 hours	3 days	45 days

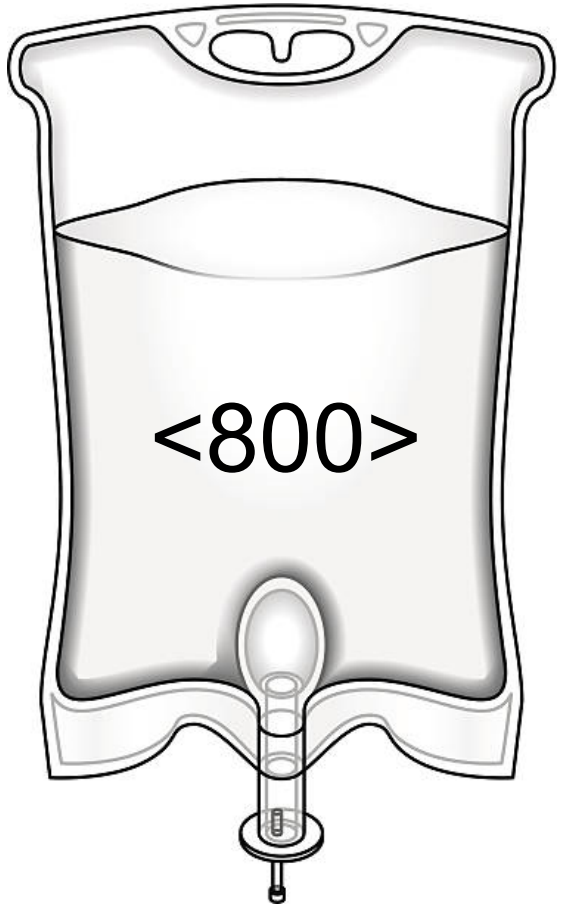
<797> Continues to Evolve with 2019 Revisions

Category	Production Environment	Previous Classification
Category 1 CSPs	Sterile Compounding Area	Low Risk in SCA
Category 2 CSPs	Cleanroom Suite	Low, Medium and High Risk

Beyond Use Dates are also Evolving with Revisions

Category	Sterilization Method	Sterility Testing Performed	Room Temperature	Refrigerator	Freezer
Category 1 CSPs	Aseptically Prepared	No	12 hours	24 hours	N/A
Category 2 CSPs	Aseptically Prepared	No	Non-sterile component(s): 1 day	Non-sterile starting component(s): 4 days	Non-sterile starting component(s): 45 days
			Sterile starting components: 4 days	Sterile starting components: 9 days	Sterile starting components: 45 days
		Yes	30 days	45 days	60 days
	Terminally Sterilized	No	14 days	28 days	45 days
		Yes	45 days	60 days	90 days

Preventing Hazardous Drug Exposure also our Duty



Hazardous Drugs have Separate Classifications

1. **Antineoplastic**
   a. Classified by ASHP/AHFS as antineoplastic and meets at least 1 hazardous criteria
2. **Non-antineoplastic**
   a. Not classified by ASHP/AHFS as antineoplastic but meets at least 1 hazardous criteria
3. **Reproductive risk**
   a. Meet only the reproductive toxicity criteria

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Hazardous Drug Exposure happens outside Pharmacy

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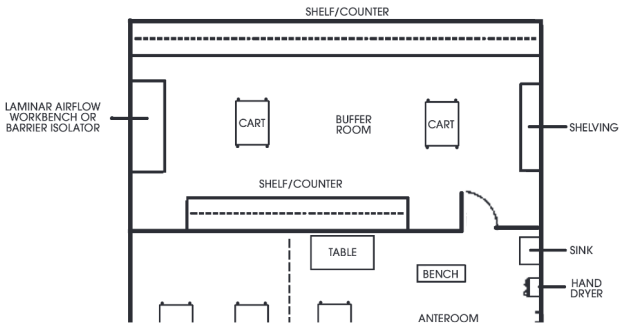
Engineering Controls also reduce Hazardous Exposure



Primary Engineering Controls

Secondary Engineering Controls

Supplemental Engineering Controls

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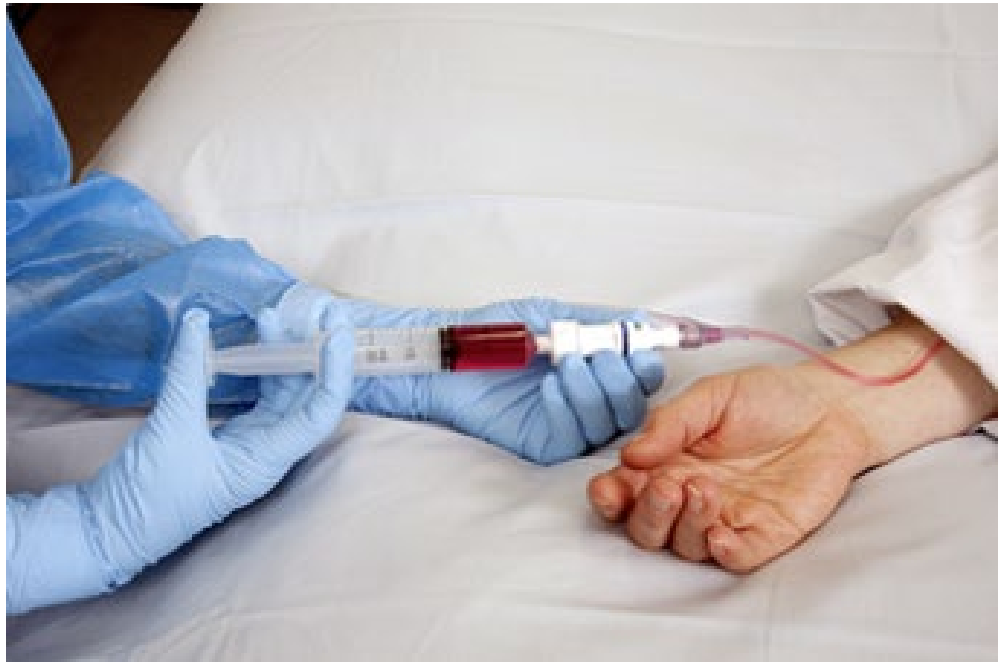
Closed System Transfer Devices Prevent Exposure

Compounding

Administration



Personal Protective Equipment is Vital

Respirator

Gloves

Gown

Head/Hair Covers

Shoe Covers

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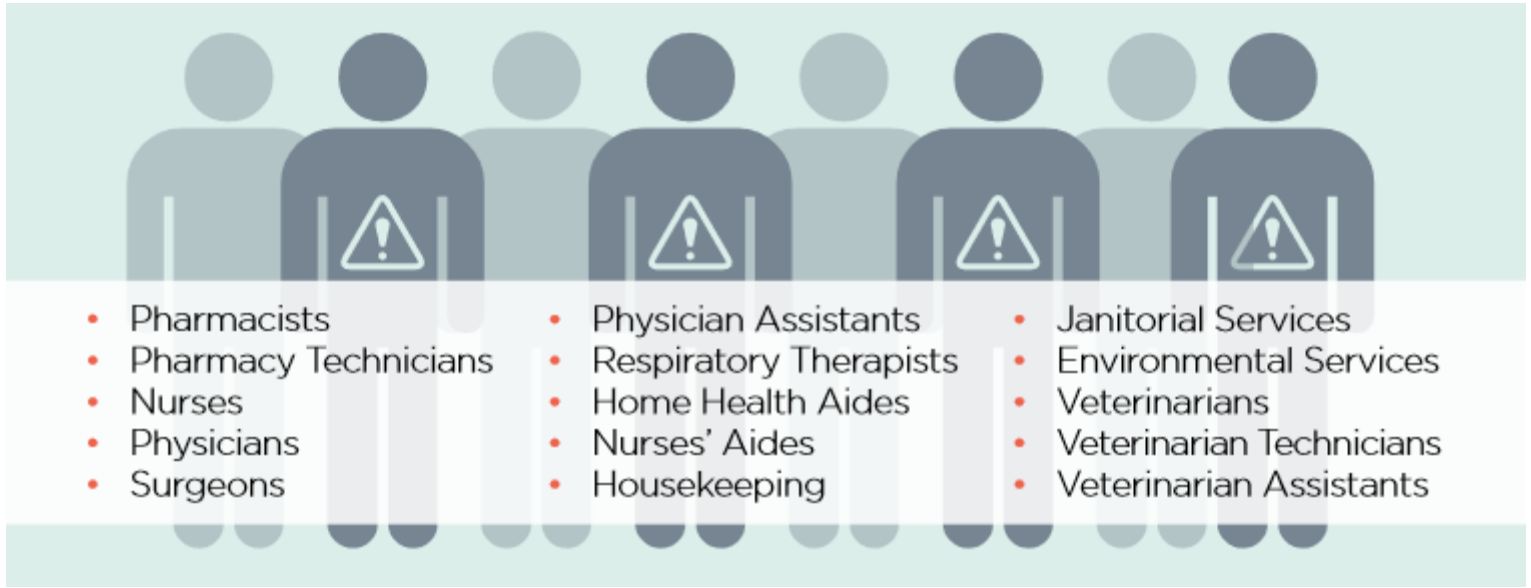
Hazardous Exposure Surveillance Methods Debated

Who to monitor?

What to monitor?



503a/b Regulation Continues to Drive Practice

503a Regulations are Important for Infection Prevention

- Limits the scope of compounding under traditional pathways
- Must have patient specific orders prior to dispensing
- Caps volume of anticipatory compounding to 30 days supply

503B Riskier, but Critical to Drug Supply Chain

- Blurring the line between compounding and manufacturing
- Compounds for office use
- Rapid response to shortages, increased utilization
- Production volume reduces cost

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