BIOTECH

Statement of Compliance

USTR 3509

Elemental Impurities Statement for Pall® Pharmaceutical-Grade Filter Cartridges / Capsules and Single-Use Components

The United States Pharmacopeia (USP <232> Elemental Impurities – Limits) and Food and Drug Administration (FDA) / International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q3D Elemental Impurities: Guidance for Industry (Sept 2015) specify limits for elemental impurities in final drug products. Elemental impurities may arise from residual catalysts intentionally added during polymer synthesis or be present as impurities related to process equipment. Twenty-four (24) elements are defined, that if known to be present, intentionally added, or have the potential to be introduced, must be below concentration limits in the final drug product. These elements are assigned into 3 Classes based on their toxicity profile and the likeliness of them occurring in a drug product, with Class 1 being the most toxic.

While the concentration limits expressed in the above referenced documents do not apply directly to process equipment or filters, Pall is pleased to provide you with the following information to assist in your risk assessment and control strategies.

Metal catalysts and metal reagents are not used in the final manufacturing steps of Pall pharmaceutical-grade filters and components for single-use systems (SUS). Additionally, Pall has implemented a global purchasing specification with our suppliers to limit or exclude the use of various substances in the materials used in our manufacturing processes. We can confirm that all Q3D Class 1 elements, and some Class 2 and Class 3 elements, are listed in the specification and therefore are not expected to be present in our filter materials of construction. Because Pall does not use metal catalysts, nor are they expected to be present in the materials we purchase, we have not set limit values nor conduct testing on a lot specific basis.

For the following families, we have conducted extraction studies with industry standard or representative solvents at a highly sensitive effective filtration area to extraction volume ratio (i.e. 1 to 5 cm^2/mL depending on the format):

Supor® EKV / EBV Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for nickel (Ni) and chromium (Cr), which were reported at a maximum concentration of 0.010 µg/cm^2 and 0.022 µg/cm^2, respectively. These elements are not known to be intentionally added into the filter materials of construction and are not expected to pose a risk concern under actual use conditions.

Supor EAV Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Class 3 elements molybdenum (Mo), antimony (Sb), barium (Ba), copper (Cu) and Cr, which were reported at no more than 0.036 µg/cm^2. Ni (Class 2) was also detected at a maximum concentration of 0.088 µg/cm^2 but is a speculated artifact related to analytical test conditions used in the study. These elements are not known to be intentionally added into the filter materials of construction and are not expected to pose a risk concern under actual use conditions.

Supor EX (ECV) Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit.

Fluorodyne® II DFL / DBL / DJL Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Ni, which was reported at a maximum concentration of 0.028 µg/cm^2. This element, which is considered an artifact arising from polyatomic matrix interference (i.e. $^{23}Na^{37}Cl^+$), is not known to be intentionally added into the filter materials of construction and is not expected to pose a risk concern under actual use conditions.

Ultipor® N66 (NF / NR / NL / NX / NB) Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Sb, Cu and gold (Au). Sb (Class 3) was reported at a maximum concentration of 0.228 µg/cm^2 and is related to the polyester materials within the filter. Cu and Au were both reported at a maximum concentration of 0.010 µg/cm^2 but are speculated artifacts related to analytical test conditions used in the study. All these elements are not expected to a pose risk concern under actual use conditions

Posidyne® (NFZ / NLZ / NTZ) Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Sb, which was reported at a maximum concentration of 0.42 µg/cm^2. This element is related to the polyester materials within the filter and is not expected to pose a risk concern under actual use conditions.

Emflon® PFR Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Au, which was reported at a maximum concentration of 0.008 µg/cm^2. This element, which is considered an artifact related to analytical test conditions used in the study, is not known to be intentionally added into the filter materials of construction and is not expected to pose a risk concern under actual use conditions.

Emflon II (V002) Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit.

HDC® II Filters

In a limited ICH Q3D elemental impurity portfolio screening (including all Class 1 and some Class 2 and 3), no ICH Q3D element detected above 20 ppb reporting limit.

Fluorodyne EX EDF Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit.

Fluorodyne EX EDT Filters

There were no ICH Q3D elements detected above the 20 ppb reporting limit except for Class 3 elements Sb, Ba, Mo, and Cr, which were reported at no more than 0.112 µg/cm^2. Ni (Class 2) was also detected at a maximum concentration of 0.016 µg/cm^2 but is a speculated artifact related to analytical test conditions used in the study. These elements are not known to be intentionally added into the filter materials of construction and are not expected to pose a risk concern under actual use conditions.

Profile® II

There were no ICH Q3D elements detected at the 20 ppb reporting limit.

Kleenpak® Presto Sterile Connectors

There were no ICH Q3D elements detected above the 20 ppb reporting threshold.

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T-Series TFF Cassettes with Omega™ Membrane

All ICH Q3D element impurities were found to be less than 0.051 µg/cm^2.

For other Pall families, Pall is currently conducting standardized extractables testing and will screen for all ICH Q3D metals in future extractables datasets and supporting validation packages. Please check with your Pall Sales representative for updates

I hope you find this information helpful. Please feel free to contact me at janet_mathus@pall.com if you require additional information.

Prepared by Pall Quality Assurance and Regulatory Affairs for Biotechnology

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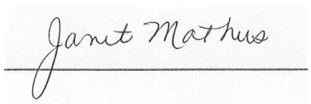
Author: Janet Mathus

Signature: 

PALL CORPORATION

Corporate Headquarters
Port Washington, NY, USA
+1-800-717-7255 toll free (USA)
+1-516-484-5400 phone

European Headquarters
Fribourg, Switzerland
+41 (0)26 350 53 00 phone

Asia-Pacific Headquarters
Singapore
+65 6389 6500 phone

Visit us on the Web at www.pall.com/biotech
Contact us at www.pall.com/contact

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