MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Epinephrine 5 mcg/mL, Lidocaine Hydrochloride 10 mg/mL Intravenous Injection (Solution, 3 mL)	FIN	F 004 764v3

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Epinephrine 0.025 mg/mL Stock Solution ††	0.60	mL				
Lidocaine Hydrochloride 12.5 mg/mL Stock Solution †††	2.40	mL				
† **Epinephrine 1 mg/mL Stock Solution**						
Epinephrine, USP	0.100	g				
Sterile Water for Injection, USP	90.0	mL				
Sterile Water for Injection, USP	q.s. to 100.0	mL				
Hydrochloric Acid 10% Solution	As required					
†† **Epinephrine 0.025 mg/mL Stock Solution**						
Epinephrine 1 mg/mL Stock Solution	1.00	mL				
Sodium Chloride, USP	0.36	g				
Sterile Water for Injection, USP	30.0	mL				
Sterile Water for Injection, USP	q.s. to 40.0	mL				
††† **Lidocaine Hydrochloride 12.5 mg/mL Stock Solution**						
Lidocaine Hydrochloride, USP	TBD					
Citric Acid (Anhydrous), USP	0.09	g				
Sodium Citrate (Dihydrate), USP	0.20	g				
Benzyl Alcohol (Parenteral Application), NF	0.1	mL				
Sterile Water for Injection, USP	8.0	mL				
Sterile Water for Injection, USP	q.s. to 10.0	mL				

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):*	*Epinephrine, Benzyl Alcohol*
Narrow Therapeutic Index	*Lidocaine Hydrochloride*
Air Sensitive *(protect from air whenever possible):*	*Epinephrine*
Moisture Sensitive *(protect from humidity whenever possible):*	*Citric Acid*

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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, sterility and endotoxin testing considerations during preparation, it is suggested to measure an additional **30 to 40%** 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).

Lidocaine Hydrochloride has a Narrow Therapeutic Index.

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 3 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Epinephrine 0.025 mg/mL Stock Solution †† §	0.60	mL			
Lidocaine Hydrochloride 12.5 mg/mL Stock Solution ††† §	2.40	mL			
† **Epinephrine 1 mg/mL Stock Solution**					
Epinephrine, USP §	0.100	g	---	---	
Sterile Water For Injection, USP §	90.0	mL	---	---	
Sterile Water For Injection, USP §	q.s. to 100.0	mL	---	---	
Hydrochloric Acid 10% Solution §	As required		---	---	
†† **Epinephrine 0.025 mg/mL Stock Solution**					
Epinephrine 1 mg/mL Stock Solution §	1.00	mL	---	---	
Sodium Chloride, USP §	0.36	g	---	---	
Sterile Water for Injection, USP §	30.0	mL	---	---	
Sterile Water for Injection, USP §	q.s. to 40.0	mL	---	---	
††† **Lidocaine Hydrochloride 12.5 mg/mL Stock Solution**					
Lidocaine Hydrochloride, USP §	TBD		---	---	
Citric Acid (Anhydrous), USP §	0.09	g	---	---	
Sodium Citrate (Dihydrate), USP §	0.20	g	---	---	
Benzyl Alcohol (Parenteral Application), NF §	0.1	mL	---	---	
Sterile Water for Injection, USP §	8.0	mL	---	---	
Sterile Water for Injection, USP §	q.s. to 10.0	mL	---	---	

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

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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.

2. † **Epinephrine 1 mg/mL Stock Solution preparation:**

   A. Incrementally add the Epinephrine (0.100 g) to the Sterile Water for Injection (90.0 mL). Then, **VERY SLOWLY** add and mix the Hydrochloric Acid 10% Solution in a drop-wise manner into the mixture. Test the pH of the solution. It should lie between 4.8 and 5.2.

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

   End result: Homogeneous liquid-like solution.

   B. Add additional Sterile Water for Injection to the mixture (Step 2A) to fill to the required amount (100.0 mL).

   Specifications: Continuously mix.

   End result: Homogeneous liquid-like solution.

3. †† **Epinephrine 0.025 mg/mL Stock Solution preparation:**

   A. Sequentially add the following ingredients into the Sterile Water for Injection (30.0 mL).

   -Epinephrine 1 mg/mL Stock Solution (1.00 mL)
   -Sodium Chloride

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

   End result: Homogeneous liquid-like solution.

   B. Add additional Sterile Water for Injection to the mixture (Step 3A) to fill to the required amount (40.0 mL).

   Specifications: Continuously mix.

   End result: Homogeneous liquid-like solution.

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4. **Ingredient quantification:**

A. Determine the potency of Lidocaine Hydrochloride based on the certificate of analysis:

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Lidocaine Hydrochloride, in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
i. Potency of Lidocaine Hydrochloride, in decimal	_____

5. **Ingredient quantification:**

A. Determine the quantity of Lidocaine Hydrochloride required to make a Lidocaine Hydrochloride 12.5 mg/mL Stock Solution, batch size (10 mL):

Quantity of Lidocaine Hydrochloride required for the Stock Solution	0.125 g
DIVIDED BY	
Potency of Lidocaine Hydrochloride, in decimal (Step 4Ai)	_____
EQUALS	
i. Quantity of Lidocaine Hydrochloride needed for the Stock Solution	_____ **g**

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6.	††† **Lidocaine Hydrochloride 12.5 mg/mL Stock Solution preparation:** A. Sequentially add the following ingredients into the Sterile Water for Injection (8.0 mL). -Lidocaine Hydrochloride (amount determined in Step 5Ai) -Citric Acid (Anhydrous) -Sodium Citrate (Dihydrate) -Benzyl Alcohol (Parenteral Application) Specifications: Continuously mix until all solid particles have completely dissolved. End result: Homogeneous liquid-like solution. B. Add additional Sterile Water for Injection to the mixture (Step 6A) to fill to the required amount (10.0 mL). Specifications: Continuously mix. End result: Homogeneous liquid-like solution.
7.	**Medium integration:** A. Incrementally add the Epinephrine 0.05 mg/mL Stock Solution (0.60 mL *plus* processing error adjustments) to the Lidocaine Hydrochloride 12.5 mg/mL Stock Solution (2.40 mL *plus* processing error adjustments). Specifications: Continuously mix. End result: Homogeneous liquid-like solution.
8.	**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 and endotoxin testing.
9.	**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.
10.	**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.

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11.	**Sterility and Endotoxin testing:** Validate the Test sample for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797. BUD based on successful endotoxin test result.	Packaging Requirements	Sterile, tightly closed, light-resistant unit-dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	6	Do not used if product changes color.
	2	Keep out of reach of children.	7	Protect from light.
	3	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).	8	Discard container after use.
	4	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.	9	May impair mental and/or physical ability. Use care when operating a car or machinery.
	5	Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.		
Pharmacist Instructions	Add any auxiliary labels specific to the active ingredients to the dispensing container as deemed necessary.			
Patient Instructions	Contact your pharmacist in the event of adverse reactions.			

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