

MEDICINAL VIPR PACKAGE

LIFETIME PERFORMANCE OF DRUG DELIVERY DEVICE

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Prepared by Medical Gases Council AHG-M.7 - Medical VIPR Flow Measurement

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1. Introduction

One of the major developments on how medicinal gases are delivered to patients has been the introduction of cylinders fitted with valves that have an integrated pressure regulator. These medical gas cylinder packages fitted with a valve with integrated pressure regulators (VIPRs) offer a number of significant benefits to both the healthcare professional and the homecare patient when administering the medicinal gas for clinical treatment. The medical VIPR packages have now been in service for more than twenty years and they have proven to be both reliable and beneficial to those administering medicinal gas from cylinders. Although the medical VIPR packages are used predominantly in medical oxygen service, they can be used for other gases and gas mixtures, including medical air and nitrous oxide/oxygen analgesic gas mixtures.

When a VIPR is fitted to the medical gas cylinder package, the gas can be administered to the patient immediately without having to fit a separate pressure regulator. This makes it possible to administer the gas rapidly in emergency situations as well as making it easier and safer to use. By turning on the VIPR shutoff valve and selecting the prescribed flow, the gas is available for immediate patient use. This obviates the need for the healthcare professional or the homecare patient from having to make high pressure connections, which can be hazardous if the connections become dirty. It also allows cylinders to be filled to a higher pressure without the end user having to purchase any additional equipment. Another benefit of the VIPR is that it removes the responsibility of maintaining the regulator equipment from the end user, meaning that the gas can be administered without any additional checks.

The requirements for VIPRs are described in the international standard EN ISO 10524-3, *Pressure regulators for use with medical gases. Pressure regulators integrated with cylinder valves* [1]¹. This standard covers the performance requirements of the valve, including the accuracy of the flow through the flow outlet and the pressure of the gas from the pressure outlet. As the VIPR is classed as a medical device it has to be CE marked in accordance with Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices [2], requiring the valve manufacturer to prepare a technical file, which provides the basic information to demonstrate the valves performance to the standard.

However, to comply with the pharmaceutical legislation, the gas companies supplying VIPR packages also have to register the medical gas packages in their marketing authorisations. As part of the licence application process, information about the safe use of the gas package shall be provided. In addition, information about testing requirements for the filled package to demonstrate that it will perform correctly shall be supplied.

Although the intended performance of the medical gas VIPR (when initially put into service) is specified in the valve manufacturer's technical file, the pharmaceutical legislation also requires the gas manufacturer to ensure that the valve is performing correctly each time the cylinder is filled and supplied for patient use over its complete service life. It is important that the VIPR will control the gas supply accurately, as both over and under administration of the gas can lead to patient harm. By establishing a process of valve performance verification and by trending any report received from the customer, it is possible to provide the appropriate assurances that the medical VIPR will function correctly.

This publication is a guideline that describes the basic requirements for the tests that the VIPR manufacturer should perform and the performance checks carried out by the gas manufacturer. This will assist to ensure that the VIPR performs as intended throughout its service life.

2. Scope and purpose

2.1 Scope

Filled medicinal VIPR packages used to administer medicinal gases by healthcare professionals and homecare patients.

The scope includes both manufacturers of VIPRs and manufacturers of medicinal gases supplying

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

medicinal VIPR packages.

2.2 Purpose

This publication is intended as a guideline to ensure that drug delivery performances are maintained throughout the lifetime of the VIPR.

The publication provides guidance on:

- testing and documentation requirements of medical VIPRs in addition to those defined in EN ISO 10524-3 and EN ISO 14246, Gas cylinders – *Cylinder valves – Manufacturing tests and examinations* [1,3]; and
- handling, filling and testing requirements of filled medicinal VIPR packages.

3. Definitions

3.1 Publication 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

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.

3.2 Technical definitions

3.2.1 First fill

Initial filling of a medical VIPR package after a new VIPR has been fitted.

3.2.2 Flow check

Check that a flow is present by any method such as audible or visible check.

3.2.3 Flow outlet

Outlet intended to deliver a controlled flow of gas.

3.2.4 Flow rate check

Using a suitable device to demonstrate that the flow rate is within an acceptable range.

3.2.5 Flow rate measurement

Using a calibrated device to measure the flow rate to a defined accuracy.

3.2.6 Flow selector

Means for selecting the flow and indicating the flow selected.

3.2.7 Flow setting

Flow position showing the intended value of delivered flow, for example, 2 L/min.

3.2.8 Lifetime

Time period after which the medical VIPR package cannot be refilled.

3.2.9 Medical VIPR package

Assembly of VIPR and cylinder for medicinal gas.

3.2.10 Nominal inlet pressure (P1)

Working pressure of the cylinder specified by the manufacturer of the VIPR for which the VIPR is intended to be used.

3.2.11 Post-maintenance fill

Initial filling of a medical VIPR package after a VIPR has been maintained (where the maintenance impacts the performance of the VIPR).

3.2.12 Pressure outlet

Outlet intended to deliver gas at a controlled pressure.

3.2.13 Nominal outlet pressure (P2)

Pressure downstream of the pressure regulator under flow conditions specified by the manufacturer.

3.2.14 Residual pressure device (RPD)

Device that is designed to prevent ingress of contaminants by maintaining a positive pressure within the cylinder relative to atmosphere by closing off its internal gas passages in the discharging direction.

[EN ISO 15996] [4]

3.2.15 Valve with integrated pressure regulator (VIPR)

Combination of a pressure regulator and cylinder valve intended to be fitted to a medical gas cylinder.

4. Intended performance of medicinal VIPRs

A medicinal VIPR package is fitted with a flow outlet and/or a pressure outlet.

NOTE According to EN ISO 10524-3, for a medicinal VIPR package fitted with a flow outlet with fixed orifices, the actual flow shall be within $\pm 30\%$ of each stated value for flows up to 1,5 L/min and $\pm 20\%$ of each stated value for flows greater than 1,5 L/min, for a cylinder pressure range between P1 to 15 bar.

For more details on other performance requirements, refer to EN ISO 10524-3 [1].

5. Test requirement for VIPR manufacturers

5.1 General

The medical VIPR manufacturer shall follow the requirements of EN ISO 14246 [3] for the shut-off valve function in addition to the ones defined below for the medical functions of the VIPR.

Manufacturing tests and examinations shall include:

- tests to be performed on every VIPR after production (though prior packaging and storage);
- inspections, verifications and examinations to be performed on a sample; and
- procedures to verify materials of construction and components to assure traceability to the original manufacturer.

Each VIPR shall be permanently marked with a unique serial number to provide the traceability of the tests results. The serial number should be marked prior any assembly operation and shall in any case be marked prior testing.

Test results and examinations shall be recorded together with the serial number of the VIPR.

5.2 Cleaning

Medicinal VIPRs shall be cleaned to meet at minimum the requirements of EN ISO 15001 *Anaesthetic and respiratory equipment – Compatibility with oxygen* [5].

5.3 Test conditions for additional tests

Additional tests to EN ISO 14246 required by this publication are carried out at the VIPR working pressure (referred as P_w in EN ISO 14246 and referred as P_1 in EN ISO 10524-3) and/or 15 bar, [3,1].

The tolerance on the inlet tests pressure shall be within $\pm 5\%$.

The test gas can be dry air or nitrogen as defined in EN ISO 14246 [2].

The VIPR shall be pressurized from the inlet connection at room temperature ($+15\text{ }^{\circ}\text{C}$ to $+30\text{ }^{\circ}\text{C}$).

It is important note for all tests with flow measuring that the test results for flows have to be corrected for the gas that the VIPR is intended to be used and in standard condition as defined in EN ISO 10524-3. [1].

5.4 Additional tests to be performed on every medicinal VIPR

5.4.1 Performance test of the residual pressure device

During the design and type approval process of the VIPR a certain opening pressure range and a closing pressure range was defined for its RPD. During production, every VIPR shall be tested to confirm that the closing pressure is within these pressure ranges.

The test shall be performed at the highest and lowest possible flows.

The result for the closing pressure test of the RPD is regarded to be satisfying if the leak rate at the flow outlet is below the value specified in ISO 15996 [4].

The closing pressure shall be recorded.

5.4.2 Flow performance test of the pressure outlet

The pressure outlet of the VIPR shall deliver a minimum flow of 40 L/min and maintain an outlet pressure of at least 3.6 bar at all inlet pressures between P_1 and 15 bar.

This requirement shall be tested on every VIPR at the inlet pressure determined by the manufacturer as the worst condition for inlet pressure with respect to the outlet performance.

The measured flow, outlet pressure, inlet pressure and test gas shall be recorded for every VIPR.

5.4.3 Flow performance tests of the flow selector

Each flow position of the flow selector of the VIPR shall be tested for accuracy of flow.

The flow result shall be recorded at each flow setting when flow selection is made from zero to the maximum setting and then back from the maximum setting to zero flow.

The test shall be performed at an inlet pressure of P1 and at 15 bar.

The acceptance limits are expected to be tighter than the accuracy requirements of EN ISO 10524-3 in order to take into account any drift or variation of the flows over the intended lifetime [1].

All the measured flow rates of the test gas and test gas inlet pressure shall be recorded for every VIPR.

5.4.4 Pressure or content gauge

There shall be a visual check that the pressure gauge pointer or display works correctly at 0 bar and P1.

Every additional function of digital gauges shall be tested according to the risk analysis.

5.4.5 Self-inspection prior release

The manufacturer shall have a written procedure for self-inspection complying with EN ISO 14246 and shall perform it prior releasing each manufactured batch [3].

Self-inspection reports shall be kept.

5.4.6 Management of change notification

An agreement should be signed between the VIPR manufacturer and the gas manufacturer concerning the notification and acceptance of any major changes to the design, materials, components and maintenance procedures for the VIPR.

6. Requirements for gas manufacturers

6.1 Initial qualification of a model of VIPR

The gas manufacturer should perform an initial qualification of samples of VIPR (serial production) with the intended gas.

This includes the verification the performance of the VIPR such as flow rates and outlet pressure.

An initial qualification should also be performed when there is a major change to an existing model of VIPR.

6.2 Incoming inspection

Incoming inspection shall be carried out according to defined procedures on each batch of VIPRs prior to fitting to the cylinder.