ANGUS CHEMICAL COMPANY
SALES SPECIFICATION

Effective Date: 11/24/2020
Supersedes Date: 08/14/2018

Name: TRIS AMINO® Ultra Pure USP/EP Tris(hydroxymethyl)-aminomethane Biologics Grade

Specification Number: 116-25-S

Additional Product Information: White crystalline solid; no odor

Final Testing Requirements

Test and Test Condition	Limit	Unit	Method	Note
Purity (dried by GC)	99.90 Min	WT%	ANGUS 5121	
Related Substances, by GC	0.10 Max	WT%	ANGUS 5121	
Water	0.2 Max	WT%	ASTM E203	
Melting Point (dried)	170.0 – 172.0	°C	ANGUS 1500	
APHA Color, 20% Aqueous Solution	20 Max		ANGUS 1000	
Loss on Drying, 105C for 3 Hrs	0.3 Max	WT%	ANGUS 1300	
Water Insoluble Matter	0.005 Max	WT%	ANGUS 1330	
Elemental Impurities (Ni) by ICP/MS	2,000 Max	ppb	ANGUS 3511	1
Residue on Ignition	0.05 Max	WT%	Current USP	
Iron, 5 Max ppm	Pass		ANGUS 3100	2
UV Abs @ 260nm, 10% Aqueous Solution	0.03 Max		ANGUS 3000	
UV Abs @ 280nm, 10% Aqueous Solution	0.02 Max		ANGUS 3000	
UV Abs @ 430nm, 10% Aqueous Solution	0.004 Max		ANGUS 3000	
UV Abs @ 290nm, 40% Aqueous Solution	0.20 Max		ANGUS 3000	
Identification A (USP)	Pass		Current USP	3
Identification B (USP)	Pass		Current USP	4
Identification C (USP)	Pass		Current USP	5

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Melting Range (dried), 168 - 172 deg C (USP)	Pass		Current USP	
pH, 5% Solution, in CO2 Free H2O (USP)	10.0 - 11.5		Current USP	
Loss on Drying, 105C for 3 Hrs (USP)	1.0 Max	WT%	Current USP	
Residue on Ignition (USP)	0.1 Max	WT%	Current USP	
Residual Solvents(USP)	Pass		Current USP	6
Assay, by Titration (USP), 99.0 - 101.0 % wt	Pass		Current USP	7
Identification B, Melting Point (EP), 168 – 174 deg C	Pass		Current EP	8
Identification C (EP)	Pass		Current EP	9
Appearance, clear & colorless (EP), 5% solution in CO2 free H2O	Pass		Current EP	
pH, 5% Solution, in CO2 Free H2O (EP)	10.0 - 11.5		Current EP	
Related Substances (EP)	Pass		Current EP	10
Chlorides (EP), 100 Max ppm	Pass		Current EP	11
Iron (EP), 10 ppm max	Pass		Current EP	12
Loss on Drying, 105C (EP)	0.5 Max	WT%	Current EP	
Sulfated Ash (EP)	0.1 Max	WT%	Current EP	

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Assay, by Titration (EP), 99.0 - 100.5 % wt	Pass		Current EP	13
Endotoxin	0.03 Max	EU/mg	ANGUS 2.012	
Bioburden	100 Max	CFU/g	ANGUS 2.036	

End of Specification

Final Testing Requirements Notes:

1 Elemental Impurities (Ni) by ICP/MS – This test is performed quarterly. In alignment with ICH Q3D, "Elemental Impurities," a risk assessment was performed to identify elemental impurities specific to this product and to determine frequency of analysis required. Analytical Instrumentation and Analytical Method, ANGUS 3511 were developed, acceptance criteria defined, and method validated in accordance with ICH Q3D, USP<232> "Elemental Impurities – Limits," and USP<233> "Elemental Impurities Procedures."

2 Iron – This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product.

3 Identification A (USP) – This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product.

4 Identification B (USP) - This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product. GC and melting point tests are performed on every batch and provide redundant identification of the product.

5 Identification C (USP) - This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product. GC and melting point tests are performed on every batch and provide redundant identification of the product.

6 Residual Solvents (USP) – Based on knowledge of the manufacturing process and the controlled handling and storage of this material, there is no potential for the Class 1, Class 2, or Class 3 solvents specified in USP # and EP 5.4 to be present in this material, with the exception of methanol (Class 2 solvent). Methanol content is controlled to less than the 3000 ppm limit requirement with a 0.3 wt% limit on the loss of drying test.

7 Assay (USP) – This test is performed quarterly. GC Method, ANGUS 5121 is performed on every product batch and has a significantly tighter specification range (99.90 wt%) than required by the USP and EP monographs. GC technology provides a more sensitive, accurate, and reproducible analytical result for product purity/impurity profile than assay by titration alone.

Final testing requirements notes continued next page

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Final Testing Requirements Notes continued:

8 Identification B (EP) - This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product. GC and melting point tests are performed on every batch and provide redundant identification of the product.

9 Identification C (EP) - This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product. GC and melting point tests are performed on every batch and provide redundant identification of the product.

10 Related Substances (EP) – This test is performed quarterly. Related substances are tested on every batch using ANGUS 5121 with a limit of 0.10 wt% maximum for the sum of all impurities, thus covering the requirements of the EP Test at 1.0 wt% maximum for any single impurity.

11 Chlorides (EP) – This test is performed quarterly. Historical data has shown 100% conformance to the test requirement for this product.

12 Iron (EP) – This test is performed quarterly. Iron is tested by AA quarterly using ANGUS method 3100 with a limit of 5 ppm maximum, a lower limit than the EP requirement of 10 ppm maximum.

13 Assay (EP) – This test is performed quarterly. GC Method, ANGUS 5121 is performed on every product batch and has a significantly tighter specification range (99.90 wt%) than required by the USP and EP monographs. GC technology provides a more sensitive, accurate, and reproducible analytical result for product purity/impurity profile than assay by titration alone.

End of Final Test Notes

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General Notes:

1 TRIS AMINO® Ultra Pure USP/EP Grade is manufactured in accordance with the site quality system and is designed to conform to both ISO 9001 and the Joint International Pharmaceutical Excipients Council (IPEC) Pharmaceutical Quality Group (PQG) Good Manufacturing Practices Guide for Pharmaceutical Excipients (current revisions).

This product is not manufactured under aseptic or sterile conditions and is considered a non-sterile product. While this product by its nature does not tend to promote or create an environment optimal for microbial presence or proliferation, ANGUS makes no statement or representation that our product is manufactured in a manner intended to meet bioburden, bacterial endotoxin specifications or remain pyrogen-free through-out the product lifecycle

It is the sole responsibility of the end user to determine the suitability of this product for any use or application contemplated. Regulatory resources available to the end user to determine precedence of use for this product:

- U.S. Food and Drug Administration (FDA) Inactive Ingredient Database (IID)
    - This product is found within the IID as “Tromethamine”
- European Drug Catalogues such as; “Dictionnaire Vidal,” (France,) or “Die Rote Liste,” (Germany.)
    - This product is found within EU drug catalogues as “Trometamol”

End of General Notes

Material Number	Packaging Size
375647	50 KG DRUM
375824	25 KG DRUM
375825	12 KG PAIL
376345	1 KG BOTTLE
376346	5 KG PAIL

LAST PAGE

READ PRECAUTIONARY INFORMATION AND MATERIAL SAFETY SHEETS. THIS PRODUCT IS SHIPPED IN COMPLIANCE WITH APPLICABLE LAWS AND REGULATIONS REGARDING CLASSIFICATION, PACKAGING, SHIPPING AND LABELING.