Evaluation

Sponsor	EnviteC-Wismar GmbH, Mr. Michael Schiffner, Alter Holzhafen 18, 23966 Wismar
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Evaluation	Biological safety - toxicology (EN ISO 10993-1, Directive 93/42/EC)
Documentation	Presented by the sponsor
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Device/material	T-adapter, component of OxiQuant oxygen monitor [1].
Manufacturer	EnviteC-Wismar GmbH
Intended use	Component of oxygen measuring device for e.g. anesthesia, intensive care, incubators, multiple use, reusable [1, 2].
Body contact	Indirect (air-mediated) with mucosal tissue of the respiratory tract, up to 30 days acc. to application [1].
Surface area	< 20 cm² (contact with air)
EN ISO 10993-1	Biological effects to be considered for material leachables are cytotoxicity, sensitization, irritation, acute systemic toxicity, subacute toxicity, genotoxicity.
Sterilization method	- (not intended) [1, 2]
Remarks	This evaluation relates only to toxic effects induced by potentially leachable substances of the tested device/material. Any material interactions with cleaning and disinfection solutions and reprocessing-related material changes are not covered by this assessment.

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Material

Polyethylene HDPE 25455N (Dow Corning) [1]

Test matrix

Toxicological tests performed on the device

Device/material	Test	Ref	Comments	Result
T-adapter, cleaned samples	Cytotoxicity EN ISO 10993-5	[3]	4.5 cm²/ml DMEM-FBS incl. 1.5 % DMSO, 24 h, 37 °C, L 929 cell cultures, 72 h, 37 °C, quantitative determination of cell proliferation	n.n.
	Chemical analysis EN ISO 10993-18	[4]	3 cm²/ml ethanol/water (1:20), 24 h, 37 °C, GC-FID, quantification of organic leachables	n.n. (< 1 µg/cm²/24 h)
		[4]	3 cm²/ml isopropanol, 24 h, 37 °C, GC-MS, characterization of organic extractables	n.n.

n.n. = no toxicologically relevant effects observed in comparison to the controls

Evaluation

The material of the T-adapter does not affect the biological safety of the patient by leachables for the following reasons:

- According to the manufacturer the device component has been marketed for 15 years without obvious material-related bioincompatibility reactions [1].
- Extracts of the component have been tested in a cell culture test system, which allows a very sensitive characterization of the resting „solubility" of materials (organic and inorganic leachables and contaminants). The test system and extraction method has been specifically designed to ensure most sensitive detection of toxic leachables on cellular level (e.g. more than 2-fold more sensitive than USP elution method). The medium was supplemented with an organic solvent (1.5 % dimethylsulfoxide) to intensify the migration of substances. No cytotoxic effects were obtained in presence of the 24 h extracts (see test matrix).
- The results of highly sensitive chemical analyses (gas chromatography, GC-FID) confirm inert properties of the material contained. The total amount of organic leachables was below the detection limit of 1 µg/cm²/24 h. As well, no organic extractables were identified in solvent extracts (isopropanol, 24 h, 37 °C) prepared under exaggerated and material-affecting conditions. Therefore, there is no indication that the material contains and/or releases substances in toxicologically relevant concentrations.

- According to the supplier the composition of the polyethylene complies to regulations for food-contacting polymers.
- The surface limited and indirect (air-mediated) contact negates the exposure of the patient to ingredients/residues in persistently hazardous concentrations.

No further toxicological testing (e.g. sensitization, mucosa/tissue irritation, systemic toxicity, genotoxicity, subchronic toxicity) was performed on extracts of the device component. This is justified because of the existing clinical experience and the insoluble properties proven by highly sensitive biological and chemical test methods. Extraction conditions and test methods used exceed actual normative requirements to provide highest possible safety level for the patients. Additionally, it is assumed that extracts will not contain substances in toxicologically relevant concentrations and/or in concentrations high enough to elucidate any responses in biological test systems. Therefore, there is no adequate sensitivity and no need of further testing.

The material insolubility of the T-adapter is in compliance with the requirements of EN ISO 10993-1 for the intended use. There is no evidence that any effects hazardous to the patient will arise by leachable ingredients and/or residues (see remarks for reprocessing).

Dr. Stephan Rossberger

Documentation []

1. EnviteC: Correspondence, specification of the device and material components, 2011.
2. EnviteC: Instructions for use, OxiQuant MC, 2009.
3. Medical Device Services: Test report 113388-20-A, cytotoxicity, T-adapter 22 mm/15 mm, 2011.
4. Medical Device Services: Test report 113389-20-A, chemical analysis, T-adapter 22 mm/15 mm, 2011.