



CGA M-25—2020
ICH Q3D RISK ASSESSMENT
REPORT ELEMENTAL
IMPURITIES IN MEDICINAL
GASES

FIRST EDITION

PREFACE

As part of a program of harmonization of industry standards, the Compressed Gas Association (CGA) has issued CGA M-25, *ICH Q3D Risk Assessment Report Elemental Impurities In Medicinal Gases*, jointly produced by members of the International Harmonization Council and originally published by the European Industrial Gases Association (EIGA) as EIGA Doc 216, *ICH Q3D Risk Assessment Report Elemental Impurities In Medicinal Gases*.

This publication is intended as an international harmonized standard for the worldwide use and application of all members of the Asia Industrial Gases Association (AIGA), Compressed Gas Association (CGA), European Industrial Gases Association (EIGA), and Japan Industrial and Medical Gases Association (JIMGA). Each association's technical content is identical, except for regional regulatory requirements and minor changes in formatting and spelling.

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1 Introduction

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) has developed a harmonised guideline for elemental impurities (EIs), Q3D in pharmaceutical products which includes medical gases, referred to as ICH Q3D [1] 1.

ICH Q3D recommends a science and risk-based approach to evaluate the potential for introduction of EIs into the drug product and to determine if additional controls need to be included in the overall control strategy to ensure product quality and safety. The overall process follows the sequence identify, evaluate and summarise.

To determine whether medicinal gases are likely to contain any EIs, specified in ICH Q3D, EIGA members performed a risk assessment (RA) which considered which EIs could theoretically be present in the licenced drug products. The maximum daily dosages (MDD) were also calculated for each medicinal gas to determine which medicinal gases were at the highest risk, see Section 4.

Although the method of production is unique for each medicinal gas, the method of filling and packaging the gases is common across all products. The same basic equipment and procedures are used to fill these products and the container closure systems (CCS) used are similar for all products. This led to a conclusion that the potential EIs present was common for all medicinal gases.

For those high risk EIs that were identified as potentially being present in the gases, appropriate test procedures were set up to determine their levels in the finished product.

The test method sampling system took product from the CCS so as to represent the gas that would be delivered to the patient for treatment. This was considered to be the worst-case scenario for all medicinal gases and gas mixtures, to determine whether the EIs would be within the permitted daily exposure (PDE) limits detailed in ICH Q3D.

From the information given in this report, the view of the EIGA companies is that the levels of EIs within the medicinal gases that they supply for patient treatment are well below the limits set out in ICH Q3D.

As and when new information becomes available, this interpretation shall be reviewed as required.

2 Scope and purpose

2.1 Scope

The scope of this publication covers all packaged medicinal gases as listed below produced by EIGA members and approved as designated medical gases by the U.S. Food and Drug Administration (FDA) or authorised as medicinal products in other jurisdictions. It covers both compressed and liquefied gases, supplied in high pressure cylinders as well as cryogenic liquids, supplied either by tankers into bulk storage tanks or in portable cryogenic containers. It considers all manufacturing processes, including the starting materials used, as well as the CCS used to supply these medicinal gases for patient use.

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.

This publication covers all licensed medicinal gases currently supplied by EIGA, CGA, AIGA, and JIMGA members as follows:

- oxygen;
- synthetic medical air;
- medical air;

¹ References are shown by bracketed numbers and are listed in order of appearance in the reference section.