MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Tadalafil 23 mg Oral Rapid-Dissolve Tablets (Solid Suspension, 30 × 750 mg [0.93 mL] Tablets)	FIN	F 007 784v2

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Tadalafil, USP	0.690	g				
Mango Flavor (Powder)	0.23	g				
Raspberry Flavor (Powder)	0.12	g				
Vanillin Flavor (Powder)	0.06	g				
Stevia Powder (Stevioside)	0.03	g				
Medi-RDT Base	TBD					

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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Hygroscopic *(protect from moisture whenever possible):* *Medi-RDT Base, Stevia Powder*

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 **12 to 15%** 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, 2016. **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** was formally published February 1, 2016 in the First Supplement to USP 39-NF 34 and has a delayed **official implementation date of December 31st, 2019**.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 795* and *USP 800*, when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All required personal protective equipment (hazardous if applicable), such as but not limited to, lab coat, protective sleeves, gloves both inner and outer if applicable, dedicated shoe covers, hairnet, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times.

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.

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 30 Tablets)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ___	Processing Error	Qty. to measure
Tadalafil, USP	0.690	g			
Mango Flavor (Powder)	0.23	g			
Raspberry Flavor (Powder)	0.12	g			
Vanillin Flavor (Powder)	0.06	g			
Stevia Powder (Stevioside) §	0.03	g			
Medi-RDT Base §	TBD				

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

Preparatory Instruction	
1.	**Mold calibration:** Determine the required quantity of Medi-RDT Base for 30 tablets based on the actual size of the tablet mold being used. Refer to the Appendix for details.
2.	**Powder preparation:** A. Pass the Medi-RDT Base through a 40 or 50 mesh sieve and weigh the required quantity (amount calculated in Appendix Step 6Aiii). B. By geometric addition, combine and triturate the following ingredients together to form a homogeneous powder blend: -Tadalafil -Mango Flavor (Powder) -Raspberry Flavor (Powder) -Stevia Powder (Stevioside) -Vanillin Flavor (Powder) C. By geometric addition, combine and mix (DO NOT TRITURATE), using a manual tumbler mixer, the following ingredients together to form a homogeneous powder blend: -Sieved Medi-RDT Base (Step 2A) -Homogeneous powder blend (Step 2B) Note: Do not use excessive force as Medi-RDT Base should not be triturated. D. Prior to filling the tablet mold cavities, pass the homogeneous powder blend (Step 2C) through a 40 or 50 mesh sieve to improve flow properties and obtain content uniformity.

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3. **Mold filling and heating:**

A. Fill the 30 tablet mold cavities by tapping and pressing the sieved homogeneous powder blend (Step 2D) into the cavities using the upper part of the mold. Repeat at least three times to ensure the cavities are completely filled. If necessary, add additional powder blend.

B. Gently heat the powder blend to 105°C – 110°C for 10 – 15 minutes. Do not overheat.

Specifications: Heat by placing the filled mold (base cavity plate only) in an appropriate oven, preheated to 105°C – 110°C.

End Result: Homogeneous solid dispersion.

4. **Cooling:**

A. Carefully remove the tablet mold from the heated oven, using a hot hand protector.

B. Immediately remove the tablets by flipping over the mold onto a piece of wax or ointment paper and gently tapping the mold with a mini mallet.

Note: Hold the tablet mold in place while tapping to avoid shaking and breaking the tablets.

C. Allow the tablets to cool for an additional 30 minutes at controlled temperature and relative humidity.

5. **Validation technique:**

A. Weigh 6 tablets separately.

B. The final weight of each tablet from Step 5A (not including the weight of the tablet mold) should be between 90 and 110% of the theoretically calculated weight (Appendix, Step 4B), in accordance to USP guidelines.

6. **Product transfer:**

Transfer the final product into the specified dispensing container (see “Packaging Requirements”).

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SUGGESTED PRESENTATION

Estimated Beyond-Use Date		6 months, as per USP*.	Packaging Requirements		Manually put into light-resistant Medi-RDT blisters and cold seal with foil labels.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	5		Cap tightly after use.
	2	Keep out of reach of children.	6		Keep in a dry place.
	3	Keep at room temperature (20°C – 23°C).	7		Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.
	4	May impair mental and/or physical ability. Use care when operating a car or machinery.	8		Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary.				
Patient Instructions	If allergic reactions occur, consult your pharmacist.				

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

REFERENCES

1. Tablets. In: Allen, LV, Jr. *The Art, Science and Technology of Pharmaceutical Compounding Fifth Edition.* American Pharmaceutical Association; 2016: 207.
2. Tadalafil . In: Sweetman SC, ed. *Martindale: The Complete Drug Reference, 36th Edition.* London, England: The Pharmaceutical Press; 2009: 2196.
3. Tadalafil (Monograph). In: O'Neil MJ. *The Merck Index 15th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #9157.
4. Tadalafil (Monograph). *United States Pharmacopeia XL / National Formulary 35*. Rockville, MD. US Pharmacopeial Convention, Inc. 2017: 6310.
5. USP <795>. *United States Pharmacopeia XL / National Formulary 35.* Rockville, MD. US Pharmacopeial Convention, Inc. 2017: 675.

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Appendix	Tablet mold calibration		

SUGGESTED CALCULATION

Preparatory Instruction	
1.	**API weighing:** A. Pass the Medi-RDT Base through a 40 or 50 mesh sieve. B. Weigh and / or measure the following ingredients: **Notes:** Measure the exact amount specified. Do not consider processing error for calibration step. Data within this calibration table are based on a 0.93 mL mold size.
2.	**Mold filling and heating:** A. Fill 5 tablet mold cavities with the Medi-RDT Base. B. Tap and press the powder blend, with the upper part of the mold, three times in the cavities to be sure they are completely filled. If necessary, add additional powder blend to fill the cavities completely. C. Gently heat the powder blend to 105°C – 110°C for 15 minutes. Do not overheat. Specifications: Heat by placing the filled mold (base cavity plate only) in an appropriate oven, preheated to 105°C – 110°C. End Result: Homogeneous solid dispersion.

Ingredient	Quantity
Medi-RDT Base	9.08 g

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3. **Cooling:**

A. Carefully remove the tablet mold from the heated oven, using a hot hand protector.

B. Immediately remove the tablets by flipping over the mold onto a piece of wax or ointment paper and gently tapping the mold with a mini mallet.

Note: Hold the tablet mold in place while tapping to avoid shaking and breaking the tablets.

C. Allow the tablets to cool for an additional 30 minutes at controlled temperature and relative humidity.

4. **Calculate the average tablet weight:**

A. Weigh the five tablets and record the total weight here (not including the weight of the empty tablet mold): _____ g

B. Calculate the average tablet weight:

Combined weight of the tablets (from Step 4A)	_____ g
DIVIDED BY	
Number of tablets	5
EQUALS	
Average (theoretical) tablet weight*	_____ **g**

***Note:** The weight of the Rapid-Dissolving Tablets is mainly affected by factors such as compression force, flow properties of the powder mixture (flow properties will vary depending on the Active Pharmaceutical Ingredient(s) and excipients in the formulation) and particle size distribution. The mixture must be sieved prior to filling.

The expected average weight of RDT's are as follows (data based on various experiments/troubleshooting completed in the past):

750mg ± 30mg (720mg - 780mg)
200mg ± 10mg (190mg - 210mg)
150mg ± 7.5mg (142.5mg - 157.5mg)
75mg ± 5mg (70mg - 80mg)

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Appendix	Tablet mold calibration		

5. **Ingredient calculation:**

A. Calculate the quantity of Medi-RDT Base required for 30 tablets:

Average tablet weight (from Step 4B)	_____ g
MINUS	
Quantity (in g) of API and other ingredients per tablet	0.038 g
EQUALS	
i. Quantity of Medi-RDT Base required per tablet	_____ g
MULTIPLIED BY	
Number of tablets required	30
EQUALS	
ii. Total quantity of Medi-RDT Base required for 30 tablets	_____ **g**
MULTIPLIED BY	
Processing error adjustments (12 to 15%)	1.12 to 1.15
EQUALS	
iii. Total quantity of Medi-RDT Base required *plus* processing error adjustments	_____ g