MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
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Suggested Formula	Levothyroxine Sodium 38 µg, Liothyronine 9 µg Slow Release Oral Capsules (Powder Blend, 100 x Size #1 Capsules)	FIN	F 007 048

IMPORTANT: This formula is for a **slow release** capsule. Please note that the rate of drug release may not be identical to the release rates of commercial formulations labeled as sustained-release, sustained action, prolonged-action, controlled-release, extended-release, timed-release, targeted release, long-acting, modified-release, etc. As such, this preparation should be prescribed and monitored under the close supervision of the prescribing physician.

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Levothyroxine Sodium 2% Stock Powder Blend †	0.190	g				
Liothyronine 0.5% Stock Powder Blend ††	0.180	g				
Hypromellose (4000 CPS) (Methocel E4M), USP	TBD					
Cellulose (Microcrystalline), NF	TBD					
Sodium Chloride, USP	As required					
† **Levothyroxine Sodium 2% Stock Powder Blend**						
Levothyroxine Sodium, USP	TBD					
Cellulose (Microcrystalline), NF	q.s. to 5.00	g				
†† **Liothyronine 0.5% Stock Powder Blend**						
Liothyronine Sodium, USP	TBD					
Cellulose (Microcrystalline), NF	q.s. to 20.00	g				

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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Narrow Therapeutic Index:	*Levothyroxine Sodium*
Light sensitive *(protect from light whenever possible):*	*Levothyroxine Sodium*
Hygroscopic *(protect from moisture whenever possible):*	*Cellulose, Hypromellose, Levothyroxine Sodium*
Oxygen Sensitive *(protect from oxygen whenever possible):*	*Levothyroxine Sodium*

Suggested Preparatory Guidelines

■ Non-Sterile Preparation ☐ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error considerations during preparation, it is suggested to measure an additional **5 to 9%** of the required quantities of ingredients.

Special Instruction: Protective apparel, such as a lab coat, disposable gloves, eyewear and face-masks should always be worn.

Levothyroxine Sodium 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 100 Size #1 Capsules)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Levothyroxine Sodium 2% Stock Powder Blend † §	0.190	g			
Liothyronine 0.5% Stock Powder Blend †† §	0.180	g			
Hypromellose (4000 CPS) (Methocel E4M), USP §	TBD				
Cellulose (Microcrystalline), NF §	TBD				
Sodium Chloride, USP	As required				
† **Levothyroxine Sodium 2% Stock Powder Blend**					
Levothyroxine Sodium, USP §	TBD		---	---	
Cellulose (Microcrystalline), NF §	q.s. to 5.00	g	---	---	
†† **Liothyronine 0.5% Stock Powder Blend**					
Liothyronine Sodium, USP	TBD		---	---	
Cellulose (Microcrystalline), NF §	q.s. to 20.00	g	---	---	

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

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Preparatory Instruction

1. **Ingredient quantification:**

A. Determine the potency of Levothyroxine Sodium based on the certificate of analysis:

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of Levothyroxine Sodium remaining after drying, in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
i. Potency of Levothyroxine Sodium, in decimal	_____

2. **Ingredient quantification:**

A. Determine the quantity of Levothyroxine Sodium required to make a Levothyroxine Sodium 2% Stock Powder Blend, batch size (5 g):

Quantity of Levothyroxine Sodium required for the Stock Powder Blend	0.100 g
DIVIDED BY	
Potency of Levothyroxine Sodium, in decimal (Step 1Ai)	_____
EQUALS	
i. Quantity of Levothyroxine Sodium needed for the stock powder blend	_____ **g**

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3. † **Levothyroxine Sodium 2% Stock Powder Blend Preparation:**

A. Triturate the Levothyroxine Sodium (amount determined in Step 2Ai) to form a fine, homogeneous powder.

B. By geometric addition, combine and mix the following ingredients together to form a homogeneous powder blend:

-Fine, homogeneous powder (Step 3A)
-Cellulose (Microcrystalline) (q.s. to 5.00 g)

4. **Ingredient quantification:**

A. Determine the potency of Liothyronine Sodium based on the certificate of analysis:

	100%
MINUS	
Loss on drying result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of dried Liothyronine Sodium, in decimal	_____
MULTIPLIED BY	
Assay on dried basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Potency of Liothyronine Sodium on dried basis, in decimal	_____
DIVIDED BY (Salt to Base conversion)	1.0338
EQUALS	
i. Potency of Liothyronine Sodium (base equivalent), in decimal	_____

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5. **Ingredient quantification:**

A. Determine the quantity of Liothyronine Sodium required to make a Liothyronine 0.5% Stock Powder Blend, batch size (20 g):

Quantity of Liothyronine (base) required for the Stock Powder Blend	0.100 g
DIVIDED BY	
Potency of Liothyronine Sodium (base equivalent), in decimal (Step 4Ai)	_____
EQUALS	
i. Quantity of Liothyronine Sodium needed for the stock powder blend	_____ **g**

6. †† **Liothyronine 0.5% Stock Powder Blend Preparation:**

A. Triturate the Liothyronine Sodium (amount determined in Step 5Ai) to form a fine, homogeneous powder.

B. By geometric addition, combine and mix the following ingredients together to form a homogeneous powder blend:

-Fine, homogeneous powder (Step 6A)
-Cellulose (Microcrystalline) (q.s. to 20.00 g)

7. **Excipient requirements for 100 x Size #1 Capsules**

A. Calculate the amount of Cellulose (Microcrystalline) and Hypromellose (4000 CPS) (Methocel E4M) required for the batch. Refer to attached appendix for details.

8. **Powder preparation:**

A. By geometric addition, combine and mix the following ingredients together:

-Levothyroxine Sodium 2% Stock Powder Blend (0.190 g *plus* processing error adjustments)
-Liothyronine 0.5% Stock Powder Blend (0.180 g *plus* processing error adjustments)
-Cellulose (Microcrystalline) (Quantity determined in appendix **(I)**)
-Hypromellose (4000 CPS) (Methocel E4M) (Quantity determined in appendix **(K)**)

End result: Homogeneous powder blend.

B. Pass the above powder mixture through a 40 or 50 mesh sieve.

C. Mix the sieved powder blend using a manual tumbler mixer to ensure homogeneity.

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9.	**Product transfer:** Fill each of 100 Size #1 Opaque Capsules with the homogeneous powder blend (Step 8C). Close each capsule tightly. Clean each capsule by placing the capsules in a container filled with Sodium Chloride, and then gently rolling the container. Pour the container contents into a 10-mesh sieve, and allow the Sodium Chloride to pass through. Finally, roll the capsules on a cloth-covered surface.
10.	**Validation technique:** The final weight of each capsule (not including capsule shell) should fall between 90 and 110% of the theoretically calculated weight, in accordance to USP 795 guidelines. The theoretically calculated weight can be determined by adding the amount in appendix **(D) + (G) + 0.0037 g** together.
11.	**Product transfer:** Transfer the final product into the specified dispensing container (see "Packaging Requirements").

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		6 months, as per USP*.	Packaging Requirements	Tightly closed, light-resistant capsule shells and vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	5	Keep in a dry place.
	2	Keep out of reach of children.	6	Protect from light.
	3	Keep at room temperature (20°C – 23°C).	7	Cap tightly after use.
	4	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 API to the dispensing container as deemed necessary.			
Patient Instructions	Contact your pharmacist in the event of adverse reactions.			

*** The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.**

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Appendix	Calculating the quantity of excipient required for the batch		

Procedure

1. **Capsule filling:**

   a. For each ingredient powder below, determine the average capsule fill weight by filling and weighing five TARED CAPSULES. Do not forget to divide the total weight by 5 to obtain an average capsule fill weight.

   Plug each amount into Step 2, column B.

2. **Volume Percent Occupied:**

Ingredients	**Column A** Quantity Required per capsule	**Column B** Average capsule fill weight	**Column C** A/B × 100 equals percent filled
a. Hypromellose	_____ **g (D)** (0.4 × column B)	_____ **g**	40%
b. Cellulose (Microcrystalline)		_____ **g**	
c. Total (add column C together)			40 %

3. **Calculate the quantity of Cellulose (Microcrystalline) and Hypromellose required for the batch:**

   a. Percent of Cellulose (Microcrystalline) required = 100% – 40% — 60 % **(E)**

   b. Average capsule fill weight of Cellulose (Microcrystalline) (from column B, Step 2b): _____ g **(F)**

   c. Quantity of Cellulose (Microcrystalline) required per capsule = [(E) ÷ 100 × (F)] – 0.0037 g* _____ g **(G)**
   *quantity of Levothyroxine Sodium and Liothyronine Stock Powder blend per capsule

   d. Total Quantity of Cellulose (Microcrystalline) required for the batch = 100 capsules × (G) _____ g **(H)**

   e. Total quantity of Cellulose (Microcrystalline) *plus* processing error = (H) × 1.05-1.09 _____ g **(I)**

   f. Total quantity of Hypromellose required for the batch = 100 capsules × (D) _____ g **(J)**

   g. Total quantity of Hypromellose *plus* processing error = (J) × 1.05-1.09 _____ g **(K)**