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Date of issue: 23 July 2021
Version 3

To whom it may concern

Re: 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a)

This document first describes the product and the manufacturing process and makes declarations concerning the manufacture of 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a).

1. 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) Overview

1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) is a product that is widely used in the pharmaceutical industry as an excipient propellant in multi-dose inhalers. It is produced from a raw material that is manufactured in a synthetic reaction of trichloroethylene with hydrogen fluoride and purified.

1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) is a liquefied gas under pressure at ambient temperature which is manufactured in a dedicated manufacturing plant which is a sealed system as the liquefied gas boils at -26°C and as such is maintained in a dedicated sealed system under pressure and is not exposed to the environment.

2. Declarations

a. Transmissible Spongiform Encephalopathy (TSE)/Bovine Spongiform Encephalopathy (BSE) Statement

This statement is to confirm that the 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) has been assessed with respect to materials identified in the "Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (EMA/410/01)".

Herewith it is confirmed that the pharmaceutical grade 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) manufactured by Koura at its Runcorn Site, Runcorn, Cheshire, United Kingdom, is neither derived from animal origin nor manufactured utilising intermediates and / or auxiliary agents which are exposed to TSE/BSE agents.

b. US Residual Solvents Statement with regards to USP<467>

This statement is to confirm that:

- No Class 1 Solvents, based on USP <467>, are used in the manufacture of the 1,1,1,2-tetrafluoroethane (ZEPHEX®134a) supplied by Koura for use in pharmaceutical metered dose inhalers.
- No Residual Solvents (Class 2, Class 3, Table 4), based on USP <467>, are present in 1,1,1,2-tetrafluoroethane supplied by Koura. No other Residual Solvents, in addition to those listed in USP <467>, are present in the 1,1,1,2-tetrafluoroethane (ZEPHEX®134a) supplied by Koura.

c. Rest of the World Residual Solvents Statement with regards to ICH Q3C(R8)

This statement is to confirm that the 1,1,1,2-tetrafluoroethane (ZEPHEX® 134a) supplied by Koura for use in pharmaceutical metered dose inhalers does not contain any of the residual solvents listed in the ICH Harmonised Tripartite Guideline Impurities: Guideline for Residual Solvents Q3C(R8).

d. HALAL Precept Statement

This statement is to confirm the following facts about manufacture of 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) supplied by Koura:

- o 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) is manufactured by Koura, at its Runcorn site, Runcorn, Cheshire, United Kingdom).
- o 1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) has been prepared exclusively from synthetic materials. No raw material, reagent or substance of animal or human origin is used for or during the manufacturing process.
- o Neither the product (1,1,1,2-Tetrafluoroethane (ZEPHEX®134a)) nor any of the raw materials, from which it is derived, are obtained by fermentation or with the aid of enzymes, bacterium or yeasts.
- o None of the raw materials are ethanol or obtained from ethanol.

e. Table of Statements with respect to Allergens, 'Other Chemicals' and GMO's

1,1,1,2-Tetrafluoroethane (ZEPHEX®134a) has been prepared exclusively from synthetic materials. No raw material, reagent or substance of animal or human origin is used for or during the manufacturing process. The following list has been prepared for specific areas currently identified as required.

Allergens 'Other Chemicals' GMO's	Present in product Yes (Y) / No (N)	Present due to cross contamination Yes (Y) / No (N)
Aflatoxins	N	N
Cyanuric acid	N	N
Dioxin	N	N
Egg	N	N
Egg Derivative	N	N
Gluten	N	N
GMO's	N	N
Latex	N	N
Lecithin	N	N
Melamine	N	N
Phthalates	N	N
Pesticides	N	N
Soy	N	N
Lactose	N	N
Wheat	N	N

For and on behalf of Koura
(Koura trading under Mexichem UK Ltd)



23 JUL 2021

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For further information on our products or concerns over usage please contact your local Koura representative who will be more than willing to help you.

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Version 3

Page 4 of 4