Avantor™ Performance Materials
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Technical Service Department
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Date: June 14, 2023

Re: Information for Select Avantor products regarding the Nitrosamine assessment for Active Pharmaceutical Ingredient (API) products manufactured by Avantor.

The FDA's *Guidance for Industry: Control of Nitrosamines in Human Drugs (effective 31 March 2021)* has recommended that API manufacturers consider pathways observed to evaluate the risk for nitrosamine contamination or formation in API and take appropriate measures to prevent unacceptable levels of nitrosamine impurities in their products. Following an internal evaluation in accordance with FDA's guidance, Avantor Performance Materials, LLC ("Avantor") has determined that nitrosamine and related compounds are not likely to be present in any of the Active Pharmaceutical Ingredients ("APIs"), manufactured by Avantor at its Phillipsburg, NJ and Paris, KY sites and listed at the end of this document. Avantor's review of these Products for risk of nitrosamine included the assessment of potential nitrogen sources, sub-contracted activities, agricultural/natural sources, and other chemistries with potential for nitrosamine impurity formation.

Avantor is able to confirm:

1. None of our manufacturing processes have reaction chemistries that utilize nitrosating agents.
2. There is no risk of producing any nitrosamine compounds in the manufacturing of our inorganic excipients. Raw materials consist of inorganic acids and bases, no catalysts are utilized, and no amines are present in the raw materials (mineral origin).
3. We do not outsource any recovered materials for 3rd parties for processing. Any return of mother liquors to the manufacturing process is controlled by Avantor and involve inorganic manufacturing processes.
4. Our bulk chemical process equipment is used to manufacture a variety of products. None provide a risk of cross-contaminating with nitrosamines as all are inorganic products as stated above. Only water is used in validated process equipment cleanout procedures. There is no cleaning agent that may contaminate the equipment or lead to the formation of nitrosamines.
5. Since our manufactured products are inorganic, no nitrosamine contamination from product degradation is considered probable.
6. Products purified by distillation are strong acids and pure solvents. The distilled products do not chemically support the formation of nitrosamines in the process, nor would carry over into the distilled product be expected.
7. No Nitrocellulose containing materials are used as final packaging components of these products.

Considering the very low potential for the presence of nitrosamines in Avantor manufactured products as set forth above, no specific testing was or is intended to be performed by Avantor to confirm the absence of nitrosamine or related compounds in the Products. Avantor makes no warranties or representations,

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express or implied, related to the presence or absence of nitrosamine or related compounds in any of the Products.

Further information on this guidance may be found at: https://www.fda.gov/media/141720/download

The following products have been assessed as Active Pharmaceutical materials, in alignment with the FDA guidance issued in 2021 [1, 2]. By this review and assessment of the materials and manufacture process for these products, Avantor found no API products that required specific testing for nitrosamine or notification to the FDA for exceeding ICH specifications for nitrosamines. A document of the evaluation is available for review by the FDA during inspection of our plant sites.

AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
9736	Ammonia Solution, Strong, N.F. Multi-Compendial
3817	di-Sodium hydrogen phosphate heptahydrate
5956	Magnesium chloride hexahydrate
2448	Magnesium Chloride, 6-Hydrate, Crystal U.S.P. - F.C.C.
2449	Magnesium Chloride, 6-Hydrate, Crystal, U.S.P. Multi-Compendial
5691	Magnesium Sulphate, 7-Hydrate, (For Parenteral Use) USP - GenAR®
5054	Magnesium Sulphate, Anhydrous U.S.P.
3250	Potassium Phosphate, Dibasic, U.S.P. Multi-Compendial Endotoxin Tested
2917	Potassium Acetate, Granular, USP Multi-Compendial
3193	Potassium Nitrate, Granular, U.S.P. Multi-Compendial
3255	Potassium Phosphate, Dibasic, Anhydrous Multi-Compendial
3247	Potassium Phosphate, Monobasic, Crystal N.F. - F.C.C.
3248	Potassium Phosphate, Monobasic, Crystal, NF Multi-Compendial
3374	Sodium Acetate, Trihydrate Multi-Compendial
3462	Sodium Acetate, Trihydrate, Crystal U.S.P. - F.C.C.
3461	Sodium Acetate, Trihydrate, Crystal, U.S.P. Multi-Compendial
3689	Sodium Fluoride, Powder U.S.P.
3803	Sodium Phosphate, Dibasic, 7-Hydrate U.S.P.
3816	Sodium Phosphate, Dibasic, 7-Hydrate, Crystal U.S.P.
3827	Sodium Phosphate, Dibasic, Anhydrous U.S.P.
3826	Sodium Phosphate, Dibasic, Anhydrous U.S.P., A.C.S.
4953	Sodium Phosphate, Dibasic, Anhydrous, U.S.P. Multi-Compendial
3820	Sodium Phosphate, Monobasic, Monohydrate, Crystal U.S.P. - F.C.C.
3821	Sodium Phosphate, Monobasic, Monohydrate, Crystal U.S.P. - F.C.C.
3802	Sodium Phosphate, Monobasic, Monohydrate, U.S.P. Multi-Compendial
3802	Sodium Phosphate, Monobasic, Monohydrate, U.S.P. Multi-Compendial
4954	Sodium Phosphate, Monobasic, Monohydrate, U.S.P. Endotoxin Tested
6325	Trehalose, Dihydrate Multi-Compendial
8872	Zinc Sulfate, 7-Hydrate, Granular U.S.P. - F.C.C.

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AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
324A-R	Potassium Phosphate, Monobasic Multi-Compendial
325A-R	Potassium Phosphate, Dibasic Multi-Compendial Endotoxin Tested

[1]Information about Nitrosamine Impurities in Medications at https://www.fda.gov/drugs/drug-safety-and-availability/information-about-nitrosamine-impurities-medications#resources.

[2]U.S. Food & Drug Administration, Control of Nitrosamine Impurities in Human Drugs, Revision 1, February 2021, https://www.fda.gov/media/141720/download.

If you have any questions or require additional information, please contact Technical Services.

Rev 0: November 30, 2022 - New document for Avantor API nitrosamine assessment.
Rev 1: June 14, 2023 – Updated the document to APM, Radnor, PA. letterhead. Included 324A, 325A-R product codes.

Prepared by the Technical Service Department