

Avantor
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Date: April 12, 2023

Re: Information for Select Avantor products regarding the EMA guidance "Information on nitrosamines for marketing authorization holders"

Following an internal evaluation in accordance with applicable regulatory authority guidance, Avantor Performance Materials, LLC and VWR Chemicals, LLC ("Avantor") has determined that nitrosamine and related compounds are not likely to be present in any of the products included in the pharmaceutical excipients (collectively, the "Products") manufactured by Avantor at its Phillipsburg, NJ, Paris, KY, and Aurora OH sites and listed below. Avantor's review of the 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. Following such assessment, Avantor is able to confirm as follows:

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, 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.ema.europa.eu/en/documents/referral/nitrosamines-emea-h-a53-1490-assessment-report_en.pdf

AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
2488	Acetic Acid, 36% N.F.
0321	Acetic Acid, 80% Solution Biotech Reagent
0375	Acetic acid 1 M Biotech Reagent Aqueous Solution
UB22	Acetic acid 6 M Biotech Reagent Aqueous Solution
9036	Acetone, N.F. Multi-Compendial
9008	Acetone N.F. - F.C.C.
2462	Acetone, NF - ACS N.F., A.C.S.
9726	Ammonia Solution, Strong N.F. - F.C.C.
3226	Ammonia Solution, Strong; Ammonium Hydroxide N.F., A.C.S.
3261	Ammonium Hydroxide (28.0-30.0% as NH ₃) N.F., A.C.S.
3226	Ammonia Solution, Strong; Ammonium Hydroxide N.F., A.C.S.
0798	Ammonium Sulphate N.F.
3523	Ammonium Sulfate, Granular N.F., A.C.S.
4628	Ammonium Sulfate N.F., A.C.S.
9039	Benzyl Alcohol, N.F. Multi-Compendial
7578	BAKERBOND® C18 Non-Endcapped Spherical, 50 µm, 120 Å Prep LC Packing SPE
0341	Citric Acid 50%, Solution Biotech Reagent
2262	Dextrose, Anhydrous, Granular U.S.P., A.C.S.
0890	Dextrose Solution, 50% (w/w) Biotech Reagent
6322	D-(+)-Galactose, NF Multi-Compendial
0516	Guanidine Hydrochloride Solution, 6M
0510	Guanidine Hydrochloride Biotech Reagent
2062	Hydrochloric Acid N.F., F.C.C., A.C.S.
V226	Hydrochloric Acid
2515	Hydrochloric Acid NF - GenAR®
2626	Hydrochloric Acid NF - GenAR®
0335	Hydrochloric Acid, 0.5N Solution Biotech Reagent
0322	Hydrochloric Acid, 0.25 N Biotech Reagent
BS24	Hydrochloric Acid, 1.0 N Solution Biotech Reagent
0325	Hydrochloric Acid, 1.0N Solution Biotech Reagent
0336	Hydrochloric Acid, 2.0N Solution Biotech Reagent
0319	Hydrochloric Acid, 5.0N Solution Biotech Reagent
0347	Hydrochloric Acid, 6.0N Solution Biotech Reagent
BS12	Hydrochloric Acid, 6.0N Solution Biotech Reagent

AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
0327	Hydrochloric Acid, 6.0N Solution Biotech Reagent
2608	Hydrochloric Acid, Diluted N.F.
2612	Hydrochloric Acid (HCl 36.5%-38.0%) N.F., F.C.C., A.C.S.
0323	Hydrochloric Acid, 25% Biotech Reagent
9544	Hydrochloric Acid, N.F. Multi-Compendial
2182	Hydrogen Peroxide, Topical, Solution, 2.5-3.5% U.S.P.
V264	Isopropyl-beta-D-thiogalactopyranoside (IPTG)
BS15	Magnesium Sulfate U.S.P.
5053	Magnesium sulphate
8814	Methanol SPECTRONORM
8818	Methanol SPECTRONORM
4874	Methylene Chloride NF - GenAR®
2097	N-Acetyl-L-Arginine Biotech Reagent
V471	Nitric Acid (Standard of SFE)
9607	Nitric Acid, 69.0-70.0% N.F.
4489	PanExcea™ MHC300G Excipient
5683	Phosphoric Acid, Diluted, N.F. Multi-Compendial
0334	Phosphoric Acid Solution, 33% (W/W) Biotech Reagent
3329	Potassium Thiocyanate Buffered Solution BAKER ANALYZED® Reagent
6696	Potassium Acetate, Crystal U.S.P.
2914	Potassium Acetate, Granular U.S.P.
3192	Potassium Nitrate, Granular U.S.P. - F.C.C.
7746	Potassium dihydrogen phosphate
3251	Potassium Phosphate, Dibasic U.S.P.
3222	Potassium Phosphate, Dibasic U.S.P., A.C.S.
7390	Potassium Phosphate, Monobasic N.F., A.C.S.
BS16	Sodium Acetate, Trihydrate Multi-Compendial
BS18	Sodium Carbonate, Anhydrous Multi-Compendial
BS21	Sodium Phosphate, Dibasic, 7-Hydrate U.S.P.
CH06	Sodium Acetate, Trihydrate Multi-Compendial
LP05	Sodium Acetate, Trihydrate Multi-Compendial
3473	Sodium Acetate, Anhydrous U.S.P. - F.C.C.
3474	Sodium Acetate, Anhydrous U.S.P. - F.C.C.
3600	Sodium Carbonate, Monohydrate, Crystal N.F. - F.C.C.
3603	Sodium carbonate monohydrate
LP08	Sodium Carbonate, Anhydrous N.F. - F.C.C.
3605	Sodium Carbonate, Anhydrous, Granular N.F. - F.C.C.

AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
3606	Sodium carbonate
5002	Sodium Hydroxide 10N PEL/USP H2O Biotech Reagent
5000	Sodium Hydroxide, 10N Solution Biotech Reagent
0896	Sodium Hydroxide Solution 40% (w/w) Biotech Reagent
0379	Sodium Hydroxide 0.1M Solution Biotech Reagent
BS26	Sodium Hydroxide, 0.5N Solution Biotech Reagent
0329	Sodium Hydroxide, 0.5N Solution Biotech Reagent
0328	Sodium Hydroxide, 1.0N Solution Biotech Reagent
0389	Sodium Hydroxide, 1.0N Solution Biotech Reagent
0312	Sodium Hydroxide, 10N Solution, Biotech Reagent Biotech Reagent
0390	Sodium Hydroxide, 2.0N Solution Biotech Reagent
0895	Sodium Hydroxide, 5.0N Solution Biotech Reagent
5668	Sodium Hydroxide, 5N Solution Biotech Reagent
0892	Sodium Hydroxide, 20% Solution Biotech Reagent
0338	Sodium Hydroxide, 25% Solution Biotech Reagent
0897	Sodium Hydroxide, 50% Solution Biotech Reagent
0339	Sodium Hydroxide, 50% Solution Biotech Reagent
3808	Sodium Phosphate, Monobasic, Monohydrate U.S.P., A.C.S.
CH04	Sodium Phosphate, Monobasic, Monohydrate Multi-Compendial
BS22	Sodium Phosphate, Monobasic, Monohydrate Multi-Compendial
LP10	Sodium Phosphate, Monobasic, Monohydrate Multi-Compendial
LP11	Sodium Phosphate, Dibasic, 7-Hydrate U.S.P.
3804	Sodium Phosphate, Dibasic, Anhydrous, U.S.P. Multi-Compendial
CH05	Sodium Phosphate, Dibasic, Anhydrous Multi-Compendial
4953	Sodium Phosphate, Dibasic, Anhydrous, U.S.P. Multi-Compendial
8028	Sodium sulphate
7803	Sodium Sulfate, Anhydrous, Powder USP - GenAR®
6321	Sucrose, NF Multi-Compendial
6320	Sucrose, NF Multi-Compendial
V225	Sulfuric Acid, NF/FCC
0331	Sulfuric Acid, 10.0N Solution Biotech Reagent
2877	Sulfuric Acid 96% Microelectronic Grade
9675	Sulfuric Acid, 95.0-98.0% N.F. - F.C.C.
9661	Sulfuric Acid N.F., A.C.S.
9671	Sulfuric Acid, N.F. Multi-Compendial
9057	tert-Butanol GenAR®
6324	Trehalose, Dihydrate, NF Multi-Compendial

AVANTOR PRODUCT CODE	MATERIAL DESCRIPTION
2910	Water for Injection Quality Water
4384	Zinc Sulfate, 7-Hydrate Granular U.S.P. - F.C.C.
4383	Zinc Sulfate, 7-Hydrate Granular, U.S.P. Multi-Compendial
4372	Zinc Sulfate, 7-Hydrate, Granular U.S.P., A.C.S.

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

Prepared by the Avantor
Technical Service Department

Rev 1: Added additional codes missed in original memo

Rev 2: Updated with language from legal review

Rev 3: Added 9736 missed in original memo

Rev 4: Added 0334 missed in original memo

Rev. 5: Feb. 21, 2022: Separated products that are being assessed as excipients and those as API materials.

Rev. 6: Mar. 16, 2022 – Added 0322 missed in original memo.

Rev 7; August 5, 2022 – Moved 6322 to Excipient; Added 6325, 324A, 325A, 3255, 3374 to API. (PT)

Rev 8; December 5, 2022 – API products removed to be documented in a separate document CIQA-0004.

Rev 9; February 27, 2023 – Updated link to EMEA guidance

Rev 10; April 17, 2023 – Added Aurora OH site and products 0375, UB22, 0379, 0892, 2910 to scope of letter.

While the above information is provided in good faith and believed to be accurate as of the date provided, Avantor makes no representations or warranties as to the accuracy or completeness of such information. All Avantor products are subject to Avantor's terms and conditions of sale including the limitations of liability contained therein and any contrary terms and conditions are expressly

rejected. As Avantor has no control over purchasers' uses of its products, Avantor expressly disclaims all liability with respect to same.