Cytiva
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USA

Nitrosamine Compliance Statement

Regarding: Hollow fiber cartridges

Background

According to the World Health Organization (WHO), nitrosamines are any compound containing a nitroso (NO) functional group. These compounds are of concern because they are potential carcinogens. Nitrosamine is formed when secondary or tertiary amines react with a nitrosating agent, such as nitrous acid. The most common source of nitrosating agents is sodium nitrite.

The European Medicines Agency (EMA) finalized a review under Article 5(3) of Regulation (EC) No 726/2004 in June 2020 to provide guidance to marketing authorization holders (MAH) on how to avoid presence of nitrosamine impurities in human medicines. Assessment report EMA/369136/2020 "Nitrosamine impurities in human medicinal products" was published on 25 June 2020 and adopted by the Committee for Medicinal Products for Human Use (CHMP).

The U.S. Food and Drug Administration (FDA) Guidance for Industry, entitled "Control of Nitrosamine Impurities in Human Drugs" and published in February 2021, recommends steps manufacturers of active pharmaceutical ingredients (APIs) and drug products should take to detect and prevent unacceptable levels of nitrosamine impurities in pharmaceutical products.

Cytiva does not manufacturer APIs or finished medicines but understands that single-use products may be used in the manufacture of finished drugs and drug products.

Statement

It is hereby stated that nitrosamines are not primary raw materials of wetted components, nor are they intentionally added or introduced during the manufacturing process of hollow fiber cartridges.

While nitrosamine levels are below our limits of detection, trace amounts of precursors were observed in the finished part. These findings are part of an extractables study, available on the Customer Regulatory Support website, *www.cytiva.com/rsf*. After registration, subscription, and approval, users can download the study entitled, *Extractables Information for Hollow Fiber*. It is recommended that customers use the extractables information to assess the risk of actionable levels of nitrosamines in their processes.

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General statements, including this one, are available on the Customer Regulatory Support website at www.cytiva.com/rsf. See "Download without a subscription" then "Statements."