MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Bacitracin 400 U/mL, Neomycin 3.5 mg/mL, Polymyxin B Sulfate 5000 U/mL Topical Wound Liquid (Solution, 500 mL)	FIN	F 007 031v3

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Bacitracin (Micronized), USP	200 000	Units				
Neomycin Sulfate, USP	TBD					
Polymyxin B Sulfate, USP	2 500 000	Units				
Sodium Chloride, USP	3.97	g				
Benzalkonium Chloride Solution (50%), NF	0.2	mL				
Sterile Water for Injection, USP	400.0	mL				
Sterile Water for Injection, USP	q.s. to 500.0	mL				
Sodium Hydroxide 10% Solution	As required					
Hydrochloric Acid 10% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):*	*Neomycin Sulfate, Polymyxin B Sulfate, Benzalkonium Chloride Solution*
Hygroscopic *(protect from moisture whenever possible):*	*Bacitracin, Neomycin Sulfate, Polymyxin B Sulfate Benzalkonium Chloride Solution*
Air Sensitive *(protect from air whenever possible):*	*Benzalkonium Chloride Solution*
Metal Reactive *(do not allow to come into contact):*	*Benzalkonium Chloride Solution*
Oxygen Sensitive *(protect from oxygen whenever possible):*	*Neomycin Sulfate*

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SPECIAL PREPARATORY CONSIDERATIONS (CONTINUED)

Suggested Preparatory Guidelines

☐ Non-Sterile Preparation ■ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, pH testing and sterility considerations during preparation, it is suggested to measure an additional **1 to 3%** of the required quantities of ingredients.

Special Instruction: This formula may contain one or more Active Pharmaceutical Ingredients (APIs) that may be classified as hazardous, please refer & verify the current NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings. At this time, **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** is informational and not compendially applicable unless otherwise specified by regulators and enforcement bodies. For information on the scope, intended applicability, and implementation context for USP General Chapter <800>, see: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797* and *USP 800* when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All heat stable, reusable materials and equipment must be sterilized and depyrogenated by dry heat sterilization at 250°C for 2 hours prior to use.

Compounder needs to verify as per USP, if every batch of final product compounded using this procedure must be sterility and endotoxin tested before being dispensed.

All required personal protective equipment (sterile and hazardous if applicable), such as but not limited to, gowns, aprons, sleeves, gloves both inner and outer if applicable, shoe covers, hairnet, head cap, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

If applicable, follow all required procedures for hazardous drug handling including but not limited to procurement, transport, storage, preparation, dispensing, administration, clean up (spills) & disposal.

Filter integrity must be validated by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.

If you are a registered 503B facility, please refer to all relevant guidance documents including but not limited to the Code of Federal Regulations (CFR), Guidance for Industry (GFIs) and Compliance Policy Guides (CPGs).

This procedure requires the use of very small quantities of ingredients. All calculations and preparation techniques must be verified before dispensing the final product.

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SUGGESTED PREPARATION (for 500 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Bacitracin (Micronized), USP §	200 000	Units			
Neomycin Sulfate, USP §	TBD				
Polymyxin B Sulfate, USP §	2 500 000	Units			
Sodium Chloride, USP §	3.97	g			
Benzalkonium Chloride Solution (50%), NF §	0.2	mL			
Sterile Water for Injection, USP §	400.0	mL			
Sterile Water for Injection, USP §	q.s. to 500.0	mL			
Sodium Hydroxide 10% Solution §	As required				
Hydrochloric Acid 10% Solution §	As required				

* Takes into account increased batch size conversions and density conversions, if required.
§ Weigh / measure just prior to use.

Preparatory Instruction **IMPORTANT: All preparatory procedures must be performed using proper Aseptic Technique**	
1.	**Equipment sterilization:** Following the manufacturer's specifications, sterilize and depyrogenate all heat stable, reusable materials and equipment, then return to ambient temperature.

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2. **Ingredient quantification:**

A. Determine the potency of Bacitracin (Micronized) based on the certificate of analysis:

	100%
MINUS	
Loss on drying (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of dried Bacitracin (Micronized), in decimal	_____
MULTIPLIED BY	
Assay on dried basis (from Certificate of Analysis)	_____ units/mg
EQUALS	
i. Potency of Bacitracin (Micronized) in (units/mg)	_____ **units/mg**

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Bacitracin required to make a 500 mL batch of Bacitracin 400 U/mL Topical Wound Liquid:

Quantity of Bacitracin (Micronized) (in Units) required for 500 mL	200 000 U
DIVIDED BY	
Bacitracin (Micronized) potency in (units/mg) (Step 2Ai)	_____ U/mg
EQUALS	
i Quantity of Bacitracin (Micronized) (in milligrams) needed for 500 mL	_____ **mg**
MULTIPLIED BY	
Multiplication factor – milligrams to grams	0.001
EQUALS	
ii Quantity of Bacitracin (Micronized) (in grams) needed for 500 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (1 to 3%)	1.01 to 1.03
EQUALS	
iii Quantity of Bacitracin (Micronized) needed *plus* processing error adjustments	_____ **g**

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4. **Ingredient quantification:**

A. Determine the potency of Neomycin Sulfate based on the certificate of analysis:

	100%
MINUS	
Loss on drying (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of dried Neomycin Sulfate, in decimal	_____
MULTIPLIED BY	
Assay (base equivalent) on dried basis result (from certificate of analysis)	_____ µg/mg
MULTIPLIED BY (Multiplication factor – µg to grams /mg to grams)	0.001
EQUALS	
i. Potency of Neomycin Sulfate (Base equivalent) in g/g	_____

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5. **Ingredient quantification:**

A. Determine the quantity (in g) of Neomycin Sulfate required to make a 500 mL batch of **Neomycin (Base)** 3.5 mg/mL Topical Wound Liquid:

Quantity of **Neomycin (Base)** required for 500 mL	1.750 g
DIVIDED BY	
Potency of Neomycin Sulfate (base equivalent), in g/g (Step 4Ai)	_____
EQUALS	
i. Quantity of Neomycin Sulfate needed for 500 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (1 to 3%)	1.01 to 1.03
EQUALS	
ii. Quantity of Neomycin Sulfate needed *plus* processing error adjustments	_____ **g**

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6. **Ingredient quantification:**

A. Determine the potency of Polymyxin B Sulfate based on the certificate of analysis:

	100%
MINUS	
Loss on drying (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of dried Polymyxin B Sulfate, in decimal	_____
MULTIPLIED BY	
Assay on dried basis (from Certificate of Analysis)	_____ units/mg
EQUALS	
i. Potency of Polymyxin B Sulfate in (units/mg)	_____ **units/mg**

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7. **Ingredient quantification:**

A. Determine the quantity (in g) of Polymyxin B Sulfate required to make a 500 mL batch of Polymyxin B Sulfate 5000 U/mL Topical Wound Liquid:

Quantity of Polymyxin B Sulfate (in Units) required for 500 mL	2 500 000 U
DIVIDED BY	
Polymyxin B Sulfate potency in (units/mg) (Step 6Ai)	_____ U/mg
EQUALS	
i Quantity of Polymyxin B Sulfate (in milligrams) needed for 500 mL	_____ **mg**
MULTIPLIED BY	
Multiplication factor – milligrams to grams	0.001
EQUALS	
ii Quantity of Polymyxin B Sulfate (in grams) needed for 500 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (1 to 3%)	1.01 to 1.03
EQUALS	
iii Quantity of Polymyxin B Sulfate needed *plus* processing error adjustments	_____ **g**

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8. **Powder-liquid preparation:**

A. In the given order, sequentially add the following ingredients to the Sterile Water for Injection (400.0 mL *plus* processing error adjustments):

-Sodium Chloride
-Benzalkonium Chloride Solution (50%)
-Bacitracin (amount determined in Step 3Aiii)
-Neomycin Sulfate (amount determined in Step 5Aii)
-Polymyxin B Sulfate (amount determined in Step 7Aiii)

Specifications: Continuously mix until all solid particles have completely dissolved.

End result: Homogeneous liquid-like solution.

Note: Add the next ingredient, once the previous one has been completely added and dissolved.

9. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 8A).

B. Test the pH of the sample. It should lie between 6.0 and 7.0.

C. If the pH < 6.0, carefully add, in a dropwise fashion, the Sodium Hydroxide 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 10% Solution.
3. Re-test the pH.
4. Continue to add the Sodium Hydroxide 10% solution until the pH of 6.0 to 7.0 is obtained.

IMPORTANT: Do not allow the pH to rise above 7.0.

D. If the pH > 7.0, carefully add, in a dropwise fashion, the Hydrochloric Acid 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Hydrochloric Acid 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Hydrochloric Acid 10% Solution.
3. Re-test the pH.
4. Continue to add the Hydrochloric Acid 10% Solution until the pH of 6.0 to 7.0 is obtained.

IMPORTANT: Do not allow the pH to fall below 6.0.

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10.	**Filling to volume:** A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (500.0 mL *plus* processing error adjustments). Specifications: Continuously mix. End result: Homogeneous liquid-like solution.
11.	**Filtering and transferring:** Aseptically filter the solution through a 0.22-µm sterile filter into the recommended dispensing container (see Packaging requirements). Transfer the remainder into a separate dispensing container. This is to be used as the Test sample for sterility testing.
12.	**Filter integrity test:** Validate filter integrity by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.
13.	**Terminal Sterilization:** In relation to the chemical composition of the formulation, final packaging, etc., select and validate an end-stage sterilization method and follow the manufacturer's specifications.
14.	**Sterility testing:** Validate the Test sample for sterility, in accordance to current USP 797 regulatory guidelines.

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SUGGESTED PRESENTATION

Estimated Beyond-Use Date		24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797.	Packaging Requirements		Sterile, tightly closed, light-resistant dispersing bottle with sterile topical applicators.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	7		Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).
	2	Keep out of reach of children.	8		Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	3	Equilibrate to room temperature before use.	9		Cap tightly after use.
	4	Do not use if product changes color.	10		Discard in the presence of particulate matter.
	5	For topical use only.	11		Protect from light.
	6	May impair mental and/or physical ability. Use care when operating a car or machinery.	12		Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
Pharmacist Instructions		Add any auxiliary labels specific to the active ingredient to the dispensing container as deemed necessary.			
Patient Instructions		Contact your pharmacist in the event of adverse reactions. **IMPORTANT:** The quantity of API administered is directly dependent on the quantity of product applied.			

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