MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

Note: Potassium Clavulanate 31.25 mg/5 mL is equivalent to Clavulanic Acid 26.23 mg/5 mL.

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Amoxicillin (Trihydrate), USP	TBD					
Potassium Clavulanate, USP	0.625	g				
Strawberry Flavor	1.0	mL				
Banana Flavor	0.5	mL				
Stevia Powder	0.50	g				
Medisca Oral Mix (Flavored Suspending Vehicle)	50.0	mL				
Medisca Oral Mix (Flavored Suspending Vehicle)	q.s. to 100.0	mL				
Sodium Hydroxide 10% Solution	As required					
Hydrochloric Acid 10% Solution	As required					

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Hygroscopic *(protect from moisture whenever possible):* *Stevia Powder, Potassium Clavulanate*

Light Sensitive *(protect from light whenever possible):* *Amoxicillin*

Suggested Preparatory Guidelines

■ Non-Sterile Preparation ☐ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error and pH adjustment 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 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.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

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
Amoxicillin (Trihydrate), USP §	TBD				
Potassium Clavulanate, USP §	0.625	g			
Strawberry Flavor	1.0	mL			
Banana Flavor	0.5	mL			
Stevia Powder §	0.50	g			
Medisca Oral Mix (Flavored Suspending Vehicle)	50.0	mL			
Medisca Oral Mix (Flavored Suspending Vehicle)	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.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

Preparatory Instruction

1. **Ingredient quantification:**

A. Determine the potency of Amoxicillin (Trihydrate) based on the certificate of analysis:

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Amoxicillin (Trihydrate), in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ µg/mg
MULTIPLIED BY (Multiplication factor – µg to grams /mg to grams)	0.001
EQUALS	
i. Potency of Amoxicillin (Trihydrate) in g/g	_____

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

2. **Ingredient quantification:**

A. Determine the quantity (in g) of Amoxicillin (Trihydrate) required to make a 100 mL batch of Amoxicillin 125 mg/5 mL Oral Liquid:

Quantity of Amoxicillin required for 100 mL	2.500 g
DIVIDED BY	
Potency of Amoxicillin (Trihydrate), in decimal (Step 1Ai)	_____
EQUALS	
i. Quantity of Amoxicillin (Trihydrate) needed for 100 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (5 to 9%):	1.05 to 1.09
EQUALS	
ii. Quantity of Amoxicillin (Trihydrate) needed *plus* processing error adjustments	_____ **g**

3. **Powder-liquid preparation:**

A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:

-Amoxicillin (Trihydrate) (amount determined in step 2Aii)
-Potassium Clavulanate
-Stevia Powder

B. Combine and mix the following ingredients together to form a homogeneous liquid-like solution:

-Strawberry Flavor
-Banana Flavor

C. Levigate the fine, homogeneous powder blend (Step 3A) with the homogeneous liquid-like solution (Step 3B).

End result: Homogeneous paste-like dispersion.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

4. **Medium integration:**

A. Incrementally add the homogeneous paste-like dispersion (Step 3C) to the Oral Mix (Flavored Suspending Vehicle) (50.0 mL *plus* processing error adjustments).

Specifications: Continuously mix, using high-shear mixing techniques.

End result: Homogeneous liquid-like dispersion.

5. **Filling to volume:**

A. Add additional Oral Mix (Flavored Suspending Vehicle) to the mixture (Step 4A) to fill to the required batch size (100.0 mL *plus* processing error adjustments).

Specifications: Continuously mix, using high-shear mixing techniques.

End result: Homogeneous liquid-like dispersion.

6. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 5A).

B. Test the pH of the sample. It should lie between 6.0 and 6.5.

C. If the pH < 6.0 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 6.0 to 6.5 is obtained.

IMPORTANT: Do not allow the pH to rise above 6.5.

D. If the pH > 6.5, 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 6.0 to 6.5 is obtained.

IMPORTANT: Do not allow the pH to fall below 6.0.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

7.	**Product transfer:** A. Transfer the final product into the specified dispensing container (see "Packaging requirements"). Note: Continuously mix the final product during the transfer process into the recommended dispensing containers in order to maintain homogeneity.

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		**10 days**, refrigerated, as per USP 795*.	Packaging Requirements		- Tightly closed, light-resistant dispensing bottle. - To be administered with a metered measuring device.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		6	Keep out of reach of children.
	2	Keep refrigerated (2°C – 8°C). Do not freeze.		7	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	3	**Shake well before use.**		8	Cap tightly after use.
	4	May impair mental and/or physical ability. Use care when operating a car or machinery.		9	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
	5	Protect from light.			
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.			

*** If the API or any other components in the CNSP have an expiration date that is earlier than the assigned BUD, the expiration date supersedes the assigned BUD and must be the assigned shortest date.**

Suggested Formula	Amoxicillin 125 mg/5 mL, Potassium Clavulanate 31.25 mg/5mL Oral Liquid (Suspension, 100 mL)	FIN	F 009 779

REFERENCES

1. Suspensions. In: Allen, LV, Jr. *The Art, Science, and Technology of Pharmaceutical Compounding Fifth Edition.* American Pharmacists Association; 2016: 279.
2. Amoxicillin. In: Sweetman SC, ed. *Martindale: The Complete Drug Reference, 38th Edition.* London, England: The Pharmaceutical Press; 2014: 216.
3. Potassium Clavulanate. In: Sweetman SC, ed. *Martindale: The Complete Drug Reference, 38th Edition.* London, England: The Pharmaceutical Press; 2014: 268.
4. Amoxicillin (Monograph). In: O'Neil MJ. *The Merck Index 15th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2012: Monograph #574.
5. Clavulanate Acid (Monograph). In: O'Neil MJ. *The Merck Index 14th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2006: #2341.
6. Amoxicillin Trihydrate-Clavulanate Potassium. In: Trissel LA. *Trissel's Stability of Compounded Formulations, 5rd Edition.* American Pharmaceutical Association; 2012: 38.
7. Amoxicillin (Monograph). *United States Pharmacopeia / National Formulary*. Rockville, MD. US Pharmacopeial Convention, Inc. 2022.
8. Clavulanate Potassium (Monograph). *United States Pharmacopeia / National Formulary.* Rockville, MD. US Pharmacopeial Convention, Inc. 2022.
9. USP <795>. *United States Pharmacopeia / National Formulary*. Rockville, MD. US Pharmacopeial Convention, Inc. 2022.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

	Excipient and Oral Vehicle Alternatives Addendum	FIN	

Please note that Medisca Network formulas are developed based on current information and available scientific literature at the time of formulation development. Modifications to the formulation by the compounder may be warranted for various situations such as: patient specific considerations, updated compatibility information or supply chain issues for excipients needed.

To aid the compounder to find alternatives to formulations when ingredients are not available, the following tables were created as options for antioxidants, oral bases, pH adjusters, preservatives and suspending agents used when compounding oral formulations.

Please verify the suitability of the alternative ingredient selected, for its compatibility and stability within the formulation.

From the tables below, only select the necessary, suitable option, as needed.

Table 1: Options for Antioxidants used in Oral Preparations

ANTIOXIDANT	SOLUBLE IN OIL OR WATER	TYPICAL CONCENTRATION (%)
Sodium Metabisulfite	Water	0.1-1.0 w/v
Vitamin E (Alpha Tocopherol)	Oil	0.001-0.05 v/v

Table 2.1: Medisca Oral Bases Options

	ORAL SUSPEND	ORAL SYRUP	ORAL MIX	ORAL SYRUP, SF	ORAL MIX, SF
APPEARANCE	Viscous off-white aqueous liquid. Thixotropic.	Clear to slightly tinted liquid	Off-white aqueous liquid	Clear to slightly tinted liquid	Off-white aqueous liquid
TASTE	Bland; Unsweetened	Cherry			
APPLICATION	Pediatric and Geriatric compounded suspensions			Pediatric and Geriatric sugar-free compounded suspensions for patients with special dietary restrictions	
INTENDED USE	Suspending vehicle	Flavored syrup vehicle	Flavored suspending vehicle	Sugar-free flavored syrup vehicle	Sugar-free flavored suspending vehicle
pH	4.0-5.0				
OSMOLALITY (mOsmol/kg) APPROXIMATE	48	2381	1231	1585	795
DYE-FREE AND ALCOHOLOL FREE	Yes				
PRESERVATIVE EFFECTIVENESS	Passes USP microbial challenge test <51>				
STABILITY DATA	BUD studies and publications available at MEDISCA.ca/studies*				

Table 2.2: Perrigo Oral Bases Options

	ORA-PLUS	ORA-SWEET	ORA-BLEND	ORA-SWEET SF	ORA-BLEND SF
APPEARANCE	Translucent, milky white, thixotropic liquid	Clear liquid with a slight tint	Opaque, pinkish liquid	Clear liquid with a slight tint	Opaque, pinkish liquid
TASTE	Very bland taste (no sweeteners or flavors)	Sweet citrus-berry flavor	Sweet citrus-berry flavor	Sweet citrus-berry flavor	Sweet citrus-berry flavor
APPLICATION	Ideal for pediatric, geriatric, and naso-gastric suspensions	Ideal for pediatric and geriatric suspensions			
INTENDED USE	Oral suspending vehicle	Flavored syrup vehicle	Flavored suspending vehicle	Sugar-Free, Alcohol-Free Syrup Vehicle	Flavored Sugar-Free Oral Suspending Vehicle
pH	4.0-4.5				
OSMOLALITY (mOsmol/kg) APPROXIMATE	157	4109	1665	1979	1027
DYE-FREE AND ALCOHOLOL FREE	Dye-free	No	No	Alcohol-free	No

PRESERVATIVE EFFECTIVENESS	Passes USP microbial challenge test <51>
STABILITY DATA	BUD studies and publications available at http://medisca.ca/ora*

Table 2.3 Alternative to Oral Vehicle Option

VEHICLE	**SUSPENDING AGENT**	**SWEETNER**	**FLAVOR**	**PRESERVATIVE**
Methylcellulose Gel 1%		Stevia 0.2-0.5%	0.2-0.5%	N/A (Contained in Methylcellulose Gel 1%)

Table 3.0 Options for pH Adjusters for Oral Preparations

ACIDIFYING AGENTS	**ALKALIZING AGENTS**
Ammonium Chloride	Ammonia Solution
Citric Acid Anhydrous	Potassium Bicarbonate
Hydrochloric Acid	Sodium Bicarbonate
Phosphoric Acid	Sodium Carbonate
Propionic Acid	Sodium Citrate Dihydrate
Sulfuric Acid	Sodium Hydroxide
Tartaric Acid	

Table 4.0 Options for Preservatives for Oral Preparations

PRESERVATIVE	**TYPICAL PERCENTAGES**	**pH of OPTIMAL ACTIVITY**
Alcohol/Ethanol	15-20% (must be above 10%)	15% is necessary to preserve at a pH of 5.0, 18% is necessary to preserve a neutral or alkaline preparation (Shrewsbury, 2001)
Benzalkonium Chloride	0.002-0.1%	4.0-10
Benzoic Acid	0.1-0.3%	Optimum activity occurs at pH below 4.5 (practically inactive over pH 5.0)
Benzyl Alcohol	1-2%	<5.0
Methylparaben	0.015-0.2%	4.0-8.0 (efficacy decreases with increase in pH)
Potassium Sorbate	0.1-0.2%	<6.0
Propylparaben	0.01-0.02%	4.0-8.0 (efficacy decreases with increase in pH)
Sodium Benzoate	0.02-0.5%	2-5 (practically inactive over pH 5.0)
Sorbic Acid	0.05-0.2%	Optimum activity occurs at pH below 4.5 (practically inactive over pH 6.0)

Table 5.0 Options for Suspending Agents for Oral Preparations

SUSPENDING AGENT	**SOLUBLE IN OIL OR WATER**	**TYPICAL CONCENTRATION (%)**
Hypromellose (4000 mPas)	Water	0.25%
Methylcellulose (1500 mPas)	Water	0.5-1.0%
Xanthan Gum	Water	0.25%
Colloidal Silicon Dioxide	Oil	0.5-1.0%

Medisca Network currently has a Formula Beyond-Use Date Databank. This databank lists several formulas that have undergone R&D stability-indicating studies to establish the evidence-based extended BUD. The suggested BUD for a specific formula is based on the **exact execution of the indicated ingredient list, quantities and procedures listed within this formulation. In the case of a R&D Bracketed BUD study, the studied concentration range will be listed and any concentration compounded at or between these strengths may apply the suggested BUD based on the exact execution of the indicated ingredient list, procedures and quantities listed within this formulation.*

If additional information and/or clarification is required, please e-mail our Compounding Services Department at compoundingservices@medisca.net or call 1-866-333-7811.

	Excipient and Oral Vehicle Alternatives Addendum	FIN	

REFERENCES

1.	USP <795>. *United States Pharmacopeia XLIII / National Formulary 38.* Rockville, MD. US Pharmacopeial Convention, Inc. 2020: 7025.
2.	Allen Jr, Loyd V. "Featured excipient: Preservatives." *International Journal of Pharmaceutical Compounding* 7.2 (1999): 142.
3.	Ferreira A: Preparações Orais Líquidas, 3rd edition. 2011.
4.	https://www.medisca.com/NDC_SPECS/MUS/2348/Downloads/ORA%20Base%20Flyer%20EN.pdf Accessed 11/30/2022
5.	https://www.medisca.com/NDC_SPECS/MUS/2512/Downloads/Medisca%20Oral%20Bases%20Sell%20Sheet%20EN.pdf Accessed 11/30/2022