TECHNICAL BULLETIN

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Use of Copper Beryllium Alloy for Medical VIPRs

This Technical Bulletin is a revision of Technical Bulletin 06 published in 2012 and takes into account the new requirements of the Medical Device Regulation, (MDR) and the lower Permissible Exposure Limit, (PEL) set in the United States of America, Occupational Safety and Health Administration (OSHA Guidance) [1,2].

Introduction

Copper beryllium (CuBe) alloy is the preferred material of construction for springs used in medical oxygen valves with integrated pressure regulators (VIPRs), where they are mainly used in the regulator, for pressure control, but can also be used in the non-return valve in filling ports or other sub-assemblies. It is the material of choice due to its resistance to ignition when in an oxygen environment, as well as its physical characteristics, including its high material strength, resistance to fatigue.

However, beryllium is also classified as a class 1B carcinogenic material [1] and its use is now controlled in medical devices by the new Medical Device Regulation, 2017/745. [2].

As the CuBe alloy only contains 2% beryllium, this Technical Bulletin describes the rationale as to why it is considered acceptable for it to be used as the material of construction for springs in gas wetted areas in medical VIPRs intended for administration of medical gases containing high concentrations of oxygen.

Although it is the responsibility of the medical VIPR manufacturer to provide this justification for the use of materials containing more than 0.1% Beryllium within their medical device, EIGA has prepared this Technical Bulletin, based on their knowledge and experience, as a generic assessment to justify the use of CuBe in the medical VIPRs.

MDR Requirements

The Medical Device Regulations [2] specify that the use of carcinogenic materials, as listed in Table 3.1 — *List of harmonised classification and labelling of hazardous substances* of the CPL Regulation, shall be controlled in the manufacture of medical devices [3].

Concerning the general safety and performance requirements of the MDR, Annex I, clause 10.4.1 addresses the design and manufacture of devices used for the administrations of gases to the patient. It states in particular that substances classified as carcinogenic 1B in a concentration that is above 0.1 % weight by weight (w/w) can be used only if:

- potential patient exposure to the substance has been duly analysed and estimated;
- possible alternative materials or designs have been thoroughly reviewed;

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- alternative materials have been demonstrated as being inappropriate in relation to maintaining the functionality and performance of the device; and
- benefit-risk ratios of the product are positive.

EIGA elemental impurity test results

To meet the pharmaceutical requirements for monitoring the elemental impurities in the medical gases, EIGA has conducted an elemental impurity assessment. The assessment, carried out on medicinal oxygen cylinder packages fitted with VIPRs, was used to demonstrate that even when administering the maximum daily dosage of medical gases to the patient, the gases are compliant with the requirements specified in ICH Q3D. Using risk management techniques, the specific elemental impurities likely to be present in the gas were identified and levels determined using validated protocols, which used ICP-MS as the measurement technique.

The results of the tests are given in EIGA Doc 216, *ICH Q3D Risk Assessment – Report on Elemental Impurities* [4].

Potential patient exposure to beryllium

The permissible exposure limits (PELs) for Beryllium, given by OSHA in its publication *Final Rule Occupational Exposure to Beryllium and Beryllium Compounds in the Federal Register* [1] sets the 8-hour time-weighted average (TWA) PEL of 0.2 µg/m^3.

Although the results of the testing did not include beryllium (as it was not specified in ICH Q3D), the levels of copper were included, and the results were within the limits.

Considering that the valves tested were fitted with copper beryllium springs:

- the results of copper levels are known as determined by ICH Q3D testing;
- the levels of beryllium within the copper beryllium spring are only at 2%;
- the valves tested had other sources of copper that could contribute to the copper levels; and
- the volumes sampled based on the maximum daily dosage;

it is possible to assess from the results the levels of beryllium and whether they are below the PEL levels.

The values for the levels of copper found in the medicinal oxygen delivered by the medical VIPRs are given in EIGA Doc 216, Table 12, *Summary of elemental impurity data for potential components*. The results show that the concentration for copper, determined in the test procedures were less than 0.54 µg/day (based on a maximum daily dosage of 10,800 litres per day). Considering that the content of beryllium in the spring was only 2% of the total mass, this would indicate that the contamination levels would be less than 0.001 µg/m^3. It should also be noted that there are other sources copper within the medical VIPRs that were tested, indicating that the results are likely to be even lower when taking this fact into account.

These results clearly show that the levels of beryllium in the gases delivered from a medical VIPR will be at least 200 times less than the PEL limits when used to administer the maximum daily dosage of oxygen to the patient

Alternative materials of construction

An alternative material that can be used for the springs in medical VIPRs is stainless steel, but this does not have such a good resistance to an ignition. The consequences of an ignition within the medical VIPR can have extreme consequences on the patient being treated as well as the healthcare professions administering the gas. Once the

spring ignites, the likelihood is that the other components of the valve and any surrounding combustible materials will also ignite, creating an extreme incident that could lead to fatalities.

EIGA has reviewed the relative risks associated with the choice of material used for medical VIPR springs and is of the opinion that the consequences of a failure due to ignition of the spring are considered as being more extreme than concerns about beryllium contamination.

EIGA Conclusion

This review shows that the:

- level of exposure that the patient will be subjected to, under the worst conditions of use, will be at least 200 times lower than the maximum permissible exposure level (PEL) set in the OSHA Guidance document [1];
- likelihood of an ignition occurring with a CuBe spring (compared to stainless steel) is significantly lower; and
- consequences of an ignition when a stainless-steel spring is used are significantly higher than with a CuBe spring

Consequently, the criteria for the acceptability of a substance, as specified in the Medical Device Regulation (Annex I, Clause 10.4) [2] are met for CuBe, allowing its safe use in the manufacture of medical VIPRs.

References

[1] 82 FR 2470 OSHA *Final Rule for Occupational Exposure to Beryllium and Beryllium Compounds in the Federal Register (January 9, 2017)* www.govinfo.gov

[2] Regulation (EU) 2017/745 *of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC* www.eur-lex.europa.eu

[3] Regulation (EC) No 1272/2008 *of the European Parliament and of the Council of of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006* www.eur-lex.europa.eu

[4] EIGA Doc 216, *ICH Q3D Risk Assessment – Report on Elemental Impurities*, www.eiga.eu

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