Infection Prevention for Pharmacy Compounding

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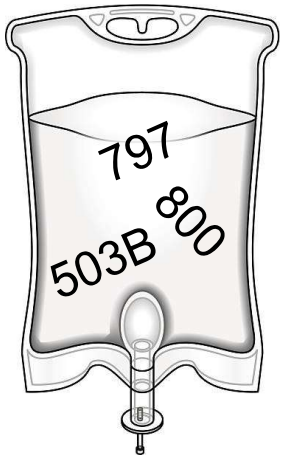
Infection Prevention Starts with Regulation



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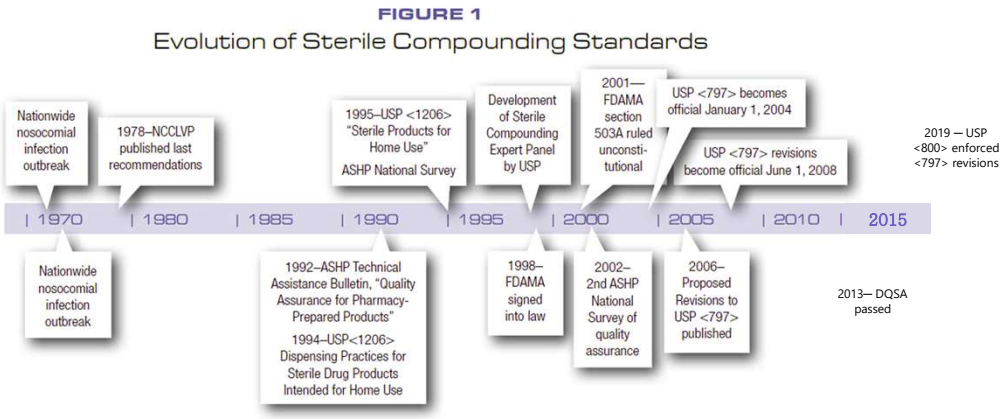
Compounding Regulation has a Rich History



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

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Regulation Informed by Compounding Misadventures

Year	State	Description	Year	State	Description
2002	Michigan	Pharmacy preparing injectable methylPREDNISolone and baclofen recalled the products because of contamination with Penicillium mo	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
2003	Missouri	Bac bat wit			eration developed VASTIN t lost vision, another
2004	Texas, New York, Michigan, Missouri	36 rec syri			ion solutions were ompounding using n a compounding
2005	New Jersey, California	Up con con			er use of the eceiving injections of om the same
2005	Minnesota	2 p oph and			gitis after receiving by a compounding um (a brown-black
2005	California	Ste bef			ain mold by a ding pharmacy was
2005	Maryland	10 con			were recalled after ons.
2006	Nevada	1 b sulf			ing a contaminated
2006	Ohio	1 c che sod			d of fosphenytoin
2007	Washington, Oregon	2, p con 0.5			ospira all issues in compounded
2009	Florida	21 horses died after receiving a compounded vitamin supplement containing vitamin B, potassium, magnesium, and selenium (product not approved in the US).	2015	Nationwide	The NIH suspends 46 clinical trials after discovering defects in the drug manufacturing process

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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.

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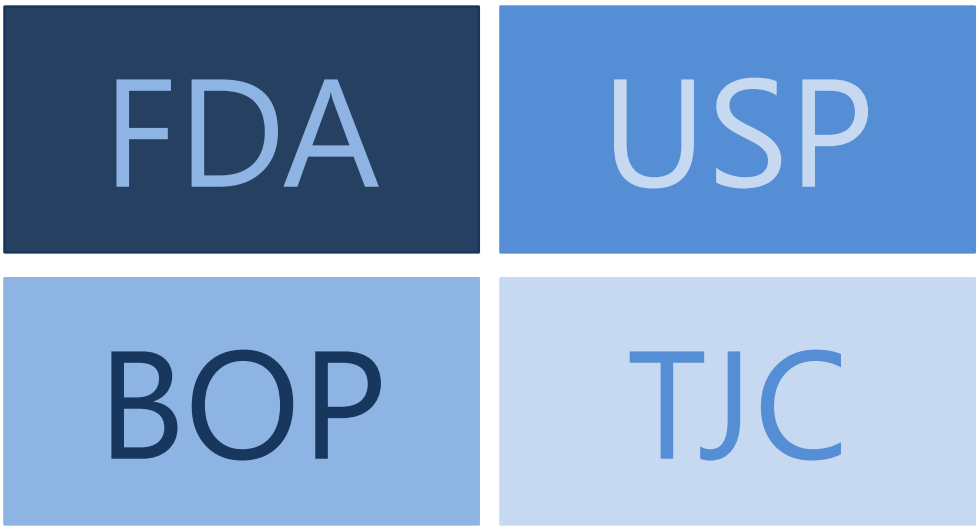
Federal and State Regulators Guide Practice



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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

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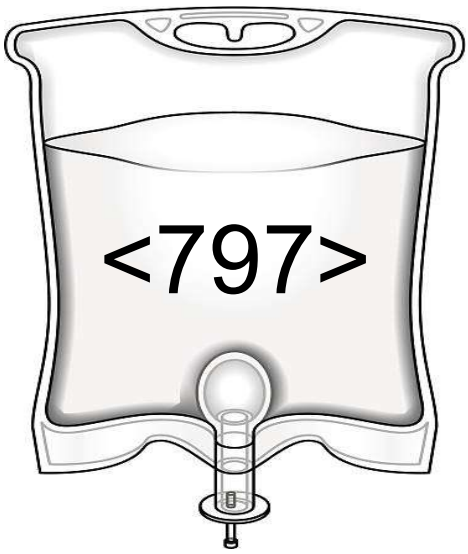
Sterile Compounding Requires Controls



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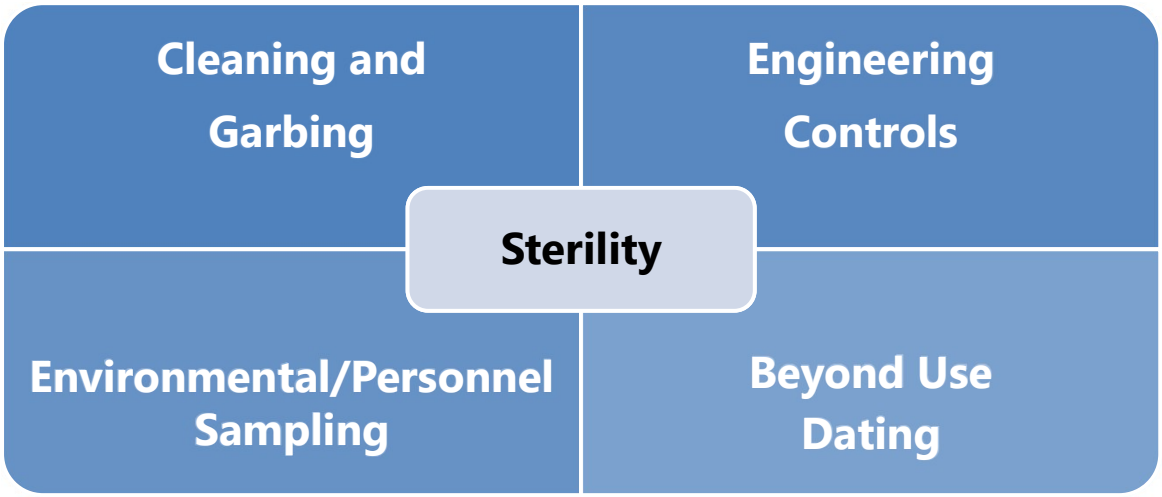
Many Variables Impact Sterile Compounding



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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

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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.	☑

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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

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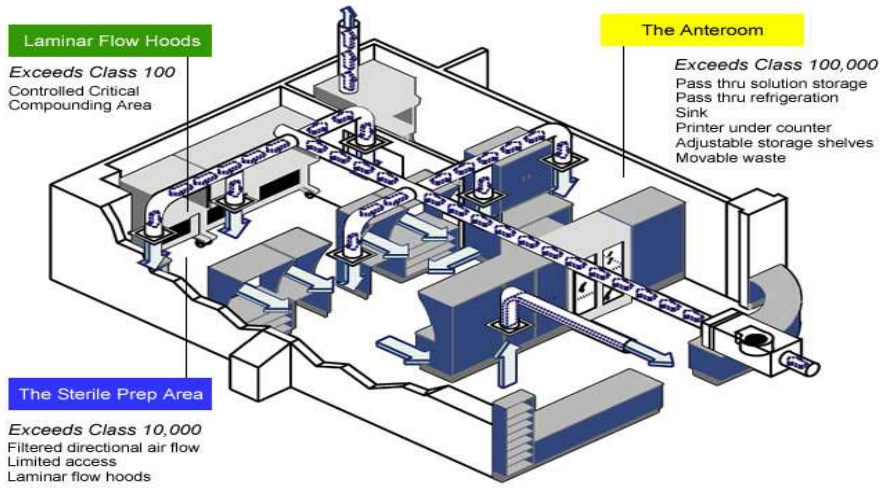
Engineering Controls Limit Particle Distribution



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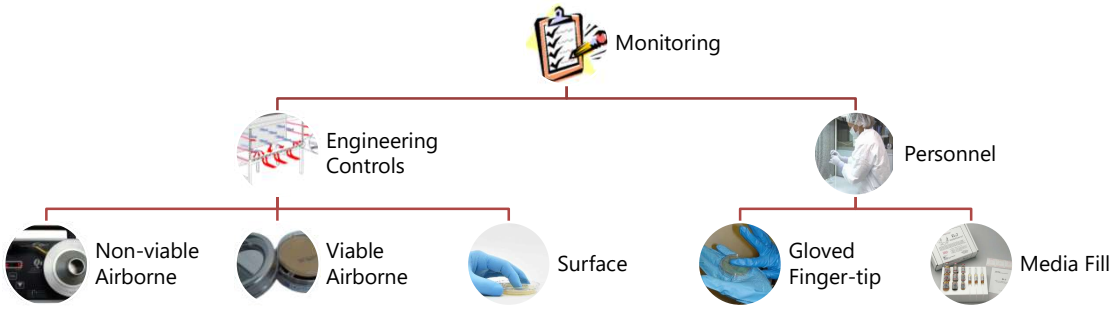
Environmental/Personnel Sampling is Critical



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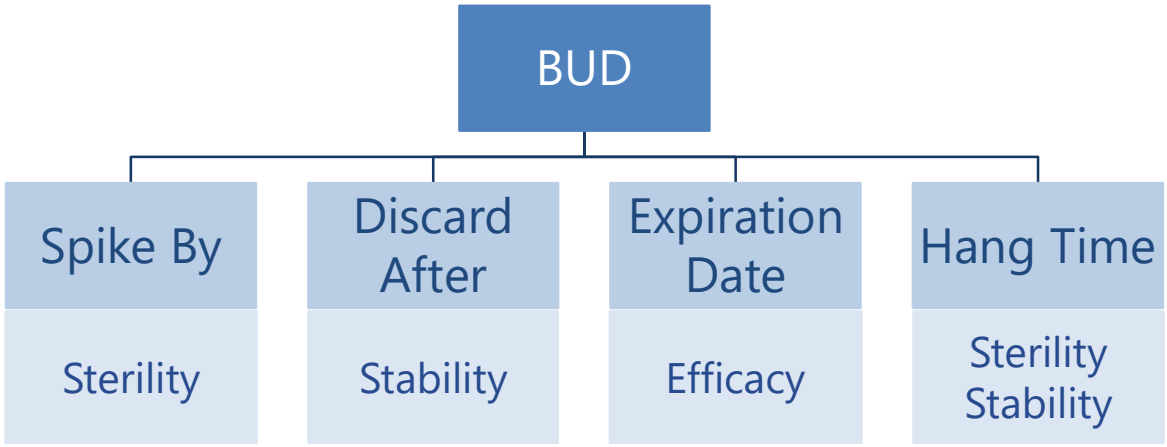
Beyond Use Dates (BUD) Mitigates Infection Risks



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Vial Type Can Also Impact Infection Risk

Single Use Vials

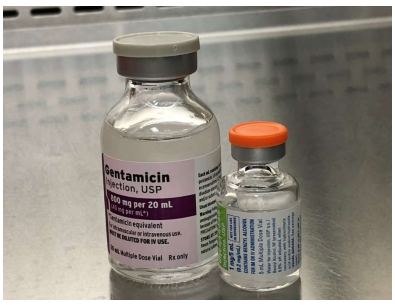
ISO 5 air: 12 hours

Or manufacturers specification

Multi Use Vials

Any air: 28 days

Or manufacturers specification



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Sterile Compounding BUDs Based on Category

Category	Sterilization Method	Sterility Testing	Non-Sterile Components	Room Temp	Fridge	Frozen
Category 1	Aseptically prepared	No	Yes	≤12 hours	≤ 24 hours	N/A
Category 2	Aseptically prepared	No	No	4 days	10 days	45 days
		No	Yes	1 day	4 days	45 days
		Yes	No	30 days	45 days	60 days
	Terminally sterilized	No	No	14 days	28 days	45 days
		Yes		45 days	60 days	90 days
Category 3	Aseptically prepared	Yes	No	60 days	90 days	120 days
	Terminally sterilized			90 days	120 days	180 days

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The "Need to Know" for Sterile Compounding BUDs

Category	Sterilization Method	Non-Sterile Components	Room Temp	Fridge
Category 1	Aseptically prepared	Yes	≤12 hours	≤ 24 hours
Category 2	Aseptically prepared	No	4 days	10 days
		Yes	1 day	4 days

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Beyond Use Dating Matters for Nonsterile Compounds

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Nonsterile BUD based on Water

Categories	BUD
Non-preserved aqueous dosage forms ($a_w \geq 0.60$)	14 days
Preserved aqueous dosage forms ($a_w \geq 0.60$)	35 days
Nonaqueous oral liquids ($a_w < 0.60$)	90 days
Other nonaqueous dosage forms ($a_w < 0.60$)	180 days

Note: 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.

a_w = water activity

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Examples of Dosage Forms & their Water Activity

Product	Water Activity (a_w)	Greatest Potential Contaminant
Nasal inhalant	0.99	Gram-negative bacteria
Hair shampoo	0.99	Gram-negative bacteria
Antacid	0.99	Gram-negative bacteria
Topical cream	0.97	Gram-positive bacteria
Oral liquid	0.90	Gram-positive bacteria and fungi
Oral suspension	0.87	Fungi
Topical ointment	0.55	None
Lip balm	0.36	None
Vaginal and rectal suppositories	0.30	None
Compressed tablets	0.36	None
Liquid-filled capsule	0.30	None

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Preventing Hazardous Drug Exposure also our Duty

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Defining Hazardous Drugs

1. Table 1 – Known or Probably carcinogens

a. Medication's "package insert" includes information to protect workers handling the drug

or

a. Classified as such by National Toxicology Program or International Agency for Research on Cancer

2. Table 2 – Hazardous as defined by NIOSH

a. Carcinogenicity
b. *Developmental toxicity (including teratogenicity)
c. *Reproductive toxicity
d. Genotoxicity
e. Organ toxicity at low doses
f. Structure and toxicity profile that mimics an exciting drug determined hazardous

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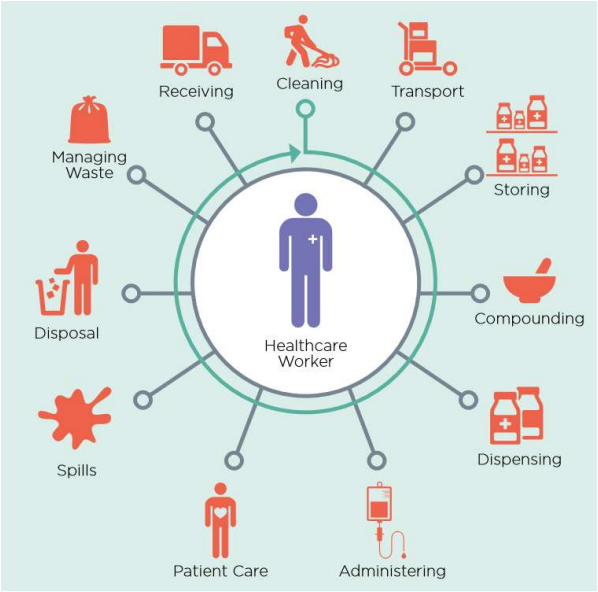
Hazardous Drug Exposure happens outside Pharmacy



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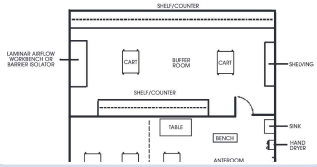
Engineering Controls also reduce Hazardous Exposure



Primary Engineering Controls

Secondary Engineering Controls

Supplemental Engineering Controls

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Closed System Transfer Devices Prevent Exposure

Compounding

Administration

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Personal Protective Equipment is Vital

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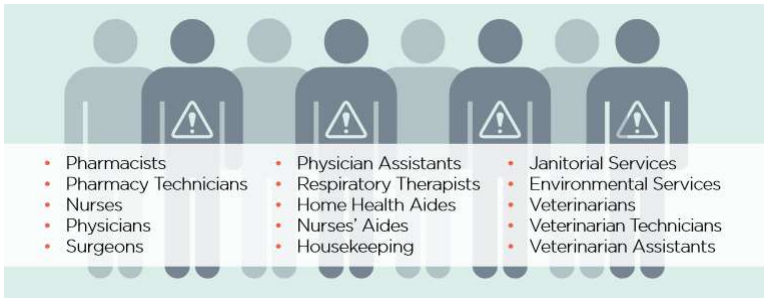
Hazardous Exposure Surveillance Methods Debated

Who to monitor?

What to monitor?



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503a/b Regulation Continues to Drive Practice

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503a Regulations are Important for Infection Prevention

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

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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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Infection Prevention for Pharmacy Compounding

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