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	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Propofol, USP	1.000	g				
Soybean Oil, USP	10.00	g				
Lecithin, NF	1.2	g				
Glycerin, USP	2.25	g				
Edetate Disodium, USP	0.005	g				
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					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Propofol, Soybean Oil, Lecithin*

Oxygen Sensitive *(protect from oxygen whenever possible):* *Propofol, Soybean Oil, Lecithin*

Hygroscopic *(protect from moisture whenever possible):* *Glycerin, Lecithin, Edetate Disodium*

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	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

SPECIAL PREPARATORY CONSIDERATIONS (CONTINUED)

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.

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	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

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
Propofol, USP §	1.000	g			
Soybean Oil, USP §	10.00	g			
Lecithin, NF §	1.2	g			
Glycerin, USP §	2.25	g			
Edetate Disodium, USP §	0.005	g			
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.
2.	**Preparatory step:** A. Prepare a hot water bath. Specifications: Temperature: 38 to 42°C.

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	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

3. **Powder-liquid preparation:**

A. Using the hot water bath, heat the Sterile Water for Injection (80.0 mL *plus* processing error adjustments) to 38°C ~ 42°C and sequentially add the following ingredients to it:

-Edetate Disodium
-Lecithin
-Glycerin

Specifications: Continuously mix.
Maintain temperature between 38°C and 42°C.

End result: Homogeneous liquid-like dispersion.

Note: Add the next ingredient, once the previous one has been completely added and dispersed.

4. **Powder-liquid preparation:**

A In a separate beaker, using the hot water bath, heat the Soybean Oil to 38°C ~ 42°C and incrementally add the Propofol to it.

Specifications: Continuously mix until all solid particles have completely dissolved.
Maintain temperature between 38°C and 42°C.

End result: Homogeneous liquid-like solution.

5. **Phase Integration:**

A. Incrementally add the homogeneous liquid-like dispersion (Step 3A) to the homogeneous liquid-like solution (Step 4A).

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

End result: Homogeneous liquid-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	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

6. **pH testing:**

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

B. Test the pH of the sample. It should lie between 5.0 and 7.5.

C. If the pH < 5.0, carefully add, in a dropwise fashion, 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.
3. Re-test the pH.
4. Continue to add the Sodium Hydroxide 10% Solution until the pH of 5.0 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 fashion, 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 5.0 to 7.5 is obtained.

IMPORTANT: Do not allow the pH to fall below 5.0.

7. **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. **Homogenize emulsion in a homogenizer until globules are less than 1 µm.**

End result: Homogeneous liquid-like emulsion.

8. **Filtering and transferring:**

A. Aseptically filter the emulsion 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 endotoxins testing.

B. Use a nitrogen blanket technique to remove oxygen from the headspace of the vial.

9. **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.

Suggested Formula	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

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

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797. BUD based on successful endotoxin test result.	Packaging Requirements	Sterile, tightly closed, light-resistant unit-dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	7	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.	8	Do not use if there is evidence of excessive creaming or aggregation, if large droplets are visible, or if there are other forms of phase separation indicating that the stability of the product has been compromised.
	3	Discard container after use.	9	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).
	4	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.	10	Protect from light.
	5	Do not use if product changes color.	11	**Preservative free solution, single use only. Discard any unused portion.**
	6	May impair mental and/or physical ability. Use care when operating a car or machinery.	12	**Shake well before use.**
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary.			

Suggested Formula	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

Patient Instructions	Contact your pharmacist in the event of adverse reactions.

Suggested Formula	Propofol 10 mg/mL Intravenous Injection (Emulsion, 100 mL)	FIN	F 008 701

REFERENCES

1.	Parenteral Preparations. In: Allen, LV, Jr. *The Art, Science, and Technology of Pharmaceutical Compounding Fifth Edition.* American Pharmacists Association; 2016: 399.
2.	Diprivan. In: Canadian Pharmacists Association. *Compendium of Pharmacists and Specialties, 2017*: 1074.
3.	Edetate Disodium. In: Sheskey, P.J., ed. *Handbook of Pharmaceutical Excipients, 8th Edition*. Pharmaceutical Press and American Pharmacists Association; 2017: 347.
4.	Glycerin. In: Sheskey, P.J., ed. *Handbook of Pharmaceutical Excipients, 8th Edition*. Pharmaceutical Press and American Pharmacists Association; 2017: 401.
5.	Lecithin. In: Sheskey, P.J., ed. *Handbook of Pharmaceutical Excipients, 8th Edition*. Pharmaceutical Press and American Pharmacists Association; 2017: 538.
6.	Soybean Oil. In: Sheskey, P.J., ed. *Handbook of Pharmaceutical Excipients, 8th Edition*. Pharmaceutical Press and American Pharmacists Association; 2017: 910.
7.	Chapter 8: Buffered and Isotonic Solutions. In: Sinko, D. J. and Singh, Y. *Martin's Physical Pharmacy and Pharmaceutical Sciences, Sixth Edition.* Philadelphia, PA: Lipponcott Williams & Wilkins; 2011: 163-181.
8.	Chapter 18: Tonicity, Osmoticity, Osmolality and Osmolarity. In: D.B Troy. *Remington: The Science and Practice of Pharmacy, 21st Edition.* Baltimore, MD: Lippincott Williams & Wilkins; 2006: 250~265.
9.	Propofol. In: Brayfield, A., ed. *Martindale: The Complete Drug Reference, 38th Edition.* London, England: The Pharmaceutical Press; 2014: 1909.
10.	Propofol (Monograph). In: O'Neil MJ. *The Merck Index 15th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #7947.
11.	Propofol (Monograph). *United States Pharmacopeia XLII / National Formulary 37.* Rockville, MD. US Pharmacopeial Convention, Inc. 2019: 3710.
12.	Propofol Systemic. Thomson Micromedex. *USP DI – Drug Information for the Health Care Professional, 26th Edition.* Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 2531.
13.	USP <797>. *United States Pharmacopeia XLII / National Formulary 37.* Rockville, MD. US Pharmacopeial Convention, Inc. 2019: 6959.