MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Enoxaparin Sodium 150 mg/mL Intravenous or Subcutaneous Injection (Solution, 100 mL)	FIN	F 008 696

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Enoxaparin Sodium, USP	TBD					
Sterile Water for Injection, USP	80.0	mL				
Sterile Water for Injection, USP	q.s. to 100.0	mL				
Sodium Hydroxide 10% Solution	As required					
Hydrochloric Acid 10% Solution	As required					

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SPECIAL PREPARATORY CONSIDERATIONS

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 **5 to 9%** 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.

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 100 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Enoxaparin Sodium, USP §	TBD				
Sterile Water for Injection, USP §	80.0	mL			
Sterile Water for Injection, USP §	q.s. to 100.0	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 Enoxaparin Sodium based on the certificate of analysis:

	100%
MINUS	
Loss on drying (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of dried Enoxaparin Sodium, in decimal	_____
MULTIPLIED BY	
Assay on dried basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
i. Potency of Enoxaparin Sodium, in decimal	_____

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Enoxaparin Sodium required to make a Enoxaparin Sodium 150 mg/mL Injection, batch size (100 mL):

Quantity of Enoxaparin Sodium required for a 100 mL Injection	15.000 g
DIVIDED BY	
Potency of Enoxaparin Sodium, in decimal (Step 2Ai)	_____
EQUALS	
i. Quantity of Enoxaparin Sodium needed for a 100 mL Injection	_____ **g**
MULTIPLIED BY	
Processing error adjustments (5 to 9%)	1.05 to 1.09
EQUALS	
ii. Quantity of Enoxaparin Sodium needed *plus* processing error adjustments	_____ **g**

4. **Powder-liquid preparation:**

A. Incrementally add the Enoxaparin Sodium (amount determined in Step 3Aii) to the Sterile Water for Injection (80.0 mL *plus* processing error adjustments).

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

End result: Homogeneous liquid-like solution.

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5. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 4A).

B. Test the pH of the sample. It should lie between 5.5 and 7.5.

C. If the pH < 5.5 carefully add in a dropwise manner 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.
2. Re-test the pH.
4. Continue to add the Sodium Hydroxide 10% Solution until the pH of 5.5 to 7.5 is obtained.

IMPORTANT: Do not allow the pH to rise above 7.5.

D. If the pH > 7.5, carefully add in a dropwise manner 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 5.5 to 7.5 is obtained.

IMPORTANT: Do not allow the pH to fall below 5.5.

6. **Filling to volume:**

A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (100.0 mL *plus* processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like solution.

7. **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.

8. **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.

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9.	**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 specification.
10.	**Sterility testing:** Validate the test samples for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		14 days, refrigerated, as per USP. BUD based on a successful sterility and endotoxin test result.	Packaging Requirements	Sterile, tightly closed unit-dose vial.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	6	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	2	Keep out of reach of children.	7	Keep refrigerated (2°C – 8°C). Do not freeze.
	3	Equilibrate to room temperature before use.	8	**Preservative free solution, single use only. Discard any unused portion.**
	4	Do not use if product changes color.	9	Discard in the presence of particulate matter.
	5	Discard container after use.		
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.			

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REFERENCES

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