# TECHNICAL BULLETIN

Prepared by: WG-7 & WG-8 TB 02/12 – February 2012

## Microbiological Quality of Medical, Pharmaceutical and Food Grade Gases

### 1 Introduction

This Technical Bulletin details EIGA's position concerning the microbiological quality of gases used in medical, pharmaceutical and food gas applications. It is intended to assist in providing responses to both end users of the gases or to Regulatory Authorities when being asked questions about the microbiological quality of gases.

There are no specific standard requirements for the levels of microbiological contamination within specifications for food grade gases but the European Pharmacopoeia specifies a general requirement for inhalation products in Chapter 5.1.4 Microbiological Quality of non-sterile pharmaceutical preparations.

Although the gases supplied for these purposes are not specified as being sterile, the processes and procedures adopted within the gas industry ensure that the manufacturing and filling processes limit the potential for microbiological contamination. All of the testing carried out by the industry, has shown typical values of microbiological contamination significantly lower than the limit set by the European Pharmacopoeia.

### 2 Scope

The scope of this document specifically covers the microbiological quality requirements for gases used for medical[1], pharmaceutical and food gas applications. It covers compressed or liquefied gases supplied in high pressure cylinders or cryogenic liquids, supplied by tankers into bulk storage tanks or in portable cryogenic containers.

It covers the quality of the gas up to the point of delivery (into the customer's storage tank) or at the outlet valve in either high pressure cylinders or portable cryogenic containers. It does not address the quality of the gas once it has been distributed to the usage point via the customer's pipeline system. It also does not cover medicinal or food grade gases that are produced using either Pressure Swing Adsorption (PSA) or Air compressing plants on the customer's premises.

This Technical Bulletin relates only to the quality of the gas and does not cover the external condition of the container.

### 3 Potential sources of contamination

The gases used for medical, pharmaceutical and food gas applications are manufactured and supplied from a number of different types of sources and processes, all of which ensure that microbiological controls are in place.

**Note 1:** The term medical in this document refers to both medicinal gases, used for administration to patients and medical gases, used as a medical device, as specified under the European Directive 93/42.

Quality risk analysis studies, carried out by the gas industry, have indicated that the levels of microbiological contamination of compressed, liquefied and cryogenic gases will be well below the levels specified in the European Pharmacopoeia Chapter 5.1.4, provided that standard procedures are followed.

The standard procedures used within the gas industry for the manufacture, filling and distribution of gases ensure the microbiological contamination levels are kept at a low level.

Contamination is controlled by manufacturing the gases in closed systems and supplying them under pressure,

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ensuring no contact with ambient air. In addition, they are maintained at extremely low moisture levels, making the conditions for microbiological growth unfavourable.

Where water comes in contact with the process gas, as part of the manufacturing process, the water quality is controlled (as defined in the EC Guide to Good Manufacturing Practice) using validated methods. Normally either drinking water or special treated water is used to ensure microbiological contamination is minimised. This ensures that the introduction of contamination into the gas stream is kept to a minimum. As part of the manufacturing process, the gases are dried prior to the final process steps, which ensure that any microbiological growth in the gas is controlled.

For gases supplied in cylinders or cryogenic containers, the valve outlets are covered immediately after filling to ensure no contamination enters the outlet. For cryogenic and liquefied gases, supplied by tanker, the transfer hose is back purged with gas prior to making the delivery to ensure that any contamination with the hose is removed prior to the product being transferred to the customer tank.

## 4 Use of gases

Whereas the gases are supplied to the end user in a controlled condition, the end user should also carry out a risk assessment of their complete system to establish if there are risks associated with their distribution pipe-work systems that could contaminate the gas. Where there is a requirement for the microbiological contamination of the gas to be controlled, appropriate bacterial or virus filters at the point of use should be used to ensure that the gas is free from any residual contamination.

Maintenance regimes should be established to ensure that filters are changed at an appropriate frequency, as defined by the manufacturer of the filter or the user.

## 5 Proposed Test Methods

The gas industry recommendation is that there is no requirement for routine microbiological testing of gases prior to supply.

However, where there is a specific need to test the gas, it should only be carried out by appropriately trained personnel who are familiar with the specific sampling requirements for gases, due to either its high pressure or cryogenic conditions.

It should be noted that the available test methods only allow the tests to be carried out on a gaseous sample. As a consequence liquefiable and cryogenic gases need to be vaporised before testing.

Correct preparation of the sampling equipment is difficult due to the need to ensure that the pressure regulator, required to reduce the pressure of the sample gas, has been prepared correctly to ensure that the gas sample is not contaminated. Generally, the sampling equipment needs to be manufactured in stainless steel to permit it to be sterilised prior to use.

Where microbiological testing of the gas is requested by the customer, the method of testing should be selected carefully. Having selected the method, care is needed to ensure that the sampling equipment has been conditioned correctly to ensure no risk of cross contamination. Special care is needed in preparing any pressure regulators used to reduce the pressure of the sample to ensure that they have been thoroughly sterilised before use.

At the current level of knowledge, better recovery rates have been observed when using the impact test method to test gases for microbiological contamination. However this method is very dependent on the specific design of the test equipment and the filtration method may be found to be adequate. It is recommended that prior to testing, checks should be made to verify the effectiveness of the selected method. Checks should also be made to identify any new methods that may be available on the market.

## 6 Conclusion

The opinion of the gas industry is that, provided they are manufactured to agreed procedures, gases used for medical, pharmaceutical and food gas applications are not susceptible to microbiological contamination.

To ensure that the risk of contamination is kept at an acceptably low level, the industry promotes a number of best

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practices in the treatment and handling of the gases to minimise the microbiological contamination. These practices include the treatment of any process water that may come into contact with the gas and the quality of the water used to hydraulically test cylinders (which is normally of drinking water quality).

Maintaining the gas in a dry condition is also seen as another preventative measure to prevent microbiological growth to assure the quality of the gas is suitable for its intended use.

Where there is a request for a statement on the microbiological quality of the gas, information should be given to indicate that the industry has carried out testing of all products and that, to date, there has been no evidence of microbiological activity found within the gas.

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