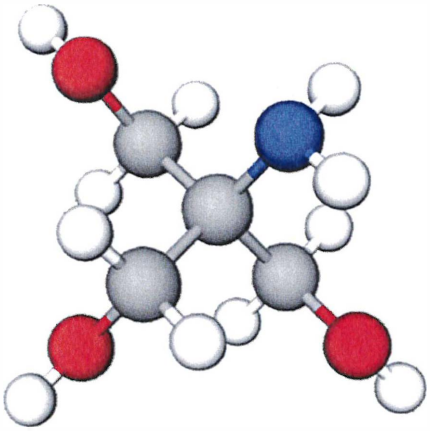
BIOSPECTRA
Premium Pharmaceutical Ingredients

TROMETHAMINE



BIO ACTIVE GRADE REGULATORY PACKET

Signature/Date:

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1. TROMETHAMINE (TRIS) BIO ACTIVE 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. Refer to Cover Sheet

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 Active Grade Tromethamine manufactured by and at the BioSpectra, Bangor, PA facility.

1.1.4. Molecular Formula:
1.1.4.1. $NH_2C(CH_2OH)_3$

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, Bio Active Grade in its Bangor, PA facility. Tromethamine is manufactured, packaged, stored, tested and released at BioSpectra's Bangor, PA facility.

1.2.2. Manufacturing:
1.2.2.1. The manufacturing of Tromethamine, Bio Active Grade is performed at BioSpectra's Bangor, 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, Bio Active Grade occurs in the following BioSpectra site: 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 is performed at the BioSpectra Bangor, PA Facility: 100 Majestic Way, Bangor, PA 18013.

1.2.5. GMP Compliance Statement:
1.2.5.1. Bio Active Grade Tromethamine is suitable for use as a non-Sterile Active Pharmaceutical Ingredient manufactured in accordance with the ICH Q7 Good Manufacturing Practice Guide. This grade of Tromethamine is not suitable to be used as a Sterile or Injectable 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. Trismethylolaminomethane
- 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 Approved Supplier Raw Material Synthesis is summarized from Supplier SN000004.
- 1.3.5.2. The BioSpectra Tris Bio Active Grade Manufacturing Process is available in the Tris Bio Active Process Flow Diagram, DCN: BSI-DGM-0039 v.2.0.
- 1.3.5.3. The Tromethamine, Bio Active Grade manufacturing process is performed by the following:

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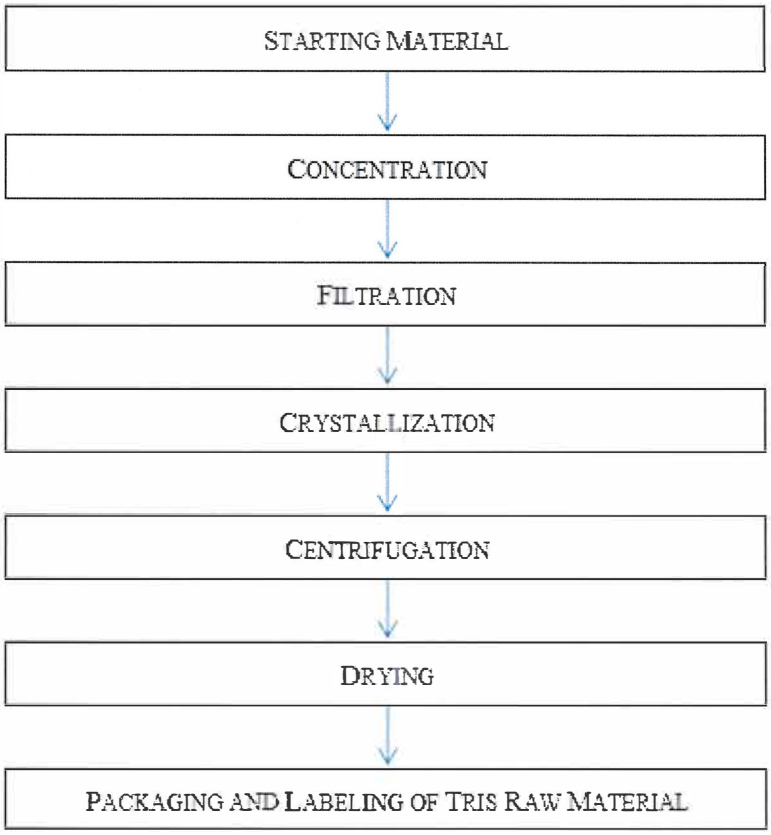
Approved Supplier Raw Material Synthesis



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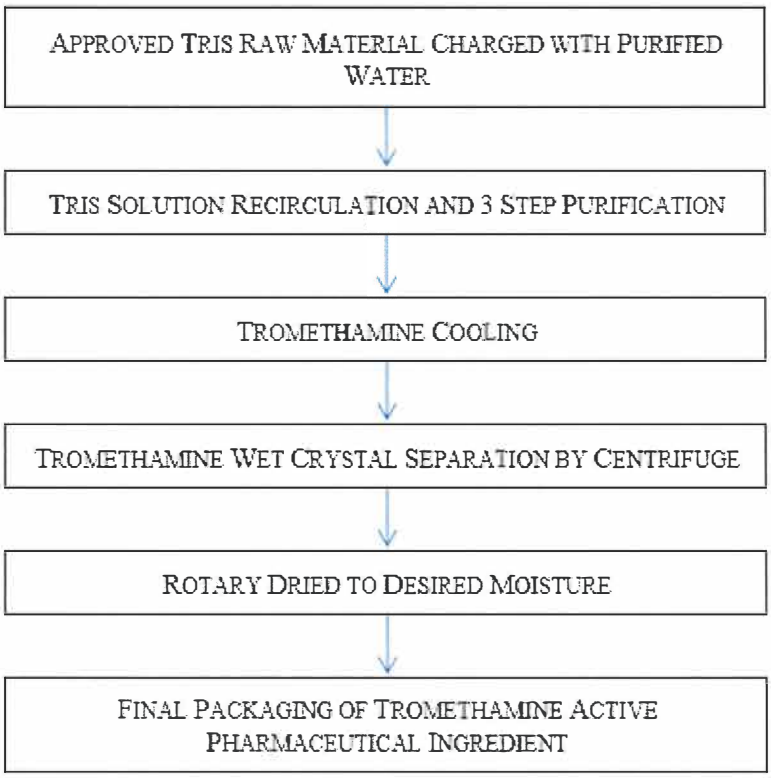
BioSpectra Tris Bio Active Manufacturing Process



1.3.6. Specifications:
1.3.6.1. Available upon request.

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1.4. Regulatory Information:

1.4.1. Compendial Compliance:

1.4.1.1. USP Monograph or EP Monograph, as indicated on the Certificate of Analysis for the specific product code purchased.

1.4.2. Master File:

1.4.2.1. Drug Master File (DMF) is available for this 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, if applicable, or contact your Commercial Team Representative for further information.

1.4.4. BSE/TSE Statement:

1.4.4.1. Tromethamine, Bio Active 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 Active Grade and its raw materials are not of animal origin.

1.4.5. Allergens Statement:

1.4.5.1. Tromethamine, Bio Active 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), Nuts i.e., Almond (*Amygdalus communis* L.), Hazelnut (*Corylus avellana*), Walnut (*Juglans regia*), Cashew (*Anacardium occidentale*), Pecan nut (*Carya illinoinensis* (Wangenh.) K. Koch), Brazil nut (*Bertholletia excelsa*), Pistachio nut (*Pistacia vera*), Macadamia nut and Queensland nut (*Macadamia ternifolia*) and products thereof, Celery and products thereof, Mustard and products thereof, Sesame seeds and products thereof, Lupin and products thereof, Molluscs and products thereof, Corn, Grains, Yeast, Starch, Preservatives, Artificial flavors / colors, Sulphur dioxide and sulphites at concentrations of more than 10 mg/kg or 10 mg/litre expressed as SO_2. 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 Active 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.

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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 Active Grade manufactured by BioSpectra complies with the requirements of the ICH Q3C Residual Solvents Guideline and USP <467> Residual Solvents. BioSpectra does not intentionally add or use any solvents in the Tromethamine, Bio Active Grade manufacturing process. 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 ICH Q3C requirements for residual solvents. BioSpectra has analyzed Tromethamine, Bio Active 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 is additionally analyzed annually for residual solvents, with specifications NMT 3000ppm Methanol and NMT 50ppm Nitromethane.

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 Active 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 small amount of a nickel compound in the manufacture of that ingredient. BioSpectra additionally analyzes Tromethamine for elemental impurities during Degradation and Impurity Profiling as part of manufacturing process validation.

1.4.9. Pallet Statement:

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

1.4.10. Elemental Impurities Statement:

1.4.10.1. BioSpectra's Tromethamine, Bio Active 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 Active 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.

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1.5. Miscellaneous Product Information:

1.5.1. Description of Batch:

1.5.1.1. The Tromethamine manufacturing process is a batch 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 per BSI-DGM-0009 BioSpectra Lot Number Identification.

1.5.2.2. A sample lot number would appear as:

1.5.2.2.1. QS6: TRIS-0124-00001

1.5.2.2.1.1. The first four digits are alpha digits which indicate the material manufactured, where TRIS represents Tromethamine. The fifth and sixth digits are numerical digits which indicate the site of final packaging, where 01 represents the Bangor, PA facility. The seventh and eighth digits are numerical digits which indicate the year the batch record was issued, where 24 represents 2024. The final five digits are numerical digits which indicate the sequential batch number, where 00001 represents the first Tromethamine batch of 2024 that is automatically generated by the ERP system. The sequential batch number automatically resets on the first of the new calendar year.

1.5.2.2.2. QS7: TRIS-E04-0125-0001

1.5.2.2.2.1. The first four digits are alpha digits which indicate the material, where TRIS represents Tromethamine. The fifth, sixth, and seventh digits are alphanumeric digits which indicate the location of manufacturing. The eighth and ninth digits are numerical digits which indicate the month of work order issuance, where 01 represents January. The tenth and eleventh digits are numerical digits which indicate the year of work order issuance, where 25 represents 2025. The final four digits are numerical digits which indicate the sequential batch number, where 0001 represents the first Tromethamine batch of 2025 that is automatically generated by the ERP system. The sequential batch number automatically resets on the first day of each calendar year.

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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 Active 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. Refer to the Tris/Tromethamine Safety Data Sheet, DCN: BSI-SDS-0004.
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/commercial-team/

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