Guidance document
Authorisation of medicinal gases

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1 Terms, definitions, abbreviations

1.1 Definitions

1.1.1 Active substance

Gases and gas mixtures (particularly of known origin and quality) which are manufactured, stored and distributed under GMP conditions and traded under GDP conditions.

Manufacturers can issue active substances to authorised recipients accompanied by a corresponding certificate of analysis and GMP certificate. Active substances are not subject to authorisation.

However, an active substance can become a medicinal product by appropriate technical processes and the designation or presentation of the gas or gas mixture as having a medicinal effect.

1.1.2 Ready-to-use medicinal products

Ready-to-use medicinal products must be authorised by Swissmedic.

Medicinal gases are considered to be ready-to-use medicinal products if they are released for the market and can be used, either directly or after further processing to the ready-to-use form, by healthcare professionals, staff members designated by them or by the patients themselves.

They comprise:

a) Gases in pressure vessels with or without a device for pressure reduction.
b) Filled containers for the storage of liquid gases with or without a device for vaporisation.

1.1.3 Ready-to-use pharmaceutical forms

Ready-to-use medicinal products which, following market release, require healthcare professionals, staff members designated by them or the patients themselves to carry out a preparatory step before they can be used. The ready-to-use pharmaceutical form of a medicinal product is always prepared from a ready-to-use medicinal product. The definition and instructions for the preparation, i.e. further processing into the ready-to-use pharmaceutical form, are part of the authorisation documentation for the ready-to-use medicinal product and are reviewed and approved together with it. The actual act of preparation does not require approval by Swissmedic, as it is the responsibility of the healthcare professional administering the product (and is subject to supervision and control by cantonal bodies) or the patient.

1.2 Abbreviations

TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, SR 812.21)
TPLO	Ordinance of the Swiss Agency for Therapeutic Products of 22 June 2006 on the Simplified Licensing of Therapeutic Products and the Licensing of Therapeutic Products by the Notification Procedure (SR 812.212.23)
TPLRO	Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (SR 812.212.22)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (Therapeutic Products Ordinance, TPO) (SR 812.212.21)

2 Introduction

This guidance document describes the requirements governing the documentation obligation for the authorisation of medicinal gases in Switzerland. The guidance document is aimed primarily at administrative bodies.

2.1 Legal basis

Art. 4, para. 1a TPA defines medicinal products as "products of chemical or biological origin which are intended to have or are presented as having a medicinal effect on the human or animal organism, in particular in the diagnosis, prevention or treatment of diseases, injuries and handicaps". If gases are intended for medical use, they are referred to as medical gases. The rules of therapeutic products legislation concerning the manufacture, authorisation and placing on the market apply to such gases. If medical gases are not medical devices (see section 5.1 below), they constitute medicinal products (so-called “medicinal gases”) and must therefore meet the requirements of the pharmacopoeia, where these are specified, before being placed on the market (Art. 8 TPA). According to Art. 9, para. 1 TPA, ready-to-use medicinal products may be placed on the market only if they have been authorised by Swissmedic. Exemptions from the authorisation obligation are listed in Art. 9, para. 2 TPA (magistral formula, officinal formula and own formula).
Under Art. 14 TPA, a simplified authorisation procedure is intended for, among other things, medicinal products with known active substances.

3 Objective

Swissmedic uses this guidance document first and foremost as a resource for applying the legal provisions on the authorisation of medicinal gases in an equitable manner. The intention of publishing this guidance document is to show private individuals what requirements have to be fulfilled according to Swissmedic practice to ensure that corresponding authorisation applications are processed and concluded as quickly and efficiently as possible.

4 Scope

This guidance document specifies the requirements governing the documentation obligation for the authorisation of medical gases as medicinal products, so-called "medicinal gases". Therefore, it does not apply to the placing on the market of industrial gases or gases as medical devices (conformity requirements).

5 Description

5.1 Gases and gas mixtures

5.1.1 Medical device

Gases and gas mixtures are classed as medical devices if their mode of action is primarily physical in nature (e.g. gas mixture for insufflation of the abdominal cavity for laparoscopy or cold liquefied nitrogen for dermatological cryosurgery). These "medical gases" are placed on the market on the basis of a conformity assessment procedure conducted by the manufacturer and are not authorised by Swissmedic.

5.1.2 Medicinal products that require authorisation

Gases and gas mixtures placed on the market as medicinal products, known as "medicinal gases", are subject to authorisation and are authorised by Swissmedic. Only ready-to-use medicinal products are authorised. However, these may still need to be reconstituted into a ready-to-use pharmaceutical form before administration (see section 1.1.3 above).
To obtain authorisation of a ready-to-use medicinal product, appropriate proof of safety, efficacy and quality in compliance with the rules stated in section 5.2 must be submitted.

5.1.3 Medicinal products exempt from authorisation

Gases and gas mixtures that are to be placed on the market as medicinal products but do not need to be authorised under Art. 9 para. 2 let. a – c^{bis} TPA should be prepared and dispensed according to the relevant legal provisions. The cantonal authorities are responsible for supervising the preparation and placing on the market of such medicinal products. The dispensing restrictions of Art. 35 TPO and the quantitative and qualitative restrictions stated in Art. 36 and Art. 37 TPO apply in particular.

5.2 Requirements for documents to be submitted

The general formal requirements for documents and the requirements for Module 1 are specified in the guidance document *Formal requirements* and the accompanying *Table of documents to be submitted*.
Two procedures exist for obtaining Swissmedic authorisation for medicinal gases.

5.2.1 Simplified authorisation

This type of authorisation is essentially linked to the requirement that the medicinal product to be authorised in the simplified procedure can refer to a reference product that is already authorised (Art. 12ff. TPLO).

Exceptionally, this reference to an authorised reference product can be omitted if "well-established use" can be demonstrated for the relevant medicinal gas (see Art. 12, para. 3 c TPLO), i.e. if it can be proved that the gas or gas mixture has been used for the proposed indication and administration route for at least 10 years and its safety and efficacy are well documented in the scientific literature and generally acknowledged. The document to be submitted should contain the following information:

Justification for the "well-established use":

a) Period of use of the gas on the market, documentation of safety and efficacy in the literature;
b) Indication;
c) Dosage;
d) Quality according to the pharmacopoeia.

Structure

a) Applicant;
b) Name of the medicinal product;
c) Ready-to-use medicinal product, possibly with name of the ready-to-use pharmaceutical form;
d) Qualitative and quantitative composition;
e) Quality of the gases;
f) Manufacturing process for the medicinal gas;
g) Tests for identity, purity and content;
h) Storage and shelf-life;
i) Labelling, expiry date/use-by period;
j) Containers.

Information

a) Details of indication and dosage of the preparation;
b) Application;
c) Definition, size and manufacturing formula for standard batches;
d) Reasons for the composition and nature of application;
e) Specifications and testing specifications for all starting substances and any starting materials;
f) Detailed description of the manufacturing process;
g) Risk assessment for the individual manufacturing steps;
h) Validation documents for the manufacturing process;
i) Specifications and testing specifications for the finished product (bulk medicinal product, ready-to-use medicinal product);
j) Certificates of analysis for the finished product;
k) Validation documents for the testing specifications;
l) Specification and suitability of the primary container;
m) Instructions for emptying, cleaning and filling the primary container;
n) Instructions for maintenance and testing of the primary container;
o) Instructions for further processing into the ready-to-use pharmaceutical form;
p) Text drafts for the packaging materials;
q) Bibliography.

5.2.2 Authorisation

An appropriate authorisation dossier in accordance with Art. 11 TPA and the TPLRO should be submitted for the authorisation of innovative gases and/or innovative gas mixtures in the standard procedure. If the ready-to-use medicinal product has to be prepared before it can be administered to patients, the authorisation application has to include a definition and instructions for further processing to produce the ready-to-use pharmaceutical forms.

5.3 Supply/dispensing category

Ready-to-use medicinal products are classified in one of four dispensing categories according to their indication, administration and risk.

The active substances contained in the medicinal product are an important criterion for assigning it to its dispensing category (Art. 40 of the Therapeutic Products Ordinance (TPO; SR 812.212.21)). The following general classifications apply to gases and gas mixtures:

Monogases	Dispensing category
Nitrous oxide (laughing gas), compressed in cylinders (N_2O)	B
Nitrous oxide (laughing gas), liquid in stationary containers (N_2O)	B
Carbon dioxide (CO_2) compressed in cylinders	B
Air for medical use, compressed in cylinders	E
Oxygen, compressed in cylinders (O_2)	E
Oxygen, liquid in mobile containers	E
Oxygen, liquid in stationary containers	E
Nitric oxide, compressed in cylinders (NO)	A

Gas mixtures	Dispensing category
Oxygen/laughing gas 50%/50%, compressed in cylinders	B
Oxygen/carbon dioxide 95%/5%, compressed in cylinders	B

5.4 Further processing of authorised ready-to-use medicinal products

5.4.1 Further processing into the ready-to-use pharmaceutical form (preparation)

Ready-to-use medicinal gases can be processed into ready-to-use pharmaceutical forms in the following ways:

a) Filling of compressed gases into systems (pressure vessels with pressure reduction), which are directly intended for withdrawal for use.
b) Filling of liquid gases into systems (containers with and without a vaporiser), which are directly intended for withdrawal for use.

c) Feeding into stationary or mobile distribution systems, for use at their withdrawal points.

Vaporising liquid gases constitutes further processing in this context, as does the mixing of several ready-to-use medicinal gases.

As regards further processing, all information associated with the ready-to-use medicinal product must be transferred to the ready-to-use pharmaceutical form in such a way that traceability and information for users and consumers are ensured in the appropriate manner (manufacturer, product name, batch number, manufacturing and expiry dates, instructions for use, warnings, indication, etc.).

5.4.2 Repackaging of ready-to-use medicinal products

The repackaging of ready-to-use medicinal gases does not count as further processing in the sense of preparation, but represents a manufacturing step that requires corresponding approval by Swissmedic.

Examples of repackaging:

a) Transferring compressed gases from one pressure vessel to another.
b) Transferring liquid gases from one container to another.
c) Liquefaction of compressed gases.

During repackaging, all the information associated with the ready-to-use medicinal product should be transferred to the new medicinal product. In addition, the process of repackaging should be documented in a traceable manner in accordance with Good Manufacturing Practice (GMP).

Change history

Version	Change	sig
2.0	Formal changes and correction of errors, deletion of nitrogen from section 5.3	wph
1.2	New layout, no content adjustments to the previous version.	dei
1.1	Formal adjustments to the header and footer No content adjustments to the previous version.	dei
1.0	Implementation of HMV4	dts