USTR 3486

Nitrosamine Statement

This statement is intended to assist customer efforts in evaluating the risk of nitrosamine impurities in manufacturing processes.

Nitrosamines are compounds of toxicologic concern, which have been known to result from manufacturing processes involving reaction of nitrites with amines. While recent regulatory guidance mainly focuses on chemically synthesized active ingredients as a source of nitrosamine contamination, polymeric materials manufactured with nitrosation-reactive functional groups and amines, or produced on manufacturing lines involving these substances, warrant risk assessment as to the likelihood of these compounds being present.

To address this concern, Pall has identified N-nitrosamine as a controlled substance in our global purchasing specification E962 (see https://www.pall.com/content/dam/pall/pall-corp/literature-library/non- gated/E962.pdf) whereby suppliers are required to identify N-nitrosamine in the materials they supply to Pall. In addition, Pall has evaluated the likelihood of nitrosamine presence in consumable products with consideration to the following factors:

- Intentional use of nitrosating agents in the Pall manufacturing process;
- Presence of secondary and tertiary amines or quaternary ammonium salts in a material of construction or a Pall manufacturing process step;
- Use and purity of solvents, reagents, and catalysts in a Pall manufacturing process step;
- Use of dedicated versus shared equipment during Pall manufacturing processes;
- Selected extractables testing of Pall products.

Pall Sterilizing Grade Filters, Pre-Filters, Virus Filters, TFF Devices (e.g. Omega™ Membrane Cassettes), and Aseptic Connectors, Biocontainers, and Mixers

Based on the above considerations, the risk of these products and components being a contributing source of nitrosamine impurities is low.

Single-Use Systems Assemblies

Based on the above considerations, the risk of these products being a contributing source of nitrosamine impurities is low.

Pall Mustang® Q Membrane Chromatography Capsules

These products utilize materials in the manufacturing process considered precursors for nitrosamine formation; specifically, secondary and tertiary amines or quaternary ammonium salts as part of the polymeric formulation. Since these amine chemistries are not intentionally used in combination with nitrosating agents, such as sodium nitrite, the risk of nitrosamine forming during Pall manufacturing processes may likely be low. For a more rigorous assessment, we are currently evaluating the possibility of trace level contributing sources of nitrite, such as process water.

Depth Filters and Depth Filter Sheets

These products utilize materials in the manufacturing process considered precursors for nitrosamine formation; specifically, secondary and tertiary amines as part of the polymeric formulation. Additionally, some depth filter sheets (activated carbon [AKS] series) contain activated carbon as a material of construction. Activated carbon may catalyze transformation of amine precursors to yield nitrosamines under environmentally relevant conditions. Such a reaction will be dependent on the presence of nitrosating agents, such as sodium nitrite, which is not intentionally used in Pall manufacturing processes. Therefore, we assess the risk of nitrosamine formation as likely low. For a more rigorous assessment, we are currently evaluating the possibility of trace level contributing sources of nitrite, such as process water.

Packaging Materials

Product contact packaging materials are not expected to be a contributing source of nitrosamine impurities.

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