

GOOD MANUFACTURING PRACTICE GUIDE PART II FOR MEDICAL GASES: BASIC REQUIREMENTS FOR ACTIVE SUBSTANCES USED AS STARTING MATERIALS

Doc 99/23/Part 2

Revision of Doc 99/17

EUROPEAN INDUSTRIAL GASES ASSOCIATION AISBL

AVENUE DE L'ASTRONOMIE 30 • B – 1210 BRUSSELS

Tel: +32 2 217 70 98

www.eiga.eu • e-mail: info@eiga.eu



Documents

Document Sharing Hub



GOOD MANUFACTURING PRACTICE GUIDE FOR MEDICAL GASES PART II: BASIC REQUIREMENTS FOR ACTIVE SUBSTANCES USED AS STARTING MATERIALS

Prepared by WG-7 Medical Gases

Disclaimer

All technical publications of EIGA or under EIGA's name, including Codes of practice, Safety procedures and any other technical information contained in such publications were obtained from sources believed to be reliable and are based on technical information and experience currently available from members of EIGA and others at the date of their issuance.

While EIGA recommends reference to or use of its publications by its members, such reference to or use of EIGA's publications by its members or third parties are purely voluntary and not binding.

Therefore, EIGA or its members make no guarantee of the results and assume no liability or responsibility in connection with the reference to or use of information or suggestions contained in EIGA's publications.

EIGA has no control whatsoever as regards, performance or non performance, misinterpretation, proper or improper use of any information or suggestions contained in EIGA's publications by any person or entity (including EIGA members) and EIGA expressly disclaims any liability in connection thereto.

EIGA's publications are subject to periodic review and users are cautioned to obtain the latest edition.

© EIGA grants permission to reproduce this publication provided the Association is acknowledged as the source

EUROPEAN INDUSTRIAL GASES ASSOCIATION AISBL
Avenue de l'Astronomie 30 B 1210 Brussels Tel: +32 2 217 70 98
E-mail: info@eiga.eu Internet: www.eiga.eu



Table of Contents

1 Introduction 1

2 Scope and purpose 1

 2.1 Scope..... 1

 2.2 Purpose 1

3 Definitions 1

 3.1 Publications terminology..... 1

 3.2 Technical definitions 2

4 General 2

 4.1 Identification of the active substance starting material..... 2

5 Guidelines 4

6 References..... 17

Tables

Table 1 Identification of the active substances starting materials (not exclusive list)..... 3

Table 2 Indication and explanation of application of GMP Part II 4

Amendments to 99/17

Section	Change
Doc	Re-affirmation without any changes

1 Introduction

According to Article 46 (f) of Directive 2001/83/EC as amended by Directive 2004/27/EC of the European Parliament on the Community code relating to medicinal products for human use and Article 50 (f) of Directive 2001/82/EC; as amended by Directive 2004/28/EC on the Community code relating to veterinary medicinal products [1 2] ¹, the manufacturing authorisation holders shall use only active substances that have been manufactured in accordance with Good Manufacturing Practice (GMP) for starting materials.

2 Scope and purpose

2.1 Scope

These guidelines cover the requirements regarding the manufacturing of the active pharmaceutical ingredients, (API) in Good Manufacturing Practice condition in the field of medicinal gases manufacturing.

In this publication, manufacturing includes all operations of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control, release, storage and distribution of active substances and the related controls.

2.2 Purpose

This publication is intended to provide guidance regarding Good Manufacturing Practice for the manufacture of active substances used in the manufacturing of medicinal gases and mixture.

3 Definitions

3.1 Publications terminology

3.1.1 Shall

Indicates that the procedure is mandatory. It is used wherever the criterion for conformance to specific recommendations allows no deviation.

3.1.2 Should

Indicates that a procedure is recommended.

3.1.3 May and Need not

Indicate that the procedure is optional.

3.1.4 Will

Is used only to indicate the future, not a degree of requirement.

3.1.5 Can

Indicates a possibility or ability.

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

3.2 Technical definitions

3.2.1 Active substance starting material

Raw material, intermediate, or an active substance that is used in the production of an active substance.

4 General

4.1 Identification of the active substance starting material

In the case of medicinal gases manufacturing the active substance starting material can be a product manufactured in large scale in industrial production or an intermediate mixture of gases called intermix.

An active substance starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house.

Active substance starting materials normally have defined specifications.

The manufacturer should designate and document the rationale for the point at which production of the active substance begins. For synthetic processes, this is known as the point at which active substance starting materials are entered into the process.

Table 1 gives guidance on the identification of the active substance starting material for the medicinal gases and mixture that are normally produced as medicinal product.

When the API starting material enters into the chemical manufacturing process then appropriate GMP as defined in this publication should be applied to these manufacturing steps.

In the remainder of this publication the term active pharmaceutical ingredient is used repeatedly and should be considered interchangeable with the term active substance.

Table 1 Identification of the active substances starting materials (not exclusive list)

GMP Part II			GMP Part I
API starting material	Chemical manufacturing process	API/drug substance	Manufacturing finished medicinal product
Industrial ammonium nitrate	Thermal decomposition and purification	Bulk nitrous oxide	Nitrous oxide in cylinder/tank
Purified ambient air	Cryogenic distillation	Bulk oxygen	Oxygen in cylinder /tank
Purified ambient air	Cryogenic distillation	Bulk nitrogen	Nitrogen excipient in cylinder /tank
Oxygen	Mixing	Synthetic medical air –premixed buffer	Synthetic medical air in cylinder
Crude / tall oil from steam reforming or natural source or fermentation	Purification	Carbon dioxide	Carbon dioxide in cylinder , mixture
Pure carbon monoxide	Mixing	Intermix	Lung function mixture
Crude / tall oil from steam reforming or catalytic partial oxidation	Purification	Carbon monoxide	Lung function mixture
Sodium nitrite / sulfuric acid	Chemical reaction and purification	Nitric oxide	Nitric oxide mixture
Pure nitric oxide	Mixture	Intermix	Nitric oxide mixture
Industrial acetylene	Purification	Pure acetylene	Lung function mixture
Pure acetylene	Mixture	Intermix	Lung function mixture
Liquid helium	Gasification	Compressed Helium	Helium mixture
Compressed helium	Mixture	Intermix	Lung function mixture
Industrial methane	Purification	Pure methane	Lung function mixture
Pure methane	Mixture	Intermix	Lung function mixture