Raw Materials for Manufacturing: Buffers

Elevate Your Process

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1. PRODUCT SCOPE AND BACKGROUND

1.1. Product Offering

The following products are in scope of this dossier. These products were qualified by site-level, quality assurance to meet the assigned quality attributes:

Biological Buffers

Code	Product Description	10KG	25KG	50KG	Configurable Packaging
T4661	**Trizma® base** ≥99.9% (titration), crystalline				✓
T6066	**Trizma® base** BioPerformance Certified, meets EP, USP testing specifications, suitable for cell culture, ≥99.9% (titration)	✓	✓		✓
T5941	**Trizma® hydrochloride** BioPerformance Certified, suitable for cell culture, ≥99.0% (titration)	✓	✓		✓
T3253	**Trizma® hydrochloride** reagent grade, ≥99.0% (titration), crystalline	✓	✓	✓	✓
H4034	**HEPES** BioPerformance Certified, ≥99.5% (titration), suitable for cell culture		✓		✓
M8250	**MES hydrate** ≥99.5% (titration)		✓	✓	✓
M2933	**MES hydrate** BioPerformance Certified, suitable for cell culture, ≥99.5%	✓			✓
G4505	**Guanidine hydrochloride** ≥99% (titration)	✓	✓		✓
G3272	**Guanidine hydrochloride** for molecular biology, ≥99%	✓			✓
B6755	**BIS-TRIS propane** ≥99.0% (titration)	✓			✓
B4429	**BIS-TRIS** BioPerformance Certified, suitable for cell culture, suitable for insect cell culture, ≥98.0%				✓
M3058	**MES sodium salt** BioPerformance Certified, suitable for cell culture	✓			✓
M5162	**MOPS** BioXtra, ≥99.5% (titration)				✓
M9024	**MOPS sodium salt** BioPerformance Certified, suitable for cell culture, ≥99.5%		✓		✓
T0377	**Tricine** ≥99% (titration)		✓		✓

Site Of Manufacturing, Testing, Packaging, and Release

Site Description	Site Information
Site of Manufacturing (Cherokee site)	Sigma-Aldrich Corporation 3300 South 2nd Street, St. Louis, MO 63118 USA
Site of Testing & Release (Dekalb site)	Sigma-Aldrich Corporation 3500 Dekalb Street, St. Louis, MO 63118 USA
Site of Packaging (Cherokee site)	Sigma-Aldrich Corporation 3300 South 2nd Street, St. Louis, MO 63118 USA

1.2. Product Background

Biological buffers provide solution stability and pH control without interfering with the biological processes of the medium. Many biochemical systems and processes can be impaired by relatively small changes in the pH. Biological buffers are selected based on their buffering capacity, pH range, chemical and biological compatibility, ionic strength, temperature stability, and other characteristics. These factors determine the buffer's suitability for use.

1.3. The products within the Elevate program referenced in this dossier:

- are for applications driven by high expectations and requiring verified process control or manufacturing control.
- are products which can be supported by quality agreements and enhanced change control.
- are 'fit-for-use' raw materials for the development and production of immunoassay and clinical chemistry for *in vitro* diagnostics (IVD).
- are for research or further manufacturing use only. Not intended for direct use in humans or animals. Non-TSCA is used only in the US.
- are not effective IVD products, and no specific disease, condition, or diagnostic performance claims are made.

1.4. Product Manufacturing and Verification

1.4.1. Product Manufacturing Process

With over 40 years of buffers manufacturing experience, we consistently produce buffer products used as raw materials in the diagnostics market. Manufacturing history and performance is reviewed, and risk assessments are performed, as needed, to identify critical control parameters, including critical control points, process scale limits, raw material specifications and equipment requirements. Additionally, primary packaging component controls are established for the products within this dossier.

1.4.2. Product Manufacturing Verification Statement

The product manufacturing procedures have been verified to have sufficient process or manufacturing controls, critical control parameters and in-process testing to produce material that consistently meets the product specifications. The batch records confirm that the product was manufactured according to the manufacturing procedures.

1.5. Product Quality Control and Verification

1.5.1 Analytical Verification Statement

The analytical methods have been verified to sufficiently perform the final batch-specific testing and release per the product specifications. Please contact your local representative to request details on an analytical method when certain criteria are met.

1.5.2 Product Certificates

The following Product Certificate table provides website links to sample certificates. If you are seeking a certificate for a specific batch, use the Documents search function. A Safety Data Sheet is also available via the Documents search function.

1.5.2.1 Specifications

All products within the Elevate program are issued with a Specification Sheet detailing the analytical tests and specifications for each product.

1.5.2.2 Certificate of Analysis

Products are issued with a Certificate of Analysis (CoA) detailing the comprehensive specifications for each product, the batch-specific testing results and release. Release testing is performed using established protocols. The sample CoAs show typical results obtained in our analytical testing.

1.5.2.3 Certificate of Origin and TSE/BSE Statement

A batch-specific Certificate of Origin (CoO) is available upon request for products within the Elevate program. TSE/BSE statement is available in **Section 9** of this document.

Product Certificate Table

Code	Product Description	Specifications	Example of CoA
T4661	**Trizma® base** ≥99.9% (titration), crystalline	Click Here	Click Here
T6066	**Trizma® base** BioPerformance Certified, meets EP, USP testing specifications, suitable for cell culture, ≥99.9% (titration)	Click Here	Click Here
T5941	**Trizma® hydrochloride** BioPerformance Certified, suitable for cell culture, ≥99.0% (titration)	Click Here	Click Here
T3253	**Trizma® hydrochloride** reagent grade, ≥99.0% (titration), crystalline	Click Here	Click Here
H4034	**HEPES** BioPerformance Certified, ≥99.5% (titration), suitable for cell culture	Click Here	Click Here
M8250	**MES hydrate** ≥99.5% (titration)	Click Here	Click Here
M2933	**MES hydrate** BioPerformance Certified, suitable for cell culture, ≥99.5%	Click Here	Click Here
G4505	**Guanidine hydrochloride** ≥99% (titration)	Click Here	Click Here
G3272	**Guanidine hydrochloride** for molecular biology, ≥99%	Click Here	Click Here
B6755	**BIS-TRIS propane** ≥99.0% (titration)	Click Here	Click Here
B4429	**BIS-TRIS** BioPerformance Certified, suitable for cell culture, suitable for insect cell culture, ≥98.0%	Click Here	Click Here
M3058	**MES sodium salt** BioPerformance Certified, suitable for cell culture	Click Here	Click Here
M5162	**MOPS** BioXtra, ≥99.5% (titration)	Click Here	Click Here
M9024	**MOPS sodium salt** BioPerformance Certified, suitable for cell culture, ≥99.5%	Click Here	Click Here
T0377	**Tricine** ≥99% (titration)	Click Here	Click Here

2. SHELF LIFE STATEMENT

For all products covered in this dossier, a product stability review has been completed or is underway following our internal shelf-life program. Stability data and trends are reviewed annually.

3. ISO CERTIFICATION

As a leader in the Life Sciences industry, we are committed to product quality, manufacturing effectiveness and meeting customer expectations. The St. Louis Cherokee site is certified to the:

ISO 9001:2015 standard: Quality management systems, requirements

ISO 9001 : 2015 Certificate

4. SITE QUALITY SELF-ASSESSMENT

A Quality Self-Assessment may be provided in lieu of a customer audit. The site self-assessment covers our quality management system for the Following regulated Activities: Manufacturing, release and packaging of biological buffers. It is based on Rx-360 Supplier Assessment Questionnaires which are well-known industry standard questionnaires.

Rx-360 is a nonprofit international consortium which addresses pharmaceutical and medical device supply chain security. We are an active member. For more information, please refer to Rx-360 (rx-360.org).

St. Louis Cherokee Site Self Assessment (Site of Manufacturing & Packaging)	St. Louis Dekalb Site Self Assessment (Site of Testing & Release)

5. QUALITY ATTRIBUTES

The M-Clarity™ matrix includes six MQ segments from MQ100 to MQ600 defining the quality attributes and the notifiable changes in each segment.

The products in this dossier meet the discriminating quality attributes assigned to the MQ400 Quality Segment.

Additonal Information on M-Clarity™

6. CHANGE NOTIFICATION

Change notifications are available on an opt-in basis. To ensure that we provide the most-up-to-date product information, we have a best-in-class Change Notification Program based on a compliant Change Control process and on our M-Clarity™ Program. We inform customers about important changes that could impact their R&D or process development programs.

The easiest and quickest method to obtain Change Notifications is to request a product specific Change Notification Commitment (CNC). By building our Change Notification program on this opt-in process, our customers should not receive non-relevant letters that could trigger unnecessary, resource-intensive investigations. Follow the link below for more information on the change control offered and how to opt-in to our change control program.

Additional Information on Change Notification

7. QUALITY AGREEMENTS

Quality Assurance Agreements (QAA) are legally binding contracts negotiated between our company and our customers.

QAAs address and define various topics related to the quality standards/systems/ services applicable to the covered products: Quality Management System standards/certifications, complaint handling, audits, recalls, documentation support, level of verification/validation, and notification of changes. Due to the extended requirements and support levels that need to be in place, QAAs are available for products with MQ segments of MQ300 and above.

The term of a QAA is five years. An expiry notice will be received two months in advance, to allow time to prepare for a renewal.

When the QAA is finalized and fully signed, the information is secured in our dedicated IT system and Change Notifications will be received for the products covered by the QAA in accordance with the M-Clarity™ program.

If you are interested in a QAA or a CNC, please contact your local representative.

8. SITE AUDITS

Site audits provide a reliable assessment of our manufacturing capabilities and facilities. Please contact your local representative to request a site-specific audit when certain criteria are met.

9. TSE/BSE STATEMENT

TSE/BSE-Certificate

ELEVATE Buffers Group Statement

The note for guidance EMA/410/01 Rev. 3 of the EC considers the requirements of raw materials used for human and veterinary medicinal products. The document introduces risk assessment into the regulatory compliance process for products derived from TSE/BSE-relevant animal species.

We certify that the following products are manufactured without the use of raw materials of animal or human origin.

They are synthetically produced.

During processing these products do not come in contact with animal material. Therefore, they do not fall under the scope of the above-mentioned guideline and are not concerned by the TSE/BSE issue.

This statement is valid only for the following catalog numbers:

B4429	BIS-TRIS	M8250	MES hydrate
B6755	BIS-TRIS propane	M9024	MOPS sodium salt
G3272	Guanidine hydrochloride	T0377	Tricine
G4505	Guanidine hydrochloride	T3253	Trizma® hydrochloride
H4034	HEPES	T4661	Trizma® base
M2933	MES hydrate	T5941	Trizma® hydrochloride
M3058	MES sodium salt	T6066	Trizma® base
M5162	MOPS		

Michelle Koranda
Quality Services

This document has been produced electronically and is valid without a signature.
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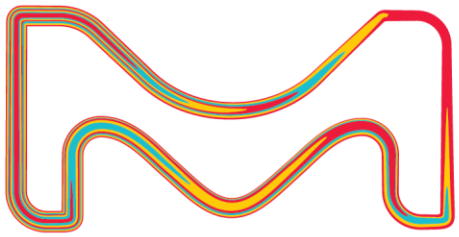

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