Infection Prevention for Pharmacy Compounding

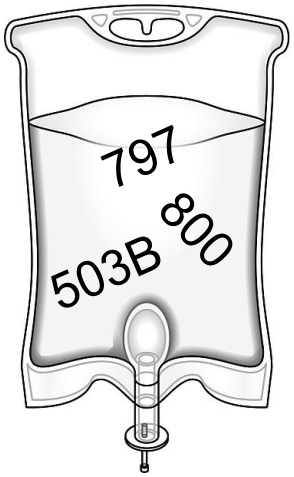
Samuel M. Eberwein, PharmD, MS, BCPS

UNC HEALTH CARE

November 6, 2019

UNC HEALTH CARE SYSTEM

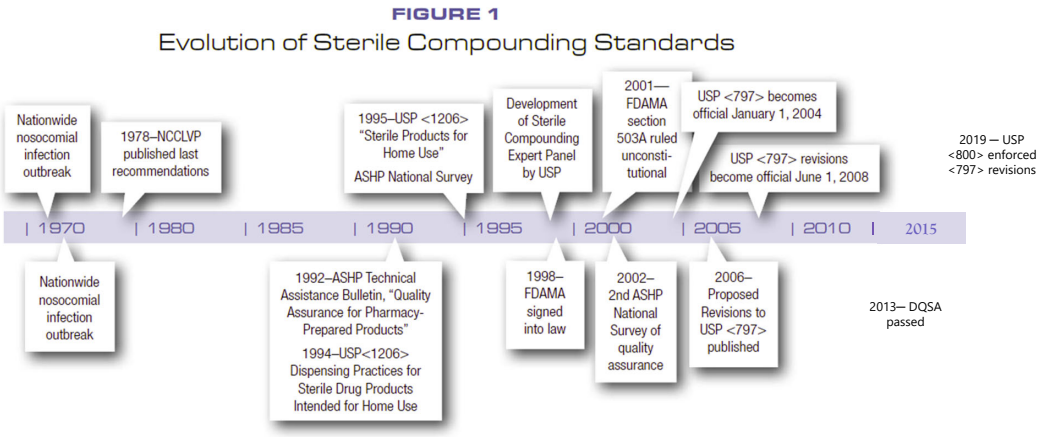
Infection Prevention Starts with Regulation



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Compounding Regulation has a Rich History



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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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 m	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	Ba ba wi			neration developed AVASTIN nt lost vision, another
2004	Texas, New York, Michigan, Missouri	3 re sy			ition solutions were compounding using in a compounding
2005	New Jersey, California	U co co			fter use of the receiving injections of rom the same
2005	Minnesota	2 op ar			ngitis after receiving d by a compounding lum (a brown-black
2005	California	St be			tain mold by a nding pharmacy was
2005	Maryland	1 co			n were recalled after ions.
2006	Nevada	1 su			ving a contaminated
2006	Ohio	1 ch so			d of fosphenytoin
2007	Washington, Oregon	2, co 0.			Hospira all issues n 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

UNC HEALTH CARE SYSTEM

Federal and State Regulators Guide Practice

FDA	USP
BOP	TJC

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

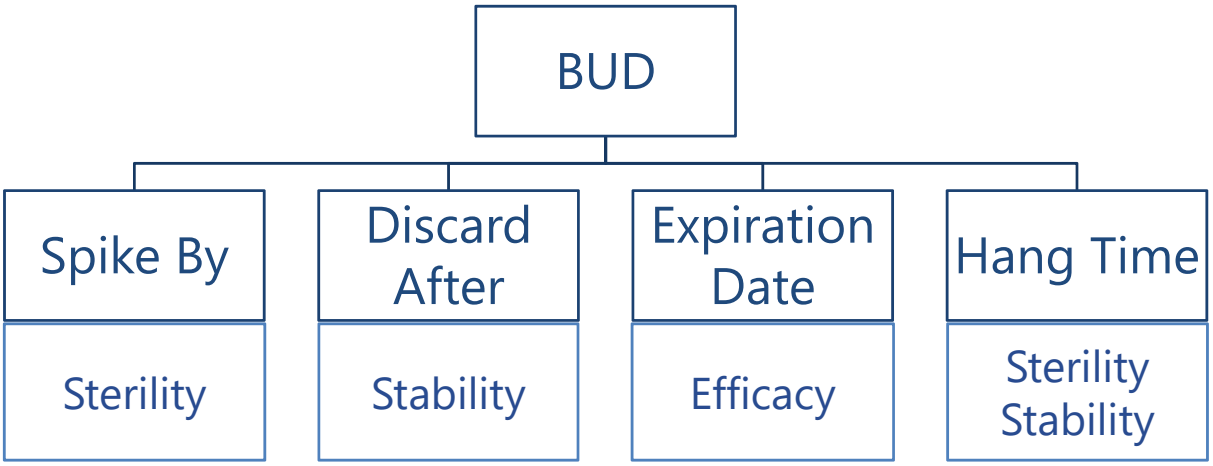
USP

- 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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Beyond Use Dates (BUD) Mitigates Infection Risks



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Beyond Use Dating Matters for Nonsterile Compounds

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

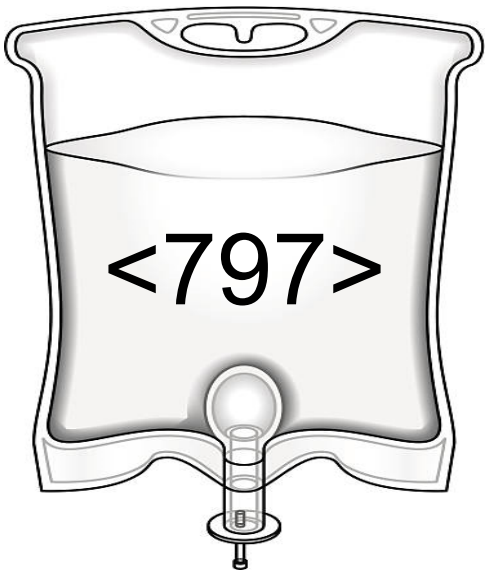
Note: no BUD should never be longer than any ingredient's expiration.

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Sterile Compounding Requires Controls



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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.

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

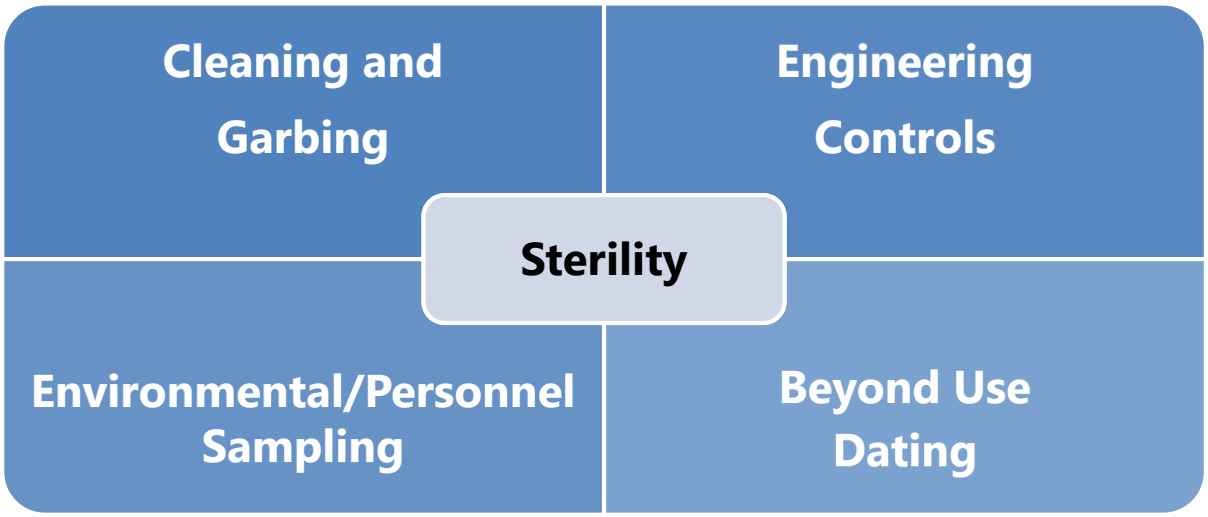
Any air: 28 days

Or manufacturers specification

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Many Variables Impact Sterile Compounding



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Hygiene and Garbing Prevent Particle Shedding

Department of Pharmacy

UNC HEALTH CARE

STOP

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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.	☑

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Engineering Controls Limit Particle Distribution

Cleanroom Particle Count Classifications

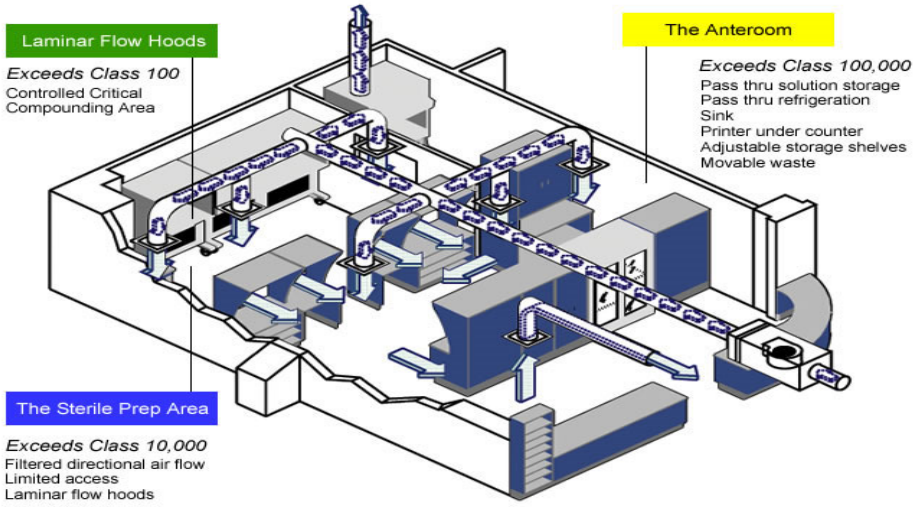
ISO 14644-1[a]		*FS 209E*[b]	*Maximum Particle Concentration (0.5 micrometers)*	
			Particles/m^3	*Particles/ft*^{3}
1				
2			4	
3		1	35	1
4		10	352	10
5	PEC/LAFW	100	3520	100
6		1000	35,200	1000
7	Buffer Room	10,000	352,000	10,000
8	Ante Room	100,000		100,000
9				1,000,000

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

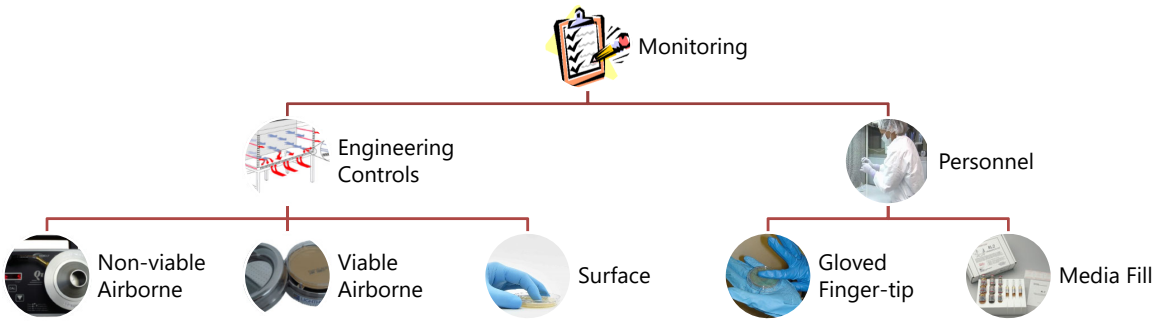
Engineering Controls Limit Particle Distribution



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Environmental/Personnel Sampling is Critical



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

<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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

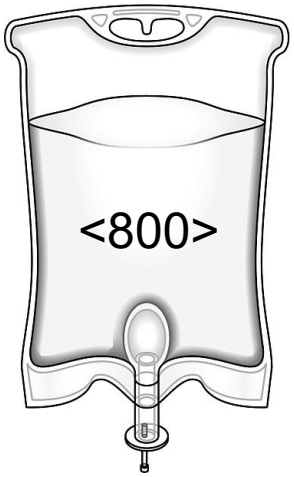
Beyond Use Dates are also Evolving with Revisions

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Preventing Hazardous Drug Exposure also our Duty



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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**

UNC HEALTH CARE

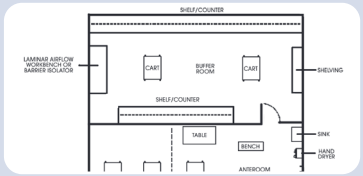
UNC HEALTH CARE SYSTEM

Hazardous Drug Exposure happens outside Pharmacy

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Engineering Controls also reduce Hazardous Exposure



Primary Engineering Controls	Secondary Engineering Controls	Supplemental Engineering Controls

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Closed System Transfer Devices Prevent Exposure

Compounding

Administration

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Personal Protective Equipment is Vital

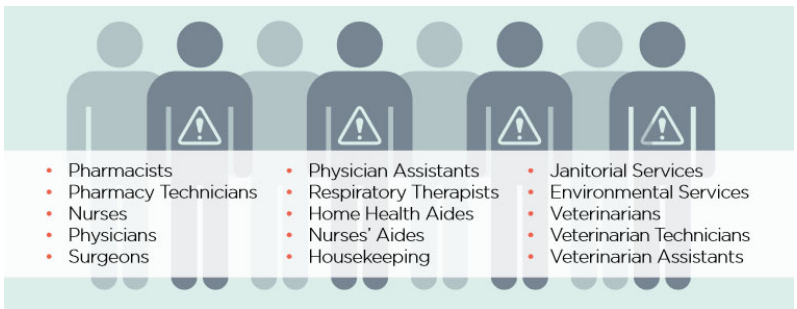
UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

Hazardous Exposure Surveillance Methods Debated

Who to monitor?

What to monitor?



UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

503a/b Regulation Continues to Drive Practice

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

UNC HEALTH CARE

UNC HEALTH CARE SYSTEM

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

UNC HEALTH CARE

Infection Prevention for Pharmacy Compounding

Samuel M. Eberwein, PharmD, MS, BCPS

UNC HEALTH CARE

November 6, 2019