PRACTICAL APPLICATION OF HAZARDOUS DRUG COMPOUNDING

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DORNEYVILLE PHARMACY

ALLENTOWN, PA

OBJECTIVES

- Describe the designated person's responsibility for training personnel in hazardous drug handling
- Discuss the importance of the NIOSH list of hazardous drugs in performing an assessment of risk (AOR)
- List several precautions for compounding, handling, storing, dispensing and disposal of HDs
- Outline the importance of workflow in compounding hazardous drugs

USP 800

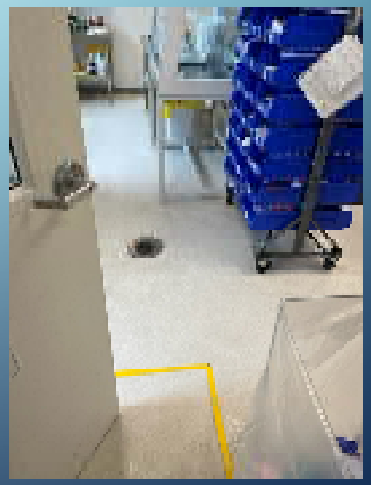
- The chapter is prescriptive, not descriptive
- How do you apply the standards to day to day activities?
- We will discuss practical application from a community pharmacy perspective

OUR COMMUNITY PRACTICE

- Compounding-only pharmacy for over 25 years
- First USP 800 compliant community compounding pharmacy in PA
- 250 SF nonsterile-HD C-SEC, 50 SF sterile-HD C-SEC (ISO 7)
- PCAB/ACHC accredited in 2018 with hazardous distinction
- Reaccredited in 2020 and 2023 with hazardous distinction
- Three pharmacists, 2 nonsterile HD technicians, 5 nonsterile technicians, 2 sterile/sterile HD technicians (also CS, HR, etc)

OUR COMMUNITY PRACTICE

NS HD LAB



NIOSH

- Assessment of risk must be conducted – using current NIOSH list with other sources (e.g. SDS)
- Active pharmaceutical ingredients (APIs) and finished products – manufactured or compounded
- Caustic substances – acids, bases, solvents (HCl, NaOH, Phenol, Benzalkonium Chloride)
- We store all HDs in C-SECs – sterile and nonsterile HD labs
- We count manufactured and compounded finished preps in HD labs on dedicated trays – no counting equipment

AORS

- HD list and AORs reviewed annually and signed by the DP
- New AORs conducted with revisions to the NIOSH list
- New AORs conducted when new HDs are added
- AORs (would be) conducted with investigational drugs, where HD status is unknown

SAMPLE AOR

DORNEYVILLE COMPOUNDING PHARMACY

Drug Name: Estriol **Date AoR Initially Performed:** 04/10/2018 **Date Reviewed or Revised:** 07/23/2020

HD Drug Category: ☐ Table 1 ☐ Table 2 ☐ Other ☒ Hazardous Chemical

Dosage form (select one):
☐ Sterile dosage compounded by a vendor and not requiring additional manipulation
☐ Dosage form of conventionally manufactured product that require only packaging or counting
☐ Dosage form of conventionally manufactured non-antineoplastic or reproductive hazard product that requires only packaging or counting
☒ Other (explain): API received from manufacturer for compounding use

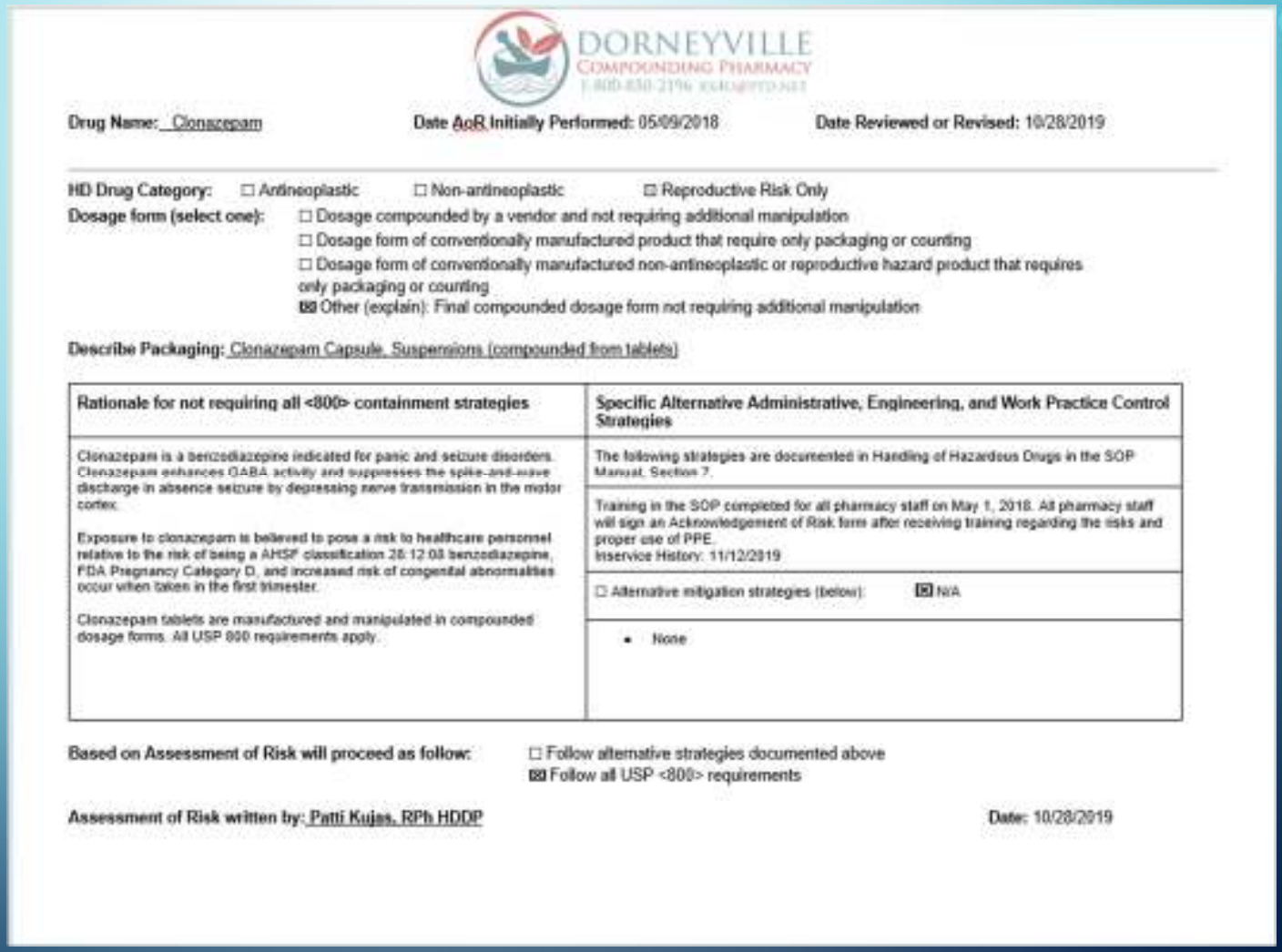
Describe Packaging: Estriol USP API

Rationale for not requiring all <800> containment strategies	Specific Alternative Administrative, Engineering, and Work Practice Control Strategies
Estriol is an estrogen derivative that is used in hormone replacement therapies. Estriol is less potent than estradiol. Estrogens modulate the pituitary secretion of gonadotropins, luteinizing hormone, and follicle-stimulating hormone through a negative feedback system. Exposure to estriol is believed to pose a risk to healthcare personnel relative to the risk of being an estrogen derivative and therefore may pose the same threat as estradiol and should thus be recognized as AHSF classification 68:16:04 estrogens and FDA Pregnancy Category X. This chemical is not on the NIOSH list; however, it may pose significant risk if not handled appropriately. Dorneyville pharmacy has deemed this a hazardous chemical, can only be used in compounding in the non-sterile HD area, following proper precautions using only under the negative pressure CVE. All USP <800> standards must be followed.	The following strategies are documented in Compounding of Hazardous Drugs in the SOP Manual, Section 7. Training in the SOP completed for all pharmacy staff on May 1, 2018. All pharmacy staff will sign an Acknowledgement of Risk form after receiving training regarding the risks and proper use of PPE. Inservice History: 11/12/2019, 08/18/2020 ☐ Alternative mitigation strategies (below) ☒ N/A • None

Based on Assessment of Risk will proceed as follow:
☐ Follow alternative strategies documented above
☒ Follow all USP <800> requirements

Assessment of Risk written by: Patti Kujas, RPh **Date:** 07/23/2020

SAMPLE AOR



DORNEYVILLE COMPOUNDING PHARMACY

Drug Name: Clonazepam **Date AoR Initially Performed:** 05/09/2018 **Date Reviewed or Revised:** 10/28/2019

HD Drug Category: ☐ Antineoplastic ☐ Non-antineoplastic ☒ Reproductive Risk Only

Dosage form (select one):
☐ Dosage compounded by a vendor and not requiring additional manipulation
☐ Dosage form of conventionally manufactured product that require only packaging or counting
☐ Dosage form of conventionally manufactured non-antineoplastic or reproductive hazard product that requires only packaging or counting
☒ Other (explain): Final compounded dosage form not requiring additional manipulation

Describe Packaging: Clonazepam Capsule, Suspensions (compounded from tablets)

Rationale for not requiring all <800> containment strategies	Specific Alternative Administrative, Engineering, and Work Practice Control Strategies
Clonazepam is a benzodiazepine indicated for panic and seizure disorders. Clonazepam enhances GABA activity and suppresses the spike-and-wave discharge in absence seizure by depressing nerve transmission in the motor cortex. Exposure to clonazepam is believed to pose a risk to healthcare personnel relative to the risk of being a AHSF classification 28:12:03 benzodiazepine, FDA Pregnancy Category D, and increased risk of congenital abnormalities occur when taken in the first trimester. Clonazepam tablets are manufactured and manipulated in compounded dosage forms. All USP 800 requirements apply.	The following strategies are documented in Handling of Hazardous Drugs in the SOP Manual, Section 7. Training in the SOP completed for all pharmacy staff on May 1, 2018. All pharmacy staff will sign an Acknowledgement of Risk form after receiving training regarding the risks and proper use of PPE. Inservice History: 11/12/2019 ☐ Alternative mitigation strategies (below): ☒ N/A • None

Based on Assessment of Risk will proceed as follow: ☐ Follow alternative strategies documented above
☒ Follow all USP <800> requirements

Assessment of Risk written by: Patti Kujas, RPh HDDP **Date:** 10/28/2019

DESIGNATED PERSON

Per USP 800, the DP must:

- Be qualified and trained to develop and implement appropriate procedures
- Ensure competency of personnel
- Ensure environmental control of the compounding and storage areas
- Identify, document, and contain the cause of any discovered contamination
- Maintain reports of sampling/testing performed, and act on the results
- Oversee compliance
- Oversee monitoring of the facility
- Review and document the review of SOPs at least every 12 months

DESIGNATED PERSON

Attachment 8 - SOP 2.010
Required Duties of the Hazardous Drug Designated Person (HDDP)

- Complete a designed HDDP program for credentialing
- Create and implement standard operations procedures (SOPs) regarding HDs
- Document an annual review of the SOPs as outlined in section 17 of USP 800
- Monitor compliance with these SOPs and other relevant regulations
- Oversee worker competency
- Coordinate worker training
- Understand and react to the risks posed by HDs to workers
- Ensure environmental control in areas where HDs are handled
- Oversee and document facility monitoring and react to unacceptable results

I hereby attest that I have read the job description, duties and responsibilities, specific to my position as a HDDP as required in the PA State Board of Pharmacy Code of Regulations.

HDDP Signature: _____ Date: _____

Pharmacy Manager Signature: _____ Date: _____

File in HR Employee File

DP IN COMMUNITY COMPOUNDING PRACTICE

- Two DPs responsible for HD compounding – both technicians
- First is DP of sterile and DP of sterile-HD with over 10 years experience in sterile and nonsterile compounding
- Second is DP of nonsterile HD compounding with over 20 years experience in nonsterile compounding
- Both are CPhTs and are considering advanced certification
- State of PA does not require licensing or registration of technicians

HD PERSONNEL TRAINING AND COMPETENCY REVIEW

- Conducted initially before independently compounding
- Competencies reviewed annually
- All HD – related activities (PPE, receipt, drug handling, storage, DDCD, spills, disposal)
- Initial training on compounding each dosage forms and annual competency review
- Potency testing every 6 months on all dosage forms using independent lab testing
- All documented in individual portfolios and in compliance tracking software

HD PERSONNEL TRAINING

Donneyville Compounding Pharmacy

HAZARDOUS DRUG TRAINING AND COMPETENCY CHECKLIST

Name: _____ Dept: Non-sterile Area

Title: _____ Date of Hire: _____

TOPIC	Needed?		Completed:			
			Training		Competency	
	Yes	No	Initials	Date	Initials	Date
Risks associated with handling HD						
List of Hazardous Drugs						
SDS (Safety Data Sheets)- Location/Interpretation						
HD SOPs						
Receipt and Storage						
Labeling, Packaging, Dispensing, &Transport						
Disposal						
Personal Protective Equipment (PPE)						
Facilities and PEC						
Compounding: Capsules						
Compounding: Liquids						
Compounding: Suppositories						
Compounding: Topicals						
Compounding: Treats						
Compounding: Triturates						
Compounding: Troches						
Deactivation, Decontamination, Cleaning and Disinfection						
Spills and Exposure Events						

When form is completed in its entirety, the Employee and the Pharmacist-in-charge will review and sign.

Employee Signature: _____ **Date:** _____

HDDP Signature: _____ **Date:** _____

File in Personnel records/Pestle

PRECAUTIONS FOR HD COMPOUNDING

- Donning and doffing PPE within line of demarcation
- Receiving new inventory of API and manufactured HDs – neutral space with proper PPE
- All HDs (manufactured drugs and APIs) stored in negative pressure space
- DDCD of C-PECs – solutions and methods in SOPs and training
- Compounding with one API (or group of APIs) at a time
- Proper hand placement within the C-PEC – ensuring they stay within the CVE
- Disposal of waste before exiting the C-PEC
- Cleaning and maintaining dedicated equipment

WORKFLOW

- Compounding software permits designation of APIs and manufactured products as HDs
- Master formulation records (MRS) identify HDs within the formula
- Compounding records are generated from MFRs for every compound
- CRs that contain HDs are printed with labeling during data entry
- HD CRs are routed to the appropriate area – nonsterile HD or sterile HD
- Work is prioritized by turn-around, API(s), shipment or pickup and dosage form

WORKFLOW

- Pharmacy uses color coding of labeling and compounding records
- Work is distributed based on color coding system (e.g. yellow clips = NS HD, red = NS, clear = sterile and sterile HD)
- Finished work is placed in HD pass-through for RPh check
- All HDs are bagged in zip-lock for non-antineoplastic and cytotoxic bag for antineoplastics
- Routing of work ensures it will be directed to proper lab and handled by trained personnel

WHAT WE COMPOUND

STERILE HDS:

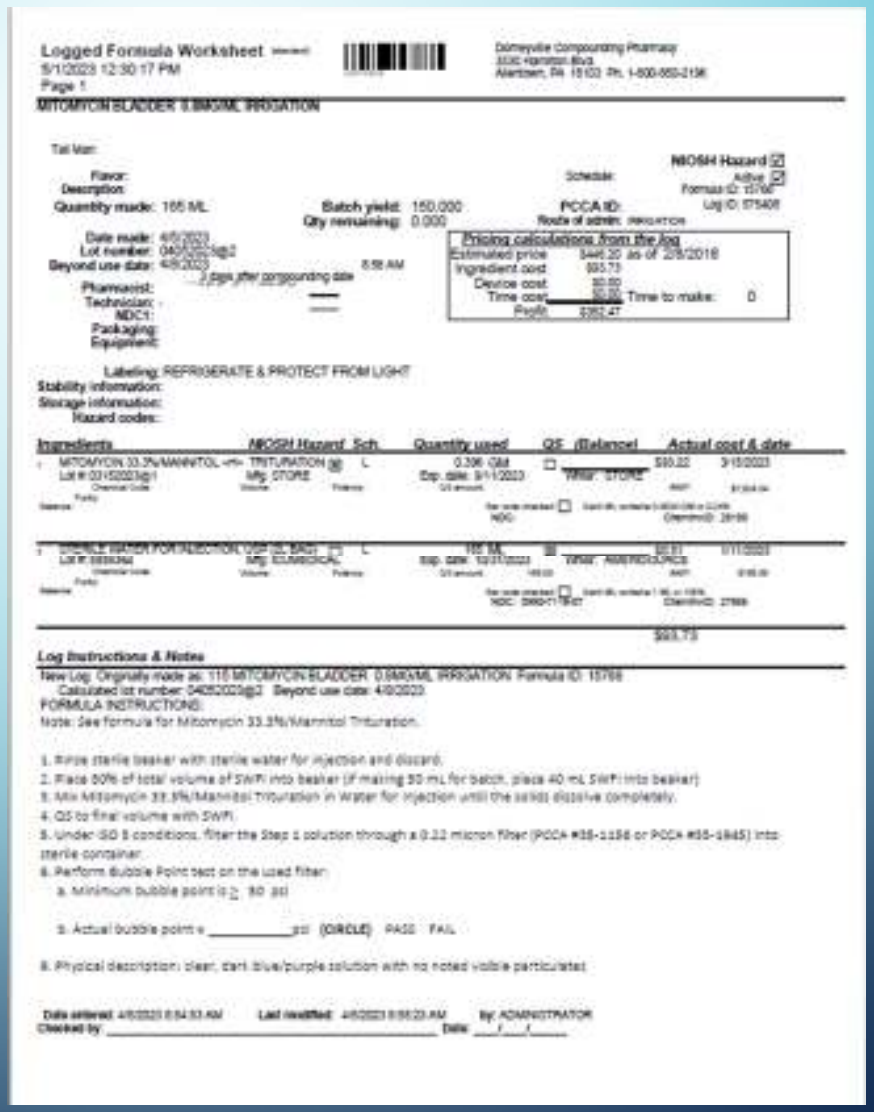
- Mitomycin – bladder irrigation, ophthalmic injection
- Testosterone injection
- Tacrolimus ophthalmic solution
- Cyclosporine ophthalmic solution
- Phenol injection
- Human and veterinary preparations primarily from active pharmaceutical ingredients (API)

WHAT WE COMPOUND

NONSTERILE HDS:

- Methimazole – transdermal, suspension, treats
- Zonisamide – capsules, suspension, treats
- Chlorambucil – capsules, suspensions
- Chloramphenicol – capsules, suspensions, treats
- HRT – estriol, estradiol, progesterone, testosterone – creams, capsules, troches
- Human and veterinary preparations primarily from active pharmaceutical ingredients (API)

SAMPLE COMPOUNDING RECORD



Logged Formula Worksheet
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Domeyville Compounding Pharmacy
3330 Hampton Blvd
Allentown, PA 18103 Ph. 1-800-555-2156

MITOMYCIN BLADDER 0.5MG/ML IRRIGATION

Tall Man:

Flavor:
Description:
Quantity made: 165 ML

Batch yield: 150.000
Qty remaining: 0.000

Schedule:
NIOSH Hazard ☑
Active ☑
Formula ID: 15768
PCCA ID:
Log ID: 575408
Route of admin: IRRIGATION

Date made: 4/5/2023
Lot number: 040520...
Beyond use date: 4/5/2023
2 days after compounding date
6:56 AM

Pharmacist:
Technician:
NDC1:
Packaging:
Equipment:

Pricing calculations from the log
Estimated price $446.20 as of 2/5/2018
Ingredient cost $83.73
Device cost $0.60
Time cost $0.00 Time to make: 0
Profit $362.47

Labeling: REFRIGERATE & PROTECT FROM LIGHT
Stability information:
Storage information:
Hazard codes:

Ingredients	NIOSH Hazard	Sch	Quantity used	QS	(Balance)	Actual cost & date
1 MITOMYCIN 33.3%/MANNITOL <H> Lot #: 031520231g1	TRITURATION (g) Mfg: STORE	L	0.306 GM Exp. date: 9/1/2023	☐	Vendor: STORE	$83.22 3/15/2023
2 SODIUM CHLORIDE FOR INJECTION, USP 0.9% Lot #: 0000M	Mfg: ECLINICAL	L	165 ML Exp. date: 10/31/2023	☑	Vendor: AMERISOURCE	$0.51 5/1/2023

$83.73

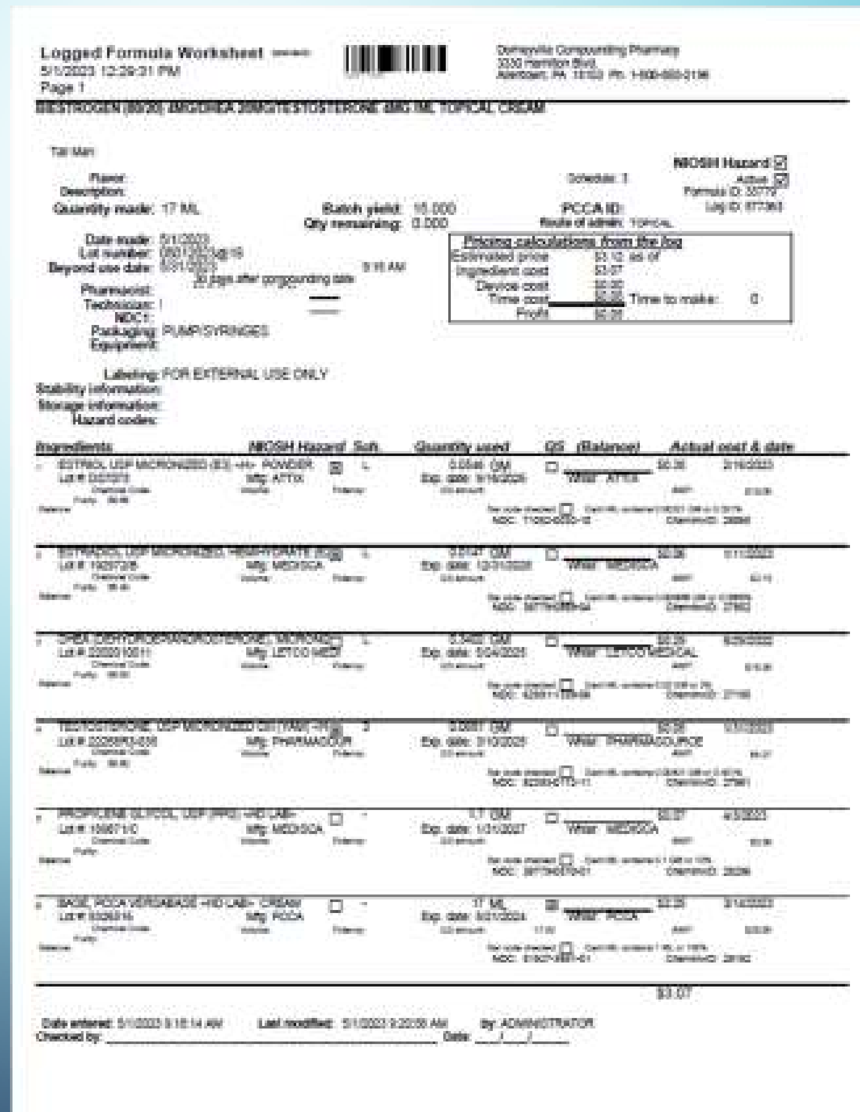
Log Instructions & Notes

New Log. Originally made as: 115 MITOMYCIN BLADDER 0.5MG/ML IRRIGATION. Formula ID: 15768
Calculated lot number: 040520231g2 Beyond use date: 4/5/2023.
FORMULA INSTRUCTIONS:
Note: See formula for Mitomycin 33.3%/Mannitol Trituration.

1. Rinse sterile beaker with sterile water for injection and discard.
2. Place 50% of total volume of SWFI into beaker (if making 50 mL for batch, place 40 mL SWFI into beaker)
3. Mix Mitomycin 33.3%/Mannitol Trituration in Water for injection until the solids dissolve completely.
4. QS to final volume with SWFI.
5. Under ISO 5 conditions, filter the Step 3 solution through a 0.22 micron filter (PCCA #85-1156 or PCCA #85-1845) into sterile container.
6. Perform Bubble Point test on the used filter:
   a. Minimum bubble point is ≥ 50 psi
   b. Actual bubble point = _____psi (CIRCLE) PASS FAIL
8. Physical description: clear, dark blue/purple solution with no noted visible particulates

Date entered: 4/5/2023 6:54:53 AM Last modified: 4/5/2023 6:56:23 AM By: ADMINISTRATOR
Checked by: _____ Date: ___/___/_____

SAMPLE COMPOUNDING RECORD



Logged Formula Worksheet
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Quantity made: 17 ML
Batch yield: 15.000
Qty remaining: 0.000
Date made: 5/1/2023
Packaging: PUMP/SYRINGES
Labeling: FOR EXTERNAL USE ONLY
Stability information:
Storage information:
Hazard codes:

Pricing calculations from the log
Time to make: 0

Ingredients	NIOSH Hazard	Sch.	Quantity used	QS	(Balance)	Actual cost & date

$3.07

Date entered: 5/1/2023
Last modified: 5/1/2023
By: ADMINISTRATOR
Checked by: ______ Date: __/__/____

HOW WE COMPOUND

- CR record is generated and directed to appropriate area – NS, NS-HD, Sterile or Nonsterile HD
- APIs measured and mixed following formula/CR directions and documented
- CR also includes order of mixing and quality assessments (e.g. appearance, pH, color, viscosity, final weight or volume, number of units)
- CSPs tested for sterility and BET
- Final preparation labeled per USP with storage requirements
- All personnel involved document steps in the process for audit trail from data entry to final preparation

HOW WE COMPOUND

EQUIPMENT

- Analytical balances – calibrated and certified annually
- Each ingredient weight or volume is documented (printed) on the CR
- All equipment is dedicated to HD – (e.g. M&P, capsule machines, electronic mortars and pestles, ointment mill, RDT and treat molds)
- C-PECs are externally vented
- C-SECs are externally vented and pressures, temp and humidity checked daily
- Certification of HD labs performed every six months

ADDITIONAL CONSIDERATIONS

- SDSs access at all computer terminals – personnel trained on access and review
- Spill team – consists of sterile and nonsterile HDDP and HR manager
- Spill drills conducted annually
- Quality and general pharmacy meetings every month – including discussion of issues with HD
- Hazardous communication policy accessible at all times
- Dedicated and laundered scrubs for HD team

CONCLUSION

- Community compounding practice meets needs of outpatients not met by manufactured medications and home infusion services (human and animal)
- Investment in facility and personnel requirements for community-based HD practice is significant
- Personnel training and competency reviews ensure compliance with USP standards
- There is no substitute for constant vigilance, which underscores the important role of the DP

REFERENCES

- U.S. Pharmacopeia. USP. http://www.usp.org/. Accessed May 1, 2023.
- *Compounding Compliance SOPs and Staff Training*, Brenda Jensen, CPhT, CNMT, MBA
- *Hazardous Drug Compounding Pharmacy Technician Education*, ASHP Section Advisory Group on Advancing Pharmacy Practice with Technicians 2018-2019