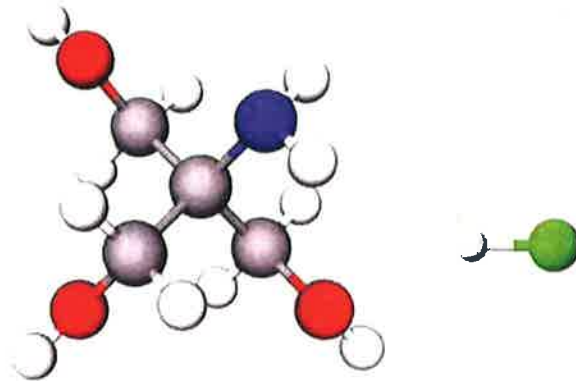




TRIS HYDROCHLORIDE



BIO EXCIPIENT GRADE REGULATORY PACKET - BANGOR

Signature/Date:

Chi M. Augusti

1/19/24



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1. TRIS HYDROCHLORIDE BIO EXCIPIENT GRADE

1.1. General Product Information

- 1.1.1 Product Name:
 - 1.1.1.1 Tris Hydrochloride
- 1.1.2 Product Code:
 - 1.1.2.1 Historic Code: TH3203, TH3220, TH3221, TH3250, TH3253, TH3254, TH3257, TH3259, and TH3260
 - 1.1.2.2 Current Code: THCL-3203, THCL-3220, THCL-3221, THCL-3250, THCL-3253, THCL-3254, THCL-3257, THCL-3259, and THCL-3260
- 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 Tris Hydrochloride manufactured by and at the BioSpectra, Bangor, PA facility.
- 1.1.4 Molecular Formula:
 - 1.1.4.1 $\text{NH}_2\text{C}(\text{CH}_2\text{OH})_3 \text{HCl}$
- 1.1.5 Molecular Weight:
 - 1.1.5.1 157.60 g/mol.

1.2. Manufacturing, Packaging, Release Site and Supplier Information

- 1.2.1 General Information:
 - 1.2.1.1 BioSpectra manufactures Tris Hydrochloride in its Bangor, PA facility. Tris Hydrochloride is manufactured, packaged, stored, tested and released at BioSpectra's Bangor, PA facility.
 - 1.2.1.2 Tris Hydrochloride is additionally stored and shipped at BioSpectra's Supply Chain Center: 51 North 3rd Street, Stroudsburg, PA 18360.
- 1.2.2 Manufacturing:
 - 1.2.2.1 The manufacturing of Tris Hydrochloride is performed at BioSpectra's Bangor, PA facility and is conducted in a dedicated processing area using only dedicated equipment. Equipment used in the manufacturing of Tris Hydrochloride is cleaned in accordance with BioSpectra's Cleaning Worksheet Procedure.
- 1.2.3 Packaging:
 - 1.2.3.1 The packaging of Tris Hydrochloride 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 Tris Hydrochloride 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 Excipient Grade Tris Hydrochloride is suitable for use as an excipient. It is manufactured in accordance with the ICH Q7 Good Manufacturing Practice Guide. This Grade of Tris Hydrochloride is not suitable to be used as an Active Pharmaceutical Ingredient, Drug Product or Household Item.

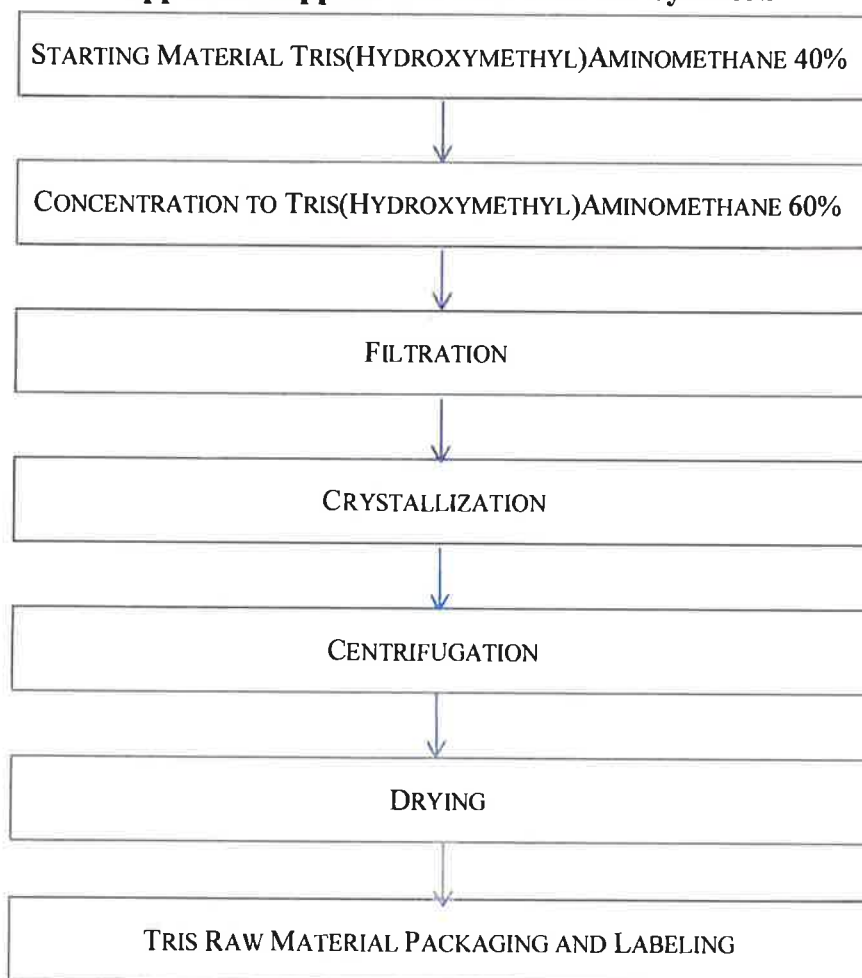
1.3. Physico-Chemical Information

- 1.3.1 CAS Number:
 - 1.3.1.1 CAS# 1185-53-1



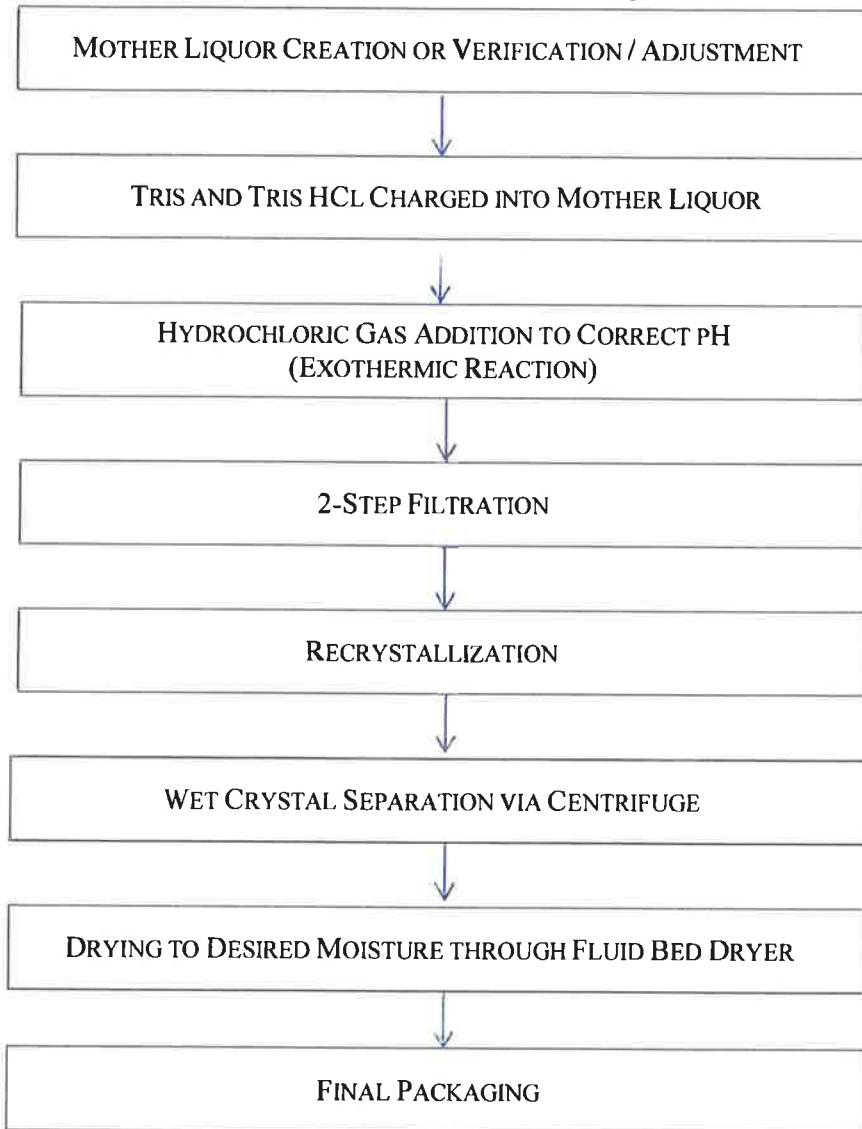
- 1.3.2 Origin:
- 1.3.2.1 The origin of Tris Hydrochloride is through synthetic chemical manufacturing using approved raw materials, which are further purified in accordance with ICH Q7 guidelines. Only raw materials of synthetic origin are used in the synthesis and purification of Tris Hydrochloride.
- 1.3.3 Synonyms:
- 1.3.3.1 2-Amino-2-(Hydroxymethyl)-1,3-Propanediol Hydrochloride
- 1.3.3.2 Tris (Hydroxymethyl) Aminomethane Hydrochloride
- 1.3.4 Morphological Form:
- 1.3.4.1 White / Crystals
- 1.3.5 Manufacturing Process:
- 1.3.5.1 The manufacturing process for Tris Hydrochloride is performed by the following:

Approved Supplier Tris Raw Material Synthesis





BioSpectra 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. Not Applicable

1.4.2 Master File:

1.4.2.1 Drug Master File (DMF) is currently not available for this product at the Bangor, PA facility.

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 Tris Hydrochloride 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 Tris Hydrochloride, Bio Excipient Grade is a synthetic chemical and has been evaluated for the source of the raw materials used in its production in through the Supplier Qualification Program. BioSpectra can state that BSE/TSE is not a concern based on this evaluation. Tris Hydrochloride, Bio Excipient Grade and its raw materials are not of animal origin.
- 1.4.5 Allergens Statement:
 - 1.4.5.1 Tris Hydrochloride, Bio Excipient Grade manufactured by BioSpectra and its raw materials are not manufactured with or using any of the following allergenic substances: Latex, 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., Almonds (*Amygdalus communis* L.), Hazelnuts (*Corylus avellana*), Walnuts (*Juglans regia*), Cashews (*Anacardium occidentale*), Pecan nuts (*Carya illinoensis* (Wangenh.) K. Koch), Brazil nuts (*Bertholletia excelsa*), Pistachio nuts (*Pistacia vera*), Macadamia or Queensland nuts (*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 10mg/litre expressed as SO₂. BioSpectra has evaluated the Raw Material Supply through the Supplier Qualification Program.
- 1.4.6 Genetically Modified Organisms (GMO) Statement:
 - 1.4.6.1 Tris Hydrochloride, 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 Tris Hydrochloride, Bio Excipient Grade manufactured by BioSpectra complies with the requirements of the ICH Q3C Residual Solvents Guideline and USP <467> Residual Solvents. There are no Class 1, 2, 3 or other solvents used or produced in the manufacturing or purification of Tris Hydrochloride with the exception of Methanol and Nitromethane, which are used in the manufacture of the Tris raw material supplied to BioSpectra. BioSpectra's approved Raw Material Supplier has stated that the Tris raw material complies with the allowed limit of 3000ppm Methanol, and that no Nitromethane is expected to remain in the final Tris raw material. BioSpectra has analyzed Tris Hydrochloride finished good for residual solvents during Degradation and Impurity Profiling and confirmed that the product complies with the limits of 3000ppm max Methanol and 50ppm max Nitromethane.

1.4.8 Metal Catalyst and Metal Reagent Residues Statement:

1.4.8.1 Tris Hydrochloride, Bio Excipient Grade is manufactured by BioSpectra without the use of metal catalysts and metal reagents. BioSpectra has evaluated the raw material supply through the Supplier Qualification Program and can state that the approved Tris raw material supplied to BioSpectra is made from an ingredient which uses a very small amount of a nickel compound in the manufacture of that ingredient. BioSpectra's approved Tris Raw Material Supplier has additionally stated that the raw material is not analyzed for nickel routinely, but occasional samples which have been tested have shown less than 10ppm of nickel. BioSpectra has additionally analyzed approved Tris raw material, as well as Tris Hydrochloride, Bio Excipient Grade finished good for elemental impurities including nickel, with results summarized in the completed Elemental Impurity Assessment.

1.4.9 Pallet Statement:

1.4.9.1 BioSpectra can state that all wooden pallets used in the shipping of Tris Hydrochloride, Bio Excipient Grade manufactured at BioSpectra are ISPM 15 compliant.

1.4.10 Elemental Impurities Statement:

1.4.10.1 BioSpectra's Tris Hydrochloride, 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 BioSpectra does not intentionally add or use melamine in the BioSpectra manufacturing process of Tris Hydrochloride, Bio Excipient Grade. BioSpectra has evaluated the raw material supply through the Supplier Qualification Program and can state that the raw materials are not expected to contain melamine based on this evaluation. BioSpectra has additionally analyzed Tris Hydrochloride for melamine, with results meeting the specification of 2.5mg/kg max.



1.5. Miscellaneous Product Information

1.5.1 Description of Batch:

1.5.1.1 The Tris Hydrochloride, Bio Excipient Grade 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: 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: THCL-0123-00001

1.5.2.1.1 The first four digits are alpha digits which indicate the material manufactured, where THCL represents Tris Hydrochloride. The fifth and sixth digits are numeric digits which indicate the site of final packaging, where 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 Tris Hydrochloride 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 Tris Hydrochloride, 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, well-ventilated area away from incompatible substances.

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>