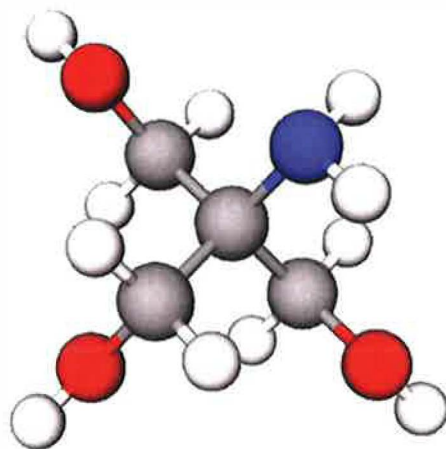




# TROMETHAMINE



## BIO EXCIPIENT GRADE REGULATORY PACKET

**Signature/Date:**



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## 1. TROMETHAMINE (TRIS) BIO EXCIPIENT GRADE

### 1.1. General Product Information:

- 1.1.1. Product Name:
  - 1.1.1.1. Tromethamine
- 1.1.2. Product Code:
  - 1.1.2.1. Historic Code: TR3220, TR3251, TR3252, TR3254, TR3255, TR3257
  - 1.1.2.2. Current Code: TRIS-3220, TRIS-3251, TRIS-3252, TRIS-3254, TRIS-3255, TRIS-3257
- 1.1.3. Scope:
  - 1.1.3.1. This regulatory packet will provide the quality and regulatory information regarding the manufacturing, testing, packaging, storage, release, shipping, and handling of Bio Excipient Grade Tromethamine manufactured by and at the BioSpectra, Stroudsburg, PA facility.
- 1.1.4. Molecular Formula:
  - 1.1.4.1.  $\text{NH}_2\text{C}(\text{CH}_2\text{OH})_3$
- 1.1.5. Molecular Weight:
  - 1.1.5.1. 121.14 g/mol

### 1.2. Manufacturing, Packaging Release Site and Supplier Information:

- 1.2.1. General Information:
  - 1.2.1.1. BioSpectra manufactures Tromethamine in its Stroudsburg, PA facility. Tromethamine is manufactured, packaged, stored, tested and released at BioSpectra's Stroudsburg, PA facility.
  - 1.2.1.2. Tromethamine is additionally stored and shipped at BioSpectra's Supply Chain Center: 51 North 3<sup>rd</sup> Street, Stroudsburg, PA 18360
- 1.2.2. Manufacturing:
  - 1.2.2.1. The manufacturing of Tromethamine is performed at BioSpectra's Stroudsburg, PA facility utilizing multiuse equipment. Equipment used in the manufacturing of Tromethamine is cleaned in accordance with BioSpectra's Cleaning Worksheet Procedure.
- 1.2.3. Packaging:
  - 1.2.3.1. The packaging of Tromethamine may occur in the following BioSpectra sites: BioSpectra Stroudsburg, PA Facility: 1474 Rockdale Lane, Stroudsburg, PA 18360, and BioSpectra Bangor, PA Facility: 100 Majestic Way, Bangor, PA 18013.
- 1.2.4. Testing for Release:
  - 1.2.4.1. Testing and release of Tromethamine may be performed at the BioSpectra Stroudsburg, PA Facility: 1474 Rockdale Lane, Stroudsburg, PA 18360, and the BioSpectra Bangor, PA Facility: 100 Majestic Way, Bangor, PA 18013.
- 1.2.5. GMP Compliance Statement:
  - 1.2.5.1. Bio Excipient Grade Tromethamine is suitable for use as an excipient. It is manufactured in accordance with the ICH Q7 Good Manufacturing Practice Guide. This grade of Tromethamine is not suitable to be used as an Active Pharmaceutical Ingredient, Drug Product or Household Item.

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### 1.3. Physico-Chemical Information:

#### 1.3.1. CAS Number:

1.3.1.1. CAS # 77-86-1

#### 1.3.2. Origin:

1.3.2.1. The origin of Tromethamine is through synthetic chemical manufacturing using approved raw materials, which are further purified in accordance with ICH Q7 guidelines. Only raw materials of synthetic origin are used in the synthesis and purification of Tromethamine.

#### 1.3.3. Synonyms:

1.3.3.1. Trometamol

1.3.3.2. THAM

1.3.3.3. Tris (Hydroxymethyl) Aminomethane

1.3.3.4. Trisaminol

1.3.3.5. Trismethylaminomethane

1.3.3.6. 2-Amino-2-(Hydroxymethyl) propane-1,3-diol

1.3.3.7. Tromethamine

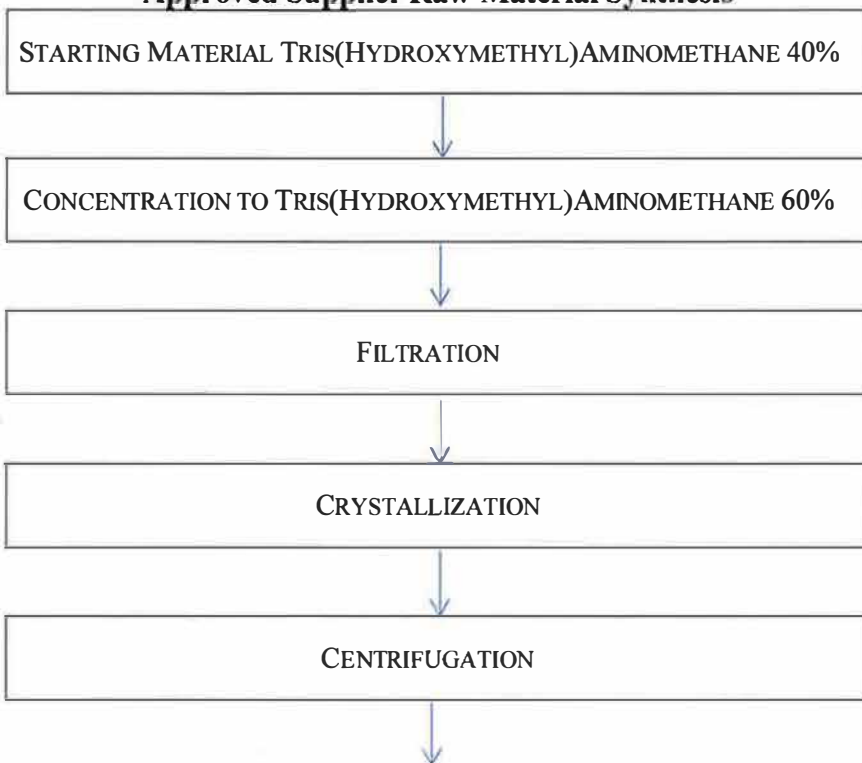
#### 1.3.4. Morphological Form:

1.3.4.1. White / Crystals

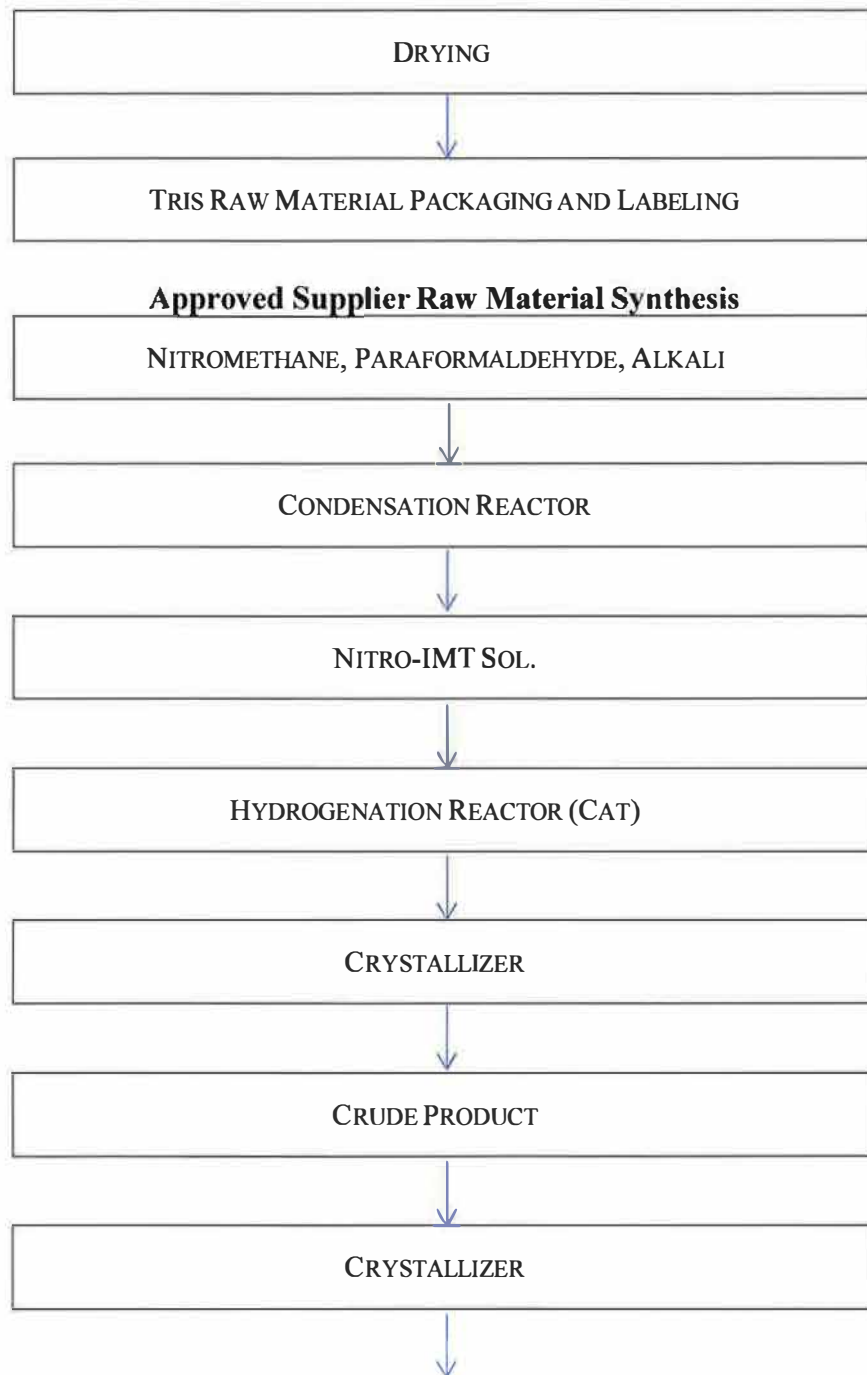
#### 1.3.5. Manufacturing Process:

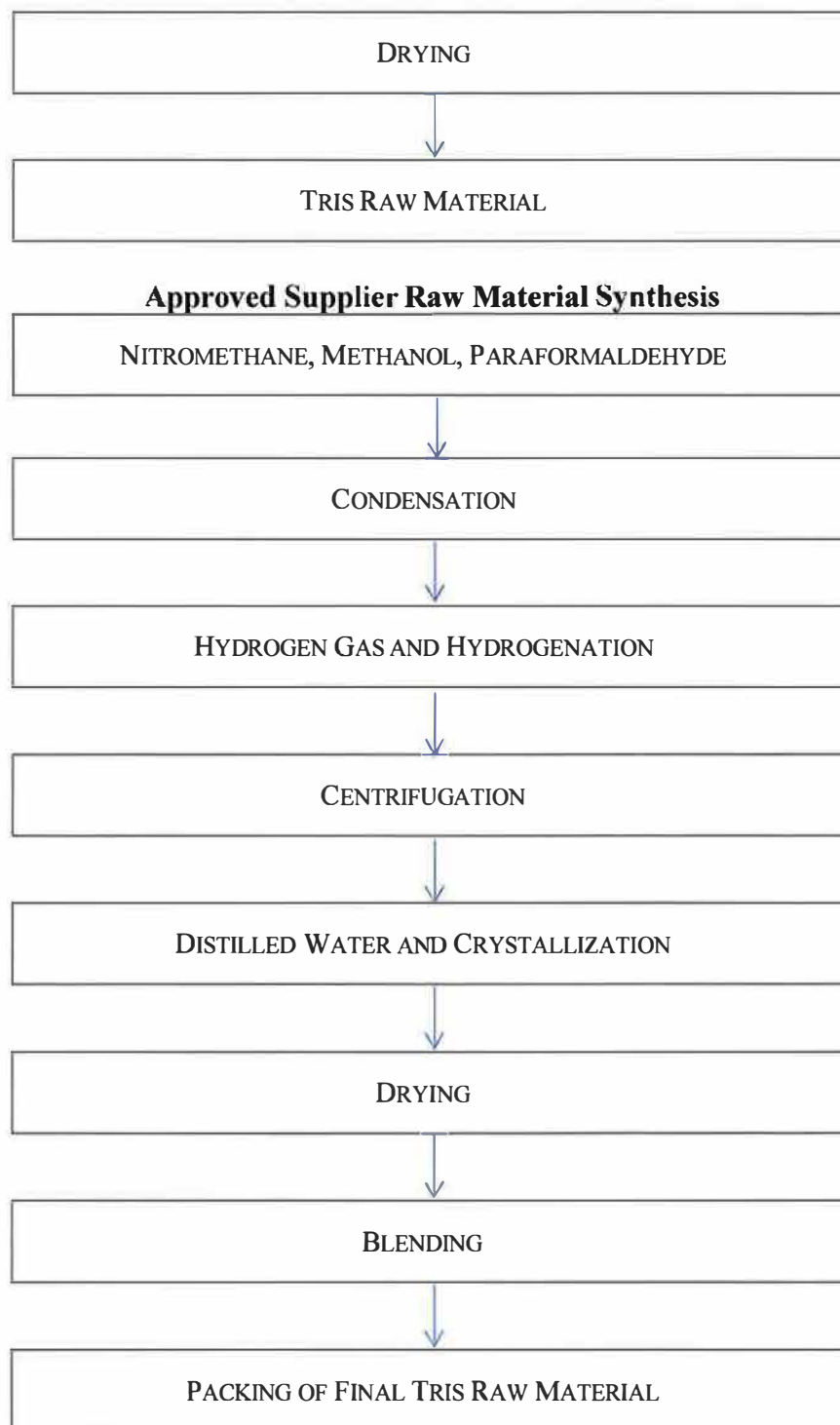
1.3.5.1. The Tromethamine, Bio Excipient Grade manufacturing process is performed by the following:

#### Approved Supplier Raw Material Synthesis



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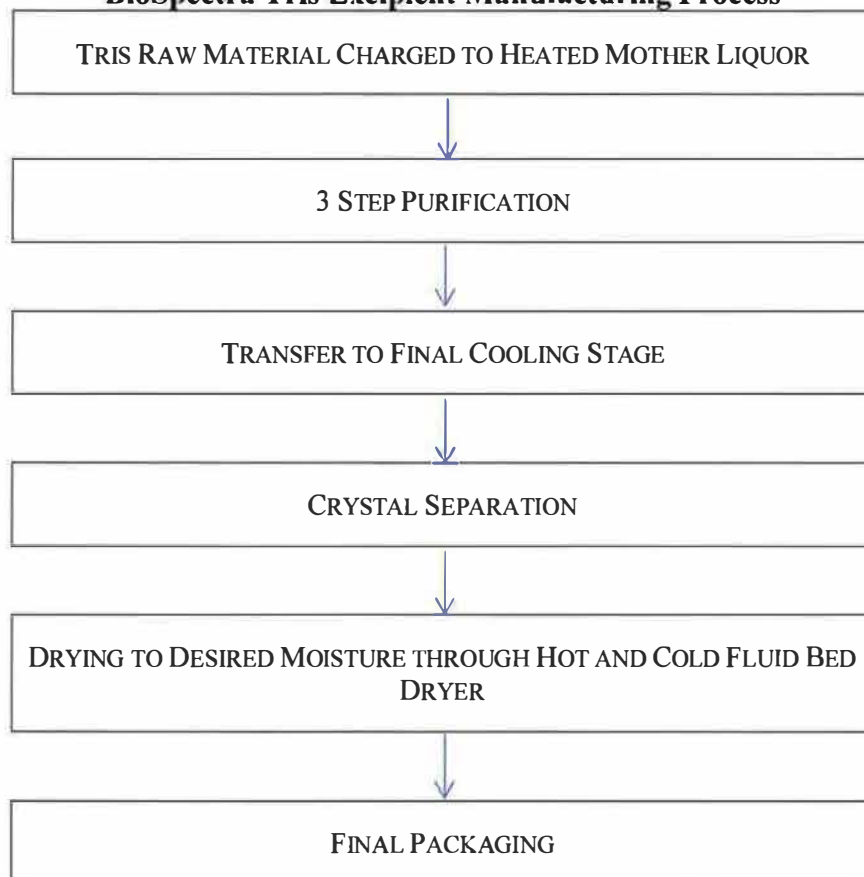




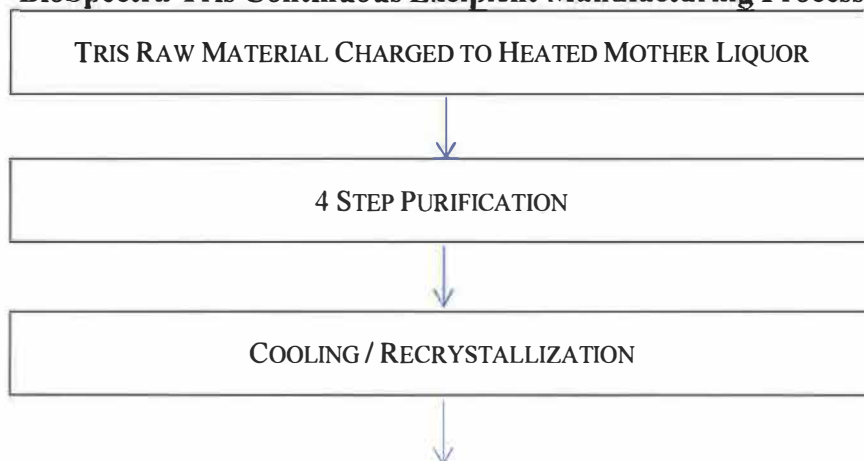
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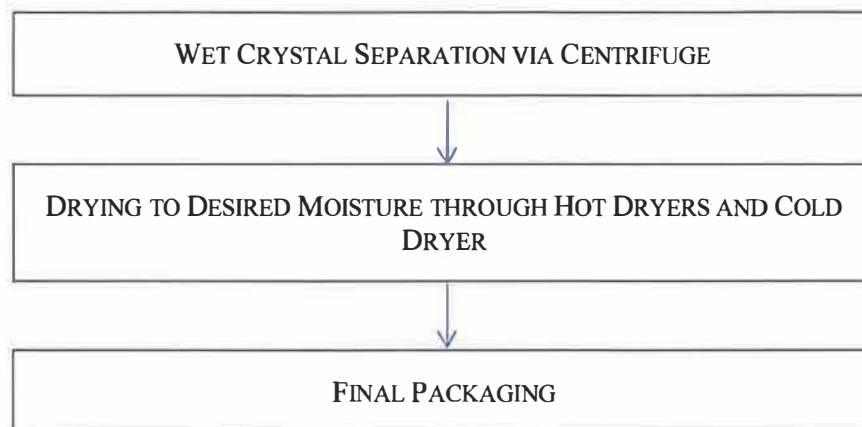


**BioSpectra Tris Excipient Manufacturing Process**



**BioSpectra Tris Continuous Excipient Manufacturing Process**





1.3.6. Specifications:

1.3.6.1. Available upon request.

**1.4. Regulatory Information:**

1.4.1. Compendial Compliance:

1.4.1.1. USP/EP Monograph based on the specific product code purchased.

1.4.2. Master File:

1.4.2.1. Drug Master File (DMF) is not available for this grade of product.

1.4.2.2. EDQM Certificate of Suitability is currently not available for this product.

1.4.3. REACH:

1.4.3.1. Refer to the Tromethamine Safety Data Sheet for the REACH Number or contact your Commercial Team Representative for further information.

1.4.4. BSE/TSE Statement:

1.4.4.1. Tromethamine, Bio Excipient Grade is a synthetic chemical and has been evaluated for the source of the raw materials used in its production through the Supplier Qualification Program. BioSpectra can state that BSE/TSE is not a concern based on this evaluation. Tromethamine, Bio Excipient Grade and its raw materials are not of animal origin.





#### 1.4.5. Allergens Statement:

1.4.5.1. Tromethamine, Bio Excipient Grade manufactured by BioSpectra and its raw materials are not manufactured using with or using any of the following substances: Cereals containing gluten (i.e., wheat, rye, barley, oats, spelt, kamut or their hybridized strains) and products thereof, Crustaceans and products thereof, Eggs and products thereof, Fish and products thereof, Peanuts and products thereof, Soybeans and products thereof, Milk and products thereof (including lactose), Celery and products thereof, Mustard and products thereof, Sesame seeds and products thereof, Lupin and products thereof, Molluscs and products thereof, Sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre expressed as SO<sub>2</sub>, Nuts i.e., Almond (*Amygdalus communis* L.), Hazelnut (*Corylus avellana*), Walnut (*Juglans regia*), Cashew (*Anacardium occidentale*), Pecan nut (*Carya illinoensis* (Wangenh.) K. Koch), Brazil nut (*Bertholletia excelsa*), Pistachio nut (*Pistacia vera*), Macadamia nut and Queensland nut (*Macadamia ternifolia*) and products thereof, Beef, Chicken, Pork, Azo Dyes, Benzoic Acid, Tartrazine, Vanillin, Cocoa, Cinnamon, Coriander, Yeast, Glutamate, Legumes, and Corn. BioSpectra has evaluated the Raw Material Supply through the Supplier Qualification Program.

#### 1.4.6. Genetically Modified Organisms (GMO) Statement:

1.4.6.1. Tromethamine, Bio Excipient Grade is a synthetic chemical and has been evaluated for the source of the raw materials used in its production through the Supplier Qualification Program. BioSpectra can state that genetic modification is not a concern based on this evaluation.

#### 1.4.7. Residual Solvents Statement:

1.4.7.1. BioSpectra can state based on the manufacturing process and the controlled handling, storage, and analysis of this product, that the Tromethamine, Bio Excipient Grade manufactured by BioSpectra complies with the requirements and specifications listed in the current USP method <467> Tables 1, 2, 3, or 4. BioSpectra has evaluated the raw material supply through the Supplier Qualification Program and can state that the Tris raw material supplied to BioSpectra is manufactured using the Class 2 residual solvents Methanol and Nitromethane, with expected concentrations meeting the requirements of ICH Q3C for residual solvents. BioSpectra analyzes Tromethamine, Bio Excipient Grade and its raw materials for Methanol and Nitromethane during Degradation and Impurity Profiling as part of process validation, with results meeting the requirements. Tromethamine, Bio Excipient Grade is additionally analyzed annually for Methanol and Nitromethane, with specifications NMT 3000ppm and NMT 50ppm respectively.



1.4.8. Metal Catalyst and Metal Reagent Residues Statement:

1.4.8.1. BioSpectra does not intentionally add or use any metal catalysts in the manufacturing process of Tromethamine, Bio Excipient Grade. BioSpectra has evaluated the raw material supply through the Supplier Qualification Program and can state that the Tris raw material is made from an ingredient which uses a very small amount of a nickel compound in the manufacture of that ingredient. BioSpectra additionally analyzes Tromethamine, Bio Excipient Grade for elemental impurities during Degradation and Impurity Profiling as part of process validation.

1.4.9. Pallet Statement:

1.4.9.1. BioSpectra can state that the wooden pallets used in the packaging and shipping of Tromethamine, Bio Excipient Grade manufactured at BioSpectra are ISPM 15 compliant.

1.4.10. Elemental Impurities Statement:

1.4.10.1. BioSpectra's Tromethamine, Bio Excipient Grade material has been profiled for elemental impurities via ICP utilizing USP <232> and <233> in accordance with ICH Q3D. The results are reported in the associated Elemental Impurity Profile and are available upon request.

1.4.11. Melamine Statement:

1.4.11.1. Tromethamine, Bio Excipient Grade has been evaluated for the source of the raw materials used in its production through the Supplier Qualification Program. BioSpectra can state that melamine is not a risk based on this evaluation. BioSpectra additionally analyzes Tromethamine annually for melamine, with a specification of 2.5 mg/kg max.

**1.5. Miscellaneous Product Information:**

1.5.1. Description of Batch:

1.5.1.1. The Tromethamine manufacturing process is a batch or continuous process where expected batch yields are established during validation in accordance with the Manufacturing Process Validation Master Plan. Individual batch yield is additionally determined for each manufactured batch and documented in the respective batch record.

1.5.2. Lot/Batch Numbering System:

1.5.2.1. The lot numbering system at BioSpectra employs the following format: 4 alphanumeric digits followed by a hyphen, 4 numerical digits followed by a hyphen, and finally 5 numerical digits. A sample lot number would appear as: TRIS-0223-00001.



- 1.5.2.1.1. The first four digits are alpha digits which indicate the material manufactured, where TRIS represents Tromethamine. The fifth and sixth digits are numeric digits which indicate the site of final packaging, where 02 represents the Stroudsburg, PA facility and 01 represents the Bangor, PA facility. The seventh and eighth digits are numeric digits which indicate the year the batch record was issued, where 23 represents 2023. The final five digits are numeric digits which indicate the sequential batch number, where 00001 represents the first Tromethamine batch of 2023 that is automatically generated by the ERP system. The sequential batch number automatically resets on the first of the new calendar year.
- 1.5.3. Expiration Date and/or Recommended Re-evaluation Interval:
- 1.5.3.1. The current recommended retest or expiration date for Tromethamine, Bio Excipient Grade is available in the BioSpectra Product Retest and Expiration Date List, DCN: BSI-LST-0239, and is based on current available stability data in accordance with BioSpectra's Stability Testing Program. Additionally, the recommended Retest or Expiration Date will be available on the Product Specific Certificate of Analysis, as applicable.
- 1.5.4. Storage and Shipping Conditions:
- 1.5.4.1. Store in a cool, dry place. Store in a cool, dry, well-ventilated area away from incompatible substances. Keep away from acids. Keep containers tightly closed.
- 1.5.5. Packaging:
- 1.5.5.1. Packaging information is available through the following:  
<https://biospectra.us/packaging>
- 1.6. Contact Information:**
- 1.6.1. <https://www.biospectra.us/about-us/commercial-marketing-team>