GUIDANCE NOTE 31

MEDICAL GASES

THE USE OF VALVES INCORPORATING RESIDUAL PRESSURE DEVICES

2017

British Compressed Gases Association

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PREFACE

The British Compressed Gases Association (BCGA) was established in l971, formed out of the British Acetylene Association, which existed since l901. BCGA members include gas producers, suppliers of gas handling equipment and users operating in the compressed gas field.

The main objectives of the Association are to further technology, to enhance safe practice, and to prioritise environmental protection in the supply and use of industrial, food and medical gases, and we produce a host of publications to this end. BCGA also provides advice and makes representations on behalf of its Members to regulatory bodies, including the UK Government.

Policy is determined by a Council elected from Member Companies, with detailed technical studies being undertaken by a Technical Committee and its specialist Sub-Committees appointed for this purpose.

BCGA makes strenuous efforts to ensure the accuracy and current relevance of its publications, which are intended for use by technically competent persons. However this does not remove the need for technical and managerial judgement in practical situations. Nor do they confer any immunity or exemption from relevant legal requirements, including by-laws.

For the assistance of users, references are given, either in the text or Appendices, to publications such as British, European and International Standards and Codes of Practice, and current legislation that may be applicable but no representation or warranty can be given that these references are complete or current.

BCGA publications are reviewed, and revised if necessary, at five-yearly intervals, or sooner where the need is recognised. Readers are advised to check the Association's website to ensure that the copy in their possession is the current version.

This document has been prepared by BCGA Technical Sub-Committee 7. It was approved for publication at BCGA Technical Committee 156. This document was first published on 20/07/2017. For comments on this document contact the Association via the website www.bcga.co.uk.

CONTENTS

* Throughout this publication the numbers in brackets refer to references in Section 11. Documents referenced are the edition current at the time of publication, unless otherwise stated.

TERMINOLOGY AND DEFINITIONS

May	Indicates an option available to the user of this Guidance Note.
Medical gas	Any gas or mixture of gases classified as a medicinal product (as defined in European Directives 2001/83/EC (3) and European Directive 2001/82/EC (2)). Throughout this document the term 'Medical Gas' is used to describe the products that are supplied in cylinder packages for medicinal use.
Minimum pressure retention valve (MPR)	A cylinder valve, which maintains a positive pressure above atmospheric pressure in a gas cylinder after use, in order to prevent internal contamination of the cylinder (as defined in EU GMP Guide (5), Annex 6) *Refer to residual pressure valve.*
Non-return valve (NRV)	Automatic valve, which allows gas to flow only in one direction (as defined in BS EN ISO 10286 (7)).
Residual pressure device (RPD)	A device that prevents ingress of contaminants by maintaining a positive differential pressure between the pressure within the cylinder and the valve outlet (as defined in BS EN ISO 10286 (7)).
Residual pressure valve (RPV)	A cylinder valve which incorporates a residual pressure device.
Shall	Indicates a mandatory requirement for compliance with this Guidance Note and may also indicate a mandatory requirement within UK law.
Should	Indicates a preferred requirement but is not mandatory for compliance with this Guidance Note.
Valve with integrated pressure regulator (VIPR)	A device intended to be permanently fitted to a gas cylinder connection and comprising a shut-off valve system and pressure reduction system.

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MEDICAL GASES

THE USE OF VALVES INCORPORATING RESIDUAL PRESSURE DEVICES

1. INTRODUCTION

This document provides advice on the inspection and filling of medical gas cylinder packages to help maintain the quality of the gas it contains.

The filling and supply of medical gas cylinders requires that the manufacturer operates under a number of licences that are issued by the UK medical Regulator, the Medicines & Healthcare products Regulatory Agency (MHRA). These licences are used to specify the quality of the gas supplied and to ensure that the procedures used for filling and testing the cylinders are compliant with the basic principles of Good Manufacturing Practice (GMP) as laid down in European Directive 2003/94/EC (4).

The need to maintain the quality of the medical gas, to avoid contamination of the gases and to prevent corrosion occurring inside the gas cylinders has led to the development of gas cylinder valves incorporating residual pressure devices (RPD).

Valves fitted with a residual pressure device are designed to maintain a small positive pressure in the cylinder to help prevent the ingress of contamination from external sources. The use of a residual pressure device is an effective way of helping to ensure that cylinders are not contaminated whilst in use.

This document provides medical gas suppliers with advice on maintaining the quality of gas within a medical gas cylinder and how that can be improved through the use of a valve fitted with a residual pressure device. It also provides Regulators and users of medical gas cylinders with information on the reasons why valves fitted with a residual pressure device are fitted to medical gas cylinders and explains how they can be used to help ensure that the quality of the medical gas being provided consistently meets the required specification.

2. SCOPE

This Guidance Note explains the use of valves fitted with a residual pressure devices in medical gas cylinders and provides guidance on the selection, installation and operation of valves fitted with a residual pressure devices, such that common practices are established across the gas industry, and the benefits of using valves fitted with a residual pressure device by both the user and the operator of gas cylinders are realised.

The *EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use* (GMP guide) (5) encourages medical gas suppliers to fit a valve fitted with a residual pressure device in a new cylinder package and as valves are replaced, in existing cylinder stock.

This Guidance Note:

- encourages the use of valves fitted with residual pressure devices in all medical gas cylinders;

- describes the benefits of valves fitted with a residual pressure devices – with reference to the risk benefits of retaining pressure in the cylinder;

- details the specification of valves fitted with a residual pressure devices – including testing requirements for selecting new valves;

- describes the testing regimes for the cylinder package when in service specifically prior to filling;

- reviews filling equipment design – and the ability to fill mixed fleet of cylinders;

- provides validation of the filling equipment to demonstrate that the use of valves fitted with a residual pressure device does not impact cylinder gas quality;

- provides customer advice on the benefits of using cylinder packages incorporating a valve fitted with a residual pressure device.

3. BACKGROUND

The European Directives as applied to medicinal gases and GMP create a minimum standard that a manufacturer is required to meet in their production processes. GMP requires that medical gases:

- meet the requirements of the marketing authorisation or product specification;

- are appropriate for their intended use;

- are of consistent high quality.

The *European Union Guide to Good Manufacturing Practice* (GMP), Annex 6 (4), [Manufacture of Medicinal Gases, Paragraph 24] requires that medical gas cylinders "*… should preferably be fitted with minimum pressure retention valves with non-return mechanism in order to provide adequate protection against contamination*".

Medical gas cylinder packages are designed and manufactured to safely contain a gas under pressure. Cylinders are closed and sealed by the use of a valve. Using a valve fitted with a residual pressure device provides additional protection to the medical gas cylinder package and its contents.

Valves fitted with a residual pressure device are designed to maintain a nominal positive pressure relative to atmosphere within the gas cylinder. This prevents the gas cylinder from being completely emptied in patient use and stops ingress of atmospheric contamination if the valve operating mechanism (main shut-off) is left open. Many of these devices include a non-

return function that protects the cylinder from back-feeding from downstream processes where more than one medical gas is connected to a medical device.

Using a valve fitted with a residual pressure device is an effective component of a system which allows the medical gas supplier to provide assurance that the gas supplied for patient use is of the appropriate quality.

The benefits from using a valve fitted with a residual pressure device include:

- ensuring the gas quality is not compromised between fills, consistently meeting a medical gas specification;

- maintaining the internal condition of the medical gas cylinder package throughout its service life;

- preventing the ingress of moisture and other atmospheric contaminants, which may lead to corrosion, especially where a valve is left open after use;

- avoiding corrosion of the cylinder, thus preventing particulate contamination of the gas contents;

- improving cylinder filling efficiency, by requiring the cylinder to only be fully vented prior to fill, therefore removing the requirement to purge and evacuate;

- preventing the possibility of contamination from back-flow from a downstream process, where the residual pressure device incorporates an integral non-return valve;

- providing anti-fill protection, which will prevent illicit filling of a cylinder, where a non-regulated valve is fitted with a residual pressure device.

4. RECOMMENDED POLICY

As described in Section 3, there are many benefits to incorporating a residual pressure device into the valve fitted on to a medical gas cylinder package.

It is recommended that:

- All valves should incorporate a residual pressure device and a non-return valve, where possible.

- When adding a new cylinder package to the Marketing Authorisation it should be supplied with a valve fitted with a residual pressure device.

- On existing cylinder packages, as valves are replaced, fit a valve fitted with a residual pressure device. A variation may be required to update the Marketing Authorisation.

NOTE: Where different valves are fitted, follow the procedures detailed in Section 7 (changeover process).

5. RISK MANAGEMENT

The following should be considered as part of the documented risk management plan:

- Device failure identified during pre-fill inspection;
- Potential use of cylinder – direct connection to the patient, or connection via pipework or medical device;
- Compatibility of the filling equipment to override the residual pressure device;
- Inspection of filling equipment prior to connection;
- Connection of cylinders to medical devices where there is more than one gas connected;
- Presence of residual batches in the current batch;
- Procedures for insertions of valves into cylinders;
- Introduction of new cylinders and valves during first fill;
- Inspection for possible tampering with valves;
- Changes to end user information or literature;
- Changes required to the Marketing Authorisation.

6. CHOOSING A VALVE

There are two main designs of valve which can be fitted to medical gas cylinders:

(i) A standard valve. This valve requires a pressure regulator to enable the gas to be supplied for patient use.

The residual pressure device fitted to a standard valve is positioned between the valve outlet and the main shut-off valve. This device will normally have the functionality of maintaining a nominal residual pressure in the cylinder if the shut–off valve is left open and incorporates a non-return valve to prevent back-feeding.

(ii) A valve with an integrated pressure regulator (VIPR). This valve has a built in pressure regulator and can be fitted with two user outlets: a flow outlet, that provides a range of flow rates (litres / minute) and a pressure outlet that reduces the pressure to 4 bar for patient administration. No additional pressure regulation is required.

The residual pressure device fitted to a valve with an integrated pressure regulator is fitted in the gas passage between the cylinder outlet and the regulator. Its only function is to retain a nominal minimal pressure in the cylinder package. The integral pressure regulator acts as a non-return valve when a high pressure is applied to either of the gas outlets.

The fill port will incorporate a non-return valve as it is normally under pressure when the valve is in use and the main shut-off valve is open.

Medical gas cylinder valves, which incorporate a residual pressure device are designed, constructed and tested in accordance with:

- BS EN ISO 10297 (8), *Gas cylinder valves. Specification and type testing*;
- BS EN ISO 10524 (9), *Pressure regulators for use with medical gases.* Part 3. *Pressure regulators integrated with cylinder valves*;
- BS EN ISO 15001 (10), *Anaesthetic and respiratory equipment. Compatibility with oxygen equipment.*
- BS EN ISO 15996 (11), *Gas cylinder. Residual pressure valves. General requirements and type testing;*

The European Industrial Gases Association (EIGA) provide additional information in EIGA Document 64 (13), *Use of residual pressure valves.*

NOTE: There are a variety of different filling connectors available and they are not all compatible with each other. Only use a fill connector supplied or recommended by the manufacturer.

For use in the UK and other European countries each valve is required to have a 'CE' mark to show that it is compliant with the appropriate legislation and standards.

Standard valves only require to be Pi marked to comply with the *Carriage of Dangerous Goods and the Use of Transportable Pressure Equipment Regulations* (CDG Regulations) (1). These are not classified as a medical device.

For valves incorporating a pressure regulator to provide either a specific flow for patient use, or a gas supply reduced to pressure of 4 bar, they also require to be CE marked to the *Medical Device Directive (MDD)* (6). These valves are considered to be a Class IIb medical device.

Further information on CE marking is available from the MHRA at:
https://www.gov.uk/guidance/medical-devices-conformity-assessment-and-the-ce-mark

The type of valve used will be determined by the gas supplier and will be included in the gas supply companies Market Authorisation for the cylinder assembly. A change in valve type, or any modification to an existing valve, will require a Marketing Authorisation variation. Refer to Section 7.

Select (refer to Section 6.1) and verify fitness for purpose (refer to Section 6.2) an appropriate valve fitted with a residual pressure device, with its documentation.

6.1 Selection of a valve fitted with a residual pressure device

- Determine your User Requirements Specification (URS) including:
    - ISO standard compliance (refer to Section 6);
    - expected valve usage and life in service;
    - Patient requirements.
- If there are flow requirements the flow device is CE marked to the MDD (6);
- Appropriately Pi marked to comply with the CDG Regulations (1);
- Permanently marked with unique batch identification and for VIPR valves with an unique serial number;
- Compatible with the intended product and pressure in the cylinder;
- Product and pressure specific filling ports;
- Where different, product specific user outlets;

6.2 Verification of a valve fitted with a residual pressure device

- It is capable of being filled with the intended gas at the working pressure of the gas cylinder;
- It delivers gas at the specified flow rate;
- Carry out a functionality test against the User Requirements Specification, specifically ensuring:
    - The residual pressure device shuts off at specified minimum and maximum flow rates;
    - When closed the residual pressure device does not leak;
    - When operating the valve is quiet in operation;

NOTE: The results of the testing should be reviewed prior to submitting the licence variation.

7. CHANGEOVER PROCESS

When introducing a cylinder assembly incorporating a valve fitted with a residual pressure device for the first time it will require a variation to the relevant Market Authorisation for the cylinder assembly.

Any significant change shall follow a management of change procedure, such as that detailed in EIGA Document 51 (12), *Management of Change*.

The gas suppliers will need to:

- Set up the filling equipment:
    - Review and modify their filling equipment where necessary taking into consideration the requirement to fill cylinders with existing valve types;
    - Include new filling connectors specific to the new valve design.
- Validate the filling process;
- Prepare and provide appropriate information, instruction and training for their staff, such that they can identify, test and fill via the new valve assembly;
- Put in place a procedure to carry out a visual and a functional check to verify there is residual pressure in the cylinder prior to the fill;
- Put in place procedures for managing cylinders found with no internal pressure.

8. IN-SERVICE TEST REGIMES FOR A VALVE FITTED WITH A RESIDUAL PRESSURE DEVICE

GMP, Annex 6 (4), requires that before filling a medical gas cylinder checks have to be carried out:

"*Checks to be performed before filling should include … a check carried out to a defined procedure, to ensure there is a positive residual pressure in each cylinder; If the cylinder is fitted with a minimum pressure retention valve, when there is no signal indicating there is a positive residual pressure, the correct functioning of the valve should be checked, and if the valve is shown not to function properly the cylinder should be sent to maintenance.".*

The filling of a medical gas cylinder fitted with a residual pressure device is very similar to filling a cylinder with a conventional valve. However, there are some differences.

As part of the routine checks carried out before filling a medical gas cylinder which incorporates a valve fitted with a residual pressure device then the filler shall carry out:

- a visual check of the valve for cleanliness and signs of damage. The visual inspection will check, where visible, that the residual pressure device has not been

removed or tampered with, and that the valve has not been contaminated with dirt, oil or grease;

- a check that the cylinder contains residual pressure.

Where a filler rejects a medical gas cylinder following these checks it shall be removed from the filling line and sent for further investigation.

The valve shall be functionally tested prior to filling. If it is a standard valve not fitted with an integrated pressure regulator, then the functionality check shall include:

- Momentarily opening the valve to check for residual pressure;
- If gas escapes the cylinder may be filled;
- If no gas escapes, the functionality of the residual pressure device shall be checked:
    - If the function test proves that the residual pressure device has retained pressure, the cylinder may be filled;
    - If the functional test reveals that the residual pressure device has not retained pressure, the cylinder shall not be filled and shall be removed from the filling line and sent to maintenance.

If it is a valve fitted with an integrated pressure regulator (VIPR), then the functionality check shall include:

- Check the contents gauge on the cylinder. If the cylinder has residual content (pressure) then the cylinder may be filled;
- If the contents gauge indicates that there is no measureable residual content (pressure) then additional checks are to be carried out;
- Open the cylinder valve slowly, select a flow on the flow selector and check for a gas flow;
- If a gas flow is detected the cylinder may be filled;
- If no flow is detected, the non-return valve in the filling port should be prodded to determine if there is a residual pressure in the cylinder. If there is evidence of residual pressure the cylinder may be filled. If there is no evidence of residual pressure the cylinder shall not be filled and shall be removed from the filling line and sent to maintenance.

Gas flow can be detected by use of a prodding device or a proprietary gas flow detector. Care should be taken to ensure any mechanical device does not damage the valve.

NOTES:

1. This functional test may not apply in cases where the cylinder is new in-service or is being returned to the filling line post maintenance following valve removal / fitting where there may be no pressurised gas inside the cylinder.

2. Prodding the non-return valve and receiving a gas release can by inference confirm that a residual pressure is retained. However, it's seal is necessarily only O Ring tight, and it's captured chamber is small, so there are cases when it can have leaked, and report a false negative. In such conditions, a retained minimum pressure might dissipate within a few days / weeks, while the cylinder is in the empties / return loop. The false negative level might be quite considerable. If, through pressure monitoring techniques capable of more finely measuring pressure than a standard gauge, a positive pressure result can be captured (for example, by the use of a pressure transducer) then a more affirmative result can be reported, with no false negatives, direct from upstream of a valve containing a residual pressure device.

Where a cylinder fails the functional test the internal condition of the cylinder shall be checked for contamination.

- If no contamination or deterioration of the inside of the cylinder is detected, the cylinder may be filled following repair or replacement of the residual pressure device or valve;

- If contamination or deterioration is detected, corrective action is to be taken or the cylinder is to be scrapped, as appropriate.

Where a valve is found to create excessive noise when there is a gas flow, it should be removed from the filling line and sent to maintenance.

Where a residual pressure device is found to have a defect or non-conformance in-service, the company shall feedback information to the valve manufacturer.

9. BENEFITS OF USING CYLINDERS WITH VALVES FITTED WITH RESIDUAL PRESSURE DEVICES

BS EN ISO 15996 (11) states that:

"Increased requirements about avoidance of contamination of gases and gas cylinders has led to the development of gas cylinder valves incorporating residual pressure devices.

These devices are designed to maintain a small positive pressure between the inlet and the outlet. This prevents the gas cylinder from being completely empty in customer use and stops ingress of atmospheric contamination. Many of these devices include a non-return function that protects the cylinder from backflow from downstream processes."

Hence the benefit of fitting a valve fitted with a residual pressure device to a medical gas cylinder package is that there will always be a residual pressure in a cylinder. This will prevent any ingress of atmospheric air and any contamination into the cylinder, particularly when the

cylinder is in-use by the end user or in transit after use, even if the main cylinder valve is left open.

The non-return functionality of the residual pressure device will also ensure that should the cylinder package be connected to a medical device where there is more than one medical gas connected there can be no back-feed into a cylinder. These two aspects of the functionality of a valve fitted with a residual pressure device ensure that the quality of any gas remaining in the cylinder remains within its specification.

As a consequence where a cylinder fitted with a valve fitted with a residual pressure device has been returned for refilling and it can be demonstrated that it holds a residual pressure then there is no additional requirement for either evacuating or purging the cylinder prior to filling.

The requirement to evacuate a cylinder prior to fill has the potential to introduce contaminants. The benefit of having a residual pressure device reduces the risk of drawing atmospheric air into the cylinder during the evacuation process prior to filling.

Over the lifetime of the cylinder it will also reduce the risk of corrosion acting on the cylinder shell by preventing the ingress of moisture.

It is acceptable that where a valve fitted with a residual pressure device is fitted and its functionality is proven to be uncompromised, cylinders will only require to be vented to atmosphere prior to fill.

10. ADVICE FOR MEDICAL GAS CYLINDER USERS

The use of a valve fitted with a residual pressure device in a medical gas cylinder will have no direct impact to the end user.

As with all gas cylinder valves, the end user should:

- always follow the gas suppliers instruction;
- always close the valve when the cylinder is not in use;
- not interfere or tamper with the valve.

For additional information refer to BCGA TIS 36 (14), *Medical gases. The safe handling and use of gas cylinders fitted with valves with integrated pressure regulators*.

11. REFERENCES

	Document Number	Title
1.	SI 2009 No. 1348	The Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations 2009 (as amended).
2.	European Directive 2001/82/EC	Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products.
3.	European Directive 2001/83/EC	Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.
4.	European Directive 2003/94/EC	European Directive 2003/94/EC – Principles and Guidelines of good manufacturing practices for medicinal products for human and veterinary use. Annex 6, Manufacture of Medicinal Gases
5.		EudraLex. The Rules Governing Medicinal Products in the European Union. Volume 4. EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use (GMP Guide)
6.	European Council Directive 93/42/EEC	Council directive 93/42/EEC of 14 June 1993 concerning medical devices. (as amended) *The Medical Device Directive (MDD).*
7.	BS EN ISO 10286	Gas cylinders. Terminology.
8.	BS EN ISO 10297	Gas cylinder valves. Specification and type testing.
9.	BS EN ISO 10524 Part 3	Pressure regulators for use with medical gases. 3. Pressure regulators integrated with cylinder valves
10.	BS EN ISO 15001	Anaesthetic and respiratory equipment. Compatibility with oxygen equipment.
11.	BS EN ISO 15996	Gas cylinders. Residual pressure valves. General requirements and type testing.
12.	EIGA IGC Document 51	Management of change.
13.	EIGA IGC Document 64	Use of residual pressure valves.
14.	BCGA Technical Information Sheet 36	Medical gases. The safe handling and use of gas cylinders fitted with valves with integrated pressure regulators.

Further information can be obtained from:

UK Legislation	www.legislation.gov.uk
EU Legislation for medicinal products - EudraLex	www.ec.europa.eu/health/documents/eudralex/vol-1_en
Medicines & Healthcare products Regulatory Agency (MHRA)	www.mhra.gov.uk
British Standards Institute (BSI)	www.bsigroup.co.uk
International Organization for Standardization (ISO)	www.iso.org
European Industrial Gases Association (EIGA)	www.eiga.eu
British Compressed Gases Association (BCGA)	www.bcga.co.uk

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