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Lactose, Monohydrate

Product Regulatory Data Sheet

Section 1 – Product Information

Products Covered

<u>Brand</u>	<u>Product Code</u>	<u>Product Description</u>	<u>MOC* code</u>
J.T.Baker®	2249	Lactose, Monohydrate, Powder N.F.	R
J.T.Baker®	2250	Lactose, Monohydrate, Powder, N.F. Multi-Compendial	R

*MOC = Management of Change

Section 2 – Manufacturing, Packaging and Release Site Information

The products in Section 1 are manufactured according to current Good Manufacturing Practices (cGMPs) as set forth by International Pharmaceutical Excipients Council (IPEC) guidelines.

A number of the cGMP produced products that are sold by Avantor may not be originally manufactured at our sites. However, we perform the analytical and stability testing for these products and repackage the products where applicable. With ISO and cGMP procedures, in place at our facilities we can ensure, and take complete responsibility for, the traceability and quality of the finished, packaged product that we offer.

For J.T.Baker® and Macron Fine Chemicals™ brand products, the Original Manufacturer and address will be referenced on the Certificate of Analysis as an alpha or alpha-numeric **manufacturer code** rather than listing the full name and address. This practice is compliant with both ICH Q7 Good Manufacturing Guidance for Active Pharmaceutical Ingredients (APIs) and IPEC guidelines and it meets cGMP requirements. For instructions to decipher the manufacturer reference code please consult the Avantor website. Instructions can be found by visiting the Ask Avantor link under the Resources tab or by directly linking to www.askavantor.com Keyword: Manufacturer Code. Additional information on Avantor suppliers may be available under NDA. Please reach out to the support contact in Section 7 for additional supplier information inquiries.

Section 3 – Physical/Chemical Information

CAS #: 64044-51-5

Manufacturing Process: Synthesis via enzymes and crystallized. Additional manufacturing process information may be disclosed under NDA upon request from the support contact in Section 7.

Raw Material Origin: Animal- Bovine Milk

Section 4 – Regulatory Information

DMF: Avantor may hold Master File(s) for specified product codes, dependant on the country of interest. Inquire with the support contact in Section 7 for additional details.

BSE/TSE Status: The Original Manufacturer confirms that Lactose products are manufactured in compliance with CPMP Guideline “Note for Guidance on Minimizing the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products”. EMEA/410/01-Rev.3, and Australian Government TGA “Transmissible Spongiform Encephalopathies (TSEs), April 2014. They confirm that based on information obtained from reputable suppliers all bovine-derived materials used in the manufacture of Lactose, all grades, were obtained from healthy cattle raised in appropriate countries that meet EU guidelines and Japan guidelines (MHLW Notification 210 and 262 and PFSA Notification No. 1069, 0414004 and 0218004). They confirm bovine milk used in the production Original Manufacturer brands of Lactose is sourced from healthy animals in the same conditions as milk collected for human consumption. No other ruminant or animal materials are used during the process to obtain the Lactose products. Enzyme products used are microbially produced and are not derived from animal sources (i.e. calf rennet is not used). Therefore, the Original Manufacturer’s Lactose products are excluded from the scope of the above stated guidance.

Thus a Certificate of Suitability from the European Directorate for the Quality of Medicines (EDQM) is not required. The Original Manufacturer applied for a Certificate of Suitability with the EDQM in June 2000. The EDQM has returned our application for a Certificate of Suitability as a result of the above stated exclusion. The EDQM has informed them “The applicants/holders of marketing applications should mention that the milk derivative is “derived from milk sourced from healthy animals in the same conditions as milk collected for human consumption. In these circumstances, no additional documentation needs to be submitted in relation to TSE for these materials neither directly to the licensing authorities nor via the Certification procedure.”

Bovines used in the production of Lactose are domiciled in the United States of America. The Lactose is derived from bovine milk supplied directly to the Original Manufacturer from US dairy farmers. Herds from which the milk is sourced are not closed herds. All farm members are in compliance with the FDA rule effective August 1997 prohibiting animal proteins in ruminant feed. Bovines used in milk production are over 30 months of age.

All Original Manufacturer brands of Lactose are produced at their US plants. No specified risk materials are used in the manufacture of Lactose.

International authorities have conducted numerous studies showing the inability of milk and milk

products to cause infection.

Lactose produced by the Original Manufacturer is not of human origin.

Allergen/Hypersensitivities Information: To the best of our knowledge the allergens listed in the [US FDA](#), [EU Directive 2003/89/EC](#), and [TG0-91/92](#) are not known additives, by products, intermediate parts, or otherwise intentionally added during the manufacturing processes of the product.

Exception: The raw material origin of this product is bovine milk.

Neither Avantor nor the Original Manufacturer produce any of the following types of products: Antibiotics, Aflatoxins, Penicillin, Semi-Synthetic Penicillins, Cephalosporins, other Beta-Lactams, Antibiotics, Cytotoxics, Steroids, Medicated Feeds, or Pesticides.

This product is manufactured using cGMP guidelines which provide controls that allow no potential for cross contamination of any allergens or other contaminants. However, this product is not tested for the presence of these or any other allergens by Avantor or the Original Manufacturer, therefore, we do not have confirmation for the absence of any allergens in the product.

GMO Information: The subject materials, including any raw materials and processing aids, are NOT subject to genetic modification.

Residual Solvents/Organic Volatile Impurities (OVI) Information: The subject materials (all lots) comply with the requirements of the ICH Q3C Residual Solvents Guideline and USP<467> Residual Solvents. No Class 1, 2, 3 or other solvents are used or produced in the manufacturing or purification of the product.

Elemental Impurities: Please see attached summary for Elemental Impurity information for listed products.

Kosher Status: The subject materials are not Kosher Certified. For J.T.Baker® and Macron Fine Chemicals™ brand products, please refer to the certificate available on AskAvantor for our most up to date listing of Kosher products. (www.askavantor.com Keyword: Kosher). For other branded products, please reach out to the support contact in Section 7 for the certificate, if available.

Halal Status: The subject materials are not Halal Certified. For J.T.Baker® and Macron Fine Chemicals™ brand products please refer to the certificate available on AskAvantor for our most up to date listing of Kosher products. (www.askavantor.com Keyword: Halal). For other branded products, please reach out to the support contact in Section 7 for the certificate, if available.

GRAS Status: The United States Food and Drug Administration (FDA) have acknowledged that some chemicals may be considered Substances Generally Recognized as Safe (GRAS) in foods when used in accordance with the requirements and limitations per specific 21 CFR regnums. For the latest information on whether or not an Avantor product is considered GRAS, please visit the [Electronic Code of Federal Regulations](#).

Section 5 – Miscellaneous Product Information

Certificate of Analysis Date Format: The Manufactured Date and Expiration/Retest Date on the CofA are reported as YYYY-MM-DD. For example, the Manufactured Date for October 1, 2021 would be reported as 2021-10-01.

Lot Numbering System and Batch Description: For J.T.Baker® and Macron Fine Chemicals™ brand products, please refer to AskAvantor for information concerning our lot/batch numbering system. (www.askavantor.com Keyword: Lot Number). For other branded products, please reach out to the support contact in Section 7 for the certificate, if available.

Batch Definition: A "batch" is a homogeneous unit of production; each batch of is from one single batch of the source supplier.

Shelf Life Information: If a product has an assigned expiration or retest period, the date will appear on the Certificate of Analysis. For products that do not have assigned dates please contact, please reach out to the support contact in Section 7 for additional stability inquiries.

Management of Change: For J.T.Baker® and Macron Fine Chemicals™ brand products, please refer to Management of Change link under Working with Avantor tab on the Avantor website. For other branded products, please reach out to the support contact in Section 7 for information on the applicable management of change process.

Country of Origin Statement: Country of Origin is indicated on the product's Certificate of Analysis. Please contact our Trade Compliance support contact in Section 7 if you require further documentation.

Storage Requirements: Please refer to the product's Certificate of Analysis or Product Specifications. In the absence of specific storage conditions listed on its specification sheet or Certificate of Analysis, products are to be stored in ambient conditions of temperature and humidity. We do not formally tie any specific temperature or humidity range with the 'ambient' storage designation, but an example of a common temperature interpretation is 15-30°C. Our products are also packaged to protect from the normal variation in humidity during storage and shipment. Further handling and storage information may be found in Section 7 of the product's SDS sheet.

Certificates of Analysis: For J.T.Baker® and Macron Fine Chemicals™ brand products, please see the current list of product specifications using our Certificate/SDS Search tool on our website [here](#). For other branded products, please see the current list of product specifications using the Certificate/SDS Search tool on our website [here](#).

Safety Data Sheet: For J.T.Baker® and Macron Fine Chemicals™ brand products, please see the current product safety information using our Certificate/SDS Search tool on our website [here](#). For other branded products, please see the current list of product specifications using the Certificate/SDS Search tool on our website [here](#).

Avantor Site Certifications: Please see the current Avantor site certifications on our website [here](#).

Site Quality Overview: Avantor maintains a self-assessment modeled after IPEC guidelines which describes site and quality system information to support the manufacturing activities of this product. Please reach out to the support contact in Section 7 for a current copy of the Site Quality Overview.

Packaging Information: Please reach out to the support contact in Section 7 for current packaging specifications.

Section 6 – Revision History

Rev. 0; Oct. 1, 2007 – IPEC EIP format

Rev. 1; March 14, 2008 – Section 4: Removed lactose from list of allergens

Rev. 2; Oct. 14, 2008 – Section 4: updated residual solvents information

Rev. 3; Aug. 4, 2009 – Section 4: To BSE/TSE statement, added "The products listed above are manufactured in compliance with CPMP Guideline "Note for Guidance on Minimizing the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products" EMEA/410/01-Rev. 2 - October 2003."; Section 7: updated contact information; Entire document: new letterhead.

Rev. 4; Apr. 28, 2011 – Section 1: Changed Mallinckrodt to Macron, added MOC codes; Section 2, added GMP statement; Section 7: updated contact information; Entire document: new letterhead and changed all references of "Solv IT Center" or " AskAvantor." Updated website links for new website; minor formatting. (JLW)

Rev. 5; Jan. 25, 2012 – HDQ address change. Section 4: Added Residual Metallic Catalysts Statement. Expanded Allergens list; Section 7: Updated contacts list (MCH)

Rev. 6; Oct. 24, 2014 – Section 3: clarified manufacturing process; Section 4: Updated BSE/TSE statement to current EMEA Rev. to match supplier's statement; updated Residual Metallic Catalysts statement; separated Kosher/Halal status and added certification statement; Section 5: Added COA Date Format statement; added Management of Change information; Section 7: removed contact list table and added CS/TS contact information. (MCH)

Rev. 7; August 25, 2017 – Entire document: new letterhead, new format; Section 1: Removed delisted product, 6270, Section 4: Updated BSE/TSE statement to supplier's current statement, Replaced Residual Metallic Catalysts with Elemental Impurities statement. (MCH)

Rev. 8; November 15, 2018 – Entire Document: New Format. (EC)

Rev. 9; November 15, 2021 – Entire Document: Updated email addresses and website from avantorinc.com to avantorsciences.com; Section 2: Minor updating to language; Section 4: Removed Compendial Compliance statement. Updated DMF statement. Updated Allergen/Hypersensitivities Information statement. Specified certificate availability for different branded products for Kosher and Halal Status statements. Generalized GRAS Status statement; Section 5: Updated Certificate of Analysis Date Format statement. Updated contact information directions for Lot Numbering System and Batch Description, Country of Origin Statement, Shelf Life Information, and Management of Change statements. Added Certificates of Analysis, Safety Data Sheet, Avantor Site Certifications,

Site Quality Overview, and Packaging Information statements; Section 7: Removed Fax number and Customer Service contact information. Added contacts. (KH)

This electronic document is valid without a signature.

Section 7 – Contact Information

Technical Service

Phone: 1-855-282-6867 and 1-610-573-2600 (outside U.S.), select option 5

Email: Technical.Service@avantorsciences.com

Regulatory Support

Email: regulatory.support@avantorsciences.com

Trade Compliance

Email: Trade.Compliance@avantorsciences.com

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The most current revision of this document is maintained on our website. Reviews and revisions are performed as warranted due to product changes or as part of the supplier audit cycle and managed under a validated document control system.

Material Name: Lactose Monohydrate **Product codes:** 2249, 2250, 6270 **Date:** January 19, 2017

Source/Type of Excipient: ☐ Mineral; ☐ Mineral derived; ☐ Plant; ☐ Plant derived; ☐ Synthetic; ☐ Fermentation derived

Other (explain): Bovine milk derived via enzymes and crystallization

Elemental Impurity		Class	Likely to be Present			If Known, Please Identify the Expected Concentration /Units (or Range)	Analytical Method Used (and Limit of Detection if Available)	Comments regarding source of information (i.e.; number of lots tested, frequency of testing, process understanding, etc.)
Arsenic (inorganic)	As	1	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Cadmium	Cd	1	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Mercury (inorganic)	Hg	1	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Lead	Pb	1	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Cobalt	Co	2A	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Nickel	Ni	2A	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Vanadium	V	2A	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Silver	Ag	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Gold	Au	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Iridium	Ir	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Osmium	Os	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches

Elemental Impurity		Class	Likely to be Present			If Known, Please Identify the Expected Concentration /Units (or Range)	Analytical Method Used (and Limit of Detection if Available)	Comments regarding source of information (i.e.; number of lots tested, frequency of testing, process understanding, etc.)
			Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>			
Palladium	Pd	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Platinum	Pt	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Rhodium	Rh	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Ruthenium	Ru	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Selenium	Se	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Thallium	Tl	2B	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Barium	Ba	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Chromium	Cr	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Copper	Cu	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<2.0 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Lithium	Li	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Molybdenum	Mo	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Antimony	Sb	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches
Tin	Sn	3	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>	Unknown <input type="checkbox"/>	<0.05 ppm	ICP-MS (MRL=0.05 ppm)	Avg. of 3 batches

Reference: ICH Q3D Guideline for Elemental Impurities, Step 4 version, September 2014



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Prepared by the Technical Service Department

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