MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Methadone Hydrochloride 10 mg/mL Injection (Solution, 50 mL)	FIN	F 001 938

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Methadone Hydrochloride, USP	0.500	g				
Chlorobutanol (Anhydrous), NF	0.25	g				
Sodium Chloride, USP	0.34	g				
Sterile Water for Injection, USP	40.0	mL				
Sterile Water for Injection, USP	q.s. to 50.0	mL				
Sodium Hydroxide 1N Solution	As required					

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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Controlled substance *(adhere to proper handling and documentation procedures)* — *Methadone Hydrochloride*

Light sensitive *(protect from light whenever possible):* — *Methadone Hydrochloride*

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 **10 to 12%** of the required quantities of ingredients.

Special Instruction: This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797*. 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.

Protective apparel, such as a sterile gown, sterile gloves, shoe covers, head cap, eyewear and face-masks should always be worn. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

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.

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 50 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Methadone Hydrochloride, USP §	0.500	g			
Chlorobutanol (Anhydrous), NF §	0.25	g			
Sodium Chloride, USP §	0.34	g			
Sterile Water for Injection, USP §	40.0	mL			
Sterile Water for Injection, USP §	q.s. to 50.0	mL			
Sodium Hydroxide 1N 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.

2. **Powder preparation:**

   A. Combine and triturate the following ingredients together:

   -Methadone Hydrochloride
   -Chlorobutanol (Anhydrous)
   -Sodium Chloride

   End result: Fine homogeneous powder blend.

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3. **Powder to medium integration:**

A. Incrementally add the fine homogeneous powder blend (Step 2A) to the following ingredient:

- Sterile Water for Injection (40.0 mL *plus* processing error adjustments)

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

End result: Homogeneous liquid-like solution.

4. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 3A).

B. Test the pH of the sample. It should lie between 4.5 and 5.5.

C. If the pH < 4.5, carefully add in a dropwise manner the Sodium Hydroxide 1N Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 1N Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 1N Solution.
3. Re-test the pH.
4. Continue to add the Sodium Hydroxide 1N Solution until the pH of 4.5 to 5.5 is obtained.

IMPORTANT: Do not allow the pH to rise above 5.5.

5. **Filling to volume:**

A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (50.0 mL *plus* processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like solution.

6. **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.

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7.	**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.
8.	**Sterility testing:** Validate the Test sample for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.

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SUGGESTED PRESENTATION

Estimated Beyond-Use Date		14 days, refrigerated. BUD based on a successful sterility and endotoxin test result.	Packaging Requirements		Sterile, light resistant unit dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		8	Discard container after use.
	2	Keep out of reach of children.		9	Keep refrigerated. Do not freeze.
	3	Protect from light.		10	**Controlled substance. Dangerous unless used as directed**
	4	**May produce psychological and/or physical dependence.**		11	**Do not take alcohol, sleep aids, tranquilizers or other CNS depressants.**
	5	**May impair mental and/or physical ability. Use care when operating a car or machinery.**		12	**Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.**
	6	Do not use if discolored.		13	Equilibrate to room temperature before use
	7	Discard in the presence of particulate matter.			
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary				
Patient Instructions	Contact your pharmacist in the event of adverse reactions.				

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REFERENCES

1. USP <797> Pharmaceutical Compounding – Sterile Preparations. US Pharmacopeial Convention, Inc. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. 2004: 2461.
2. Sodium Chloride. In: Rowe RC. *Handbook of Pharmaceutical Excipients, 4th Edition*. American Pharmaceutical Association; 2003: 556.
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4. Chapter 18: Tonicity, Osmoticity, Osmolaltiy and Osmolarity. In: Gennaro AR. *Remington: The Science and Practice of Pharmacy, 20th Edition.* Baltimore, MD: Lippincott Williams & Wilkins; 2000: 246.
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