MEDICAL GASES

DESIGN CONSIDERATIONS AND GUIDANCE FOR THE SAFE USE OF MEDICAL GAS VIPR

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Prepared by Medical Gases Council Ad Hoc Group M-8

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Amendments from 183/13

Section	Change
	Rewrite to reflect current practices

1 Introduction

EIGA Member Companies have been successfully using valves with an integrated pressure regulator (VIPR) for many years in medical gases applications. The VIPR represents a major improvement compared to the former practice when separate customer owned and maintained pressure regulators were used, see EIGA Doc 104, *Safety Principles for Pressure Regulators for Medical Oxygen Cylinders* [1].

VIPR come under the scope of two European regulations, the Transportable Pressure Equipment Directive [2] (TPED) and the Medical Devices Directive, (MDD,) [3].

There have been incidents involving medical gas cylinder packages, (primarily oxygen) using VIPRs. These incidents are well known within the gases industry as well as to the medical gas regulatory authorities.

Since the first publication of this document a decrease of the severity of oxygen ignition incidents involving VIPRs has been observed, even though the numbers in service has been increasing. This publication has been revised to include additional information on VIPR design and operation.

2 Scope and purpose

2.1 Scope

This publication covers medical gas cylinders fitted with VIPRs, designed in accordance with EN ISO 10524-3, *Pressure regulators for use with medical gases. Pressure regulators integrated with cylinder valves -- Part 3*, [4].

2.2 Purpose

The purpose of this publication is to:

- Provide recommendations for those responsible for specifying, designing, manufacturing, cylinder filling and maintaining such devices as well as for end-users and authorities. These recommendations are based on a review of the known incidents involving medical gas cylinders fitted with VIPRs designed and filled up to 300 bar;
- Describes the life time of medical VIPRs; and
- Provides guidance both to gas companies and to healthcare providers as how to treat VIPR-equipped cylinders along the supply chain, in the filling, handling, transportation, storage and maintenance processes.

3 Definitions

For the purpose of this publication, the following definitions apply.

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

Indicates 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 Valve with Integrated Pressure Regulator (VIPR)

Combination of a pressure regulator and cylinder valve intended to be fitted to a medical gas cylinder, EN ISO 10524-3 [4])

4 Feedback from incident reports and investigations

EIGA member companies have reported incidents with VIPRs from different valve manufacturers.

Recommendations are based on individual incidents review and resulting expertise. The incidents have occurred at both customer premises and gas company filling facilities.

The investigations showed that the VIPR incidents could be broken down into the following types:

- Type 1: Failure without ignition
    - failure of gauges;
    - wrong flow / no flow;
    - leakages; and
    - failure leading to the activation of the pressure relief device.
- Type 2: Failure with internal ignition
    - on the high-pressure side (shut off mechanism, residual pressure unit or filling port); and
    - on low pressure side (pressure regulation seat and regulator).

Where the causes for both types of the incidents were identified, they included:

- improper design;
- inappropriate materials;
- improper spare parts
- improper manufacture
- improper operation, and
- internal contamination, for example external debris ingress.

Following incident reviews, the resulting actions have included:

- withdrawal of the VIPR from service via a product recall;
- improvements to the user instructions and training;
- improvement of the cylinder filling procedures (including pre and post fill check) and personnel training;
- improvement in the maintenance procedures and personnel training;
- redesign of the VIPR; and
- improvement of the VIPR manufacturing process and procedures.

5 Design considerations

The minimum design requirements for VIPR are defined in EN ISO 10524-3 [4]. Additional recommendations are outlined below. EIGA Safety Information 21 *Cylinder Valves - Design Considerations* provides information for safe valve design [5].

The design of VIPR should minimise the need for testing and maintenance over its service life.

5.1 Usability and Ergonomics

The usability, defined as the characteristic of the user interface that facilitates use and thereby establishes effectiveness, efficiency and user satisfaction, shall be considered by the VIPR manufacturer as it can have a direct impact on safety.

VIPRs are used routinely in healthcare facilities by professional users, for example nurses, and at patient homes by non-professional users including the patient or family members.

They are also used in applications such as intensive care units, helicopters, ambulances and in emergency situations, when the caregiver is already busy managing a stressful activity. Therefore, the usability shall take into account the user specified applications.

The usability shall also take into account the combination of the VIPR and valve guard.

The points of particular attention for the VIPR are:

- sequence of operations which are required to supply a flow of gas, usually from opening the valve to selection of the flow;
- identification of the status open/close of the valve;
- selection of the flow settings: unambiguity, such as ".5" can be confused with "5" or "6" can be confused with "9", when the cylinder is upside down, ease of selection including grip, force to be applied, self-capability;
- protection against inadvertent change of settings;
- resistance to excessive force applied by the user on the controls and mobile parts;
- legibility of the flow settings, indicators and markings;

- ease of connection of the various accessories such as flexible hoses, tubing, humidifiers or filling connectors; and

- ability to use the VIPR with the cylinder in various positions including standing and laying on the ground in various orientations.

The points of particular attention for the valve guard are:

- ease of carrying the cylinder, including with gloves;

- visibility access to the settings and indicators; and

- handling of the moving parts such as bed hangers or protections and plugs.

5.2 Materials

Selection of materials is critical to the development of a safe VIPR. All components in the VIPR shall be reviewed for gas compatibility and fit for purpose. In addition, the operating conditions should be reviewed for materials selection including:

- pressure;

- flowrate;

- temperature;

- component exposure to gas, in normal or fault condition; and

- flow path, whether impingement or not impingement area.

Guidance of material selection criteria can be found in EN ISO 15001 *Anaesthetic and respiratory equipment -- Compatibility with oxygen* and EIGA Doc 13, *Oxygen pipeline and piping system* [6,7].

VIPRs and their associated filling connectors shall be tested to validate the material selection, see 5.7. This validation shall be in the form of a test for resistance to ignition of the VIPR and its associated filling connector as described in EN ISO 10524-3. [4]

An accelerated life cycle endurance test and environmental testing on the VIPR shall also be undertaken as part of the validation of the design as required in EN ISO 10524-3 [4].

Non-metallic components are the most susceptible to ignition and therefore their use in the gas wetted areas of the VIPR shall be minimised. Typical examples of uses of non-metallic components include, but are not restricted to valve seats, O-rings, diaphragms and lubricants.

The material selection of non-metallic components shall consider not only the compatibility with the intended gas, for example, oxygen but also the consequence of ignition

There are restrictions in medical applications on the use of polymers that can give off a toxic gas during combustion, such as halogenated polymers, see EN ISO 15001 and EIGA Doc 73, *Design Considerations to Mitigate the Potential Risks of Toxicity when using Non-Metallic Materials in High Pressure Oxygen Breathing Gas Systems* [6,8].

Design should be as such that non-metallic components are protected against direct stream of the gas. Non-metallic surfaces in contact with gas should be minimized.

Lubricants and oils for the low-pressure sections are preferred to be of a grade suitable for high pressure to prevent risk due to migration in high pressure section.

Non-metallic components, as well as lubricants, can be affected over time and operation due to creep and ageing. These factors shall be considered during the risk assessment of VIPR components considering the service life. The implementation of a quality control process is essential to ensure components used are of the correct composition and specification.

Metallic components are more resistant to combustion than non-metallic components; however correct material choice is no less important as in a pure oxygen environment many metals will burn with a large release of energy and can propagate a fire. Aluminium alloys and stainless steels are examples of metals that can burn at low oxygen pressure, see EN ISO 10524-3 *Pressure regulators for use with medical gases - Part 3: Pressure regulators integrated with cylinder valves (VIPRs)* and EN ISO 11114-1 *Gas cylinders. Compatibility of cylinder and valve materials with gas contents. Metallic materials* [4,9]. Their use shall be reviewed following material selection rules, and whenever possible an alternative material chosen, which is more resistant to combustion and subsequent propagation due to higher exemption pressure. Materials can include brass or Monel®.

Consideration shall be given to the heat conductivity, since low heat conductivity can increase the probability of ignition. Where it is not possible to use an alternative, the material shall be assessed and its compatibility with oxygen demonstrated via a suitable test, for example, ASTM G175 *Standard Test Method for Evaluating the Ignition Sensitivity and Fault Tolerance of Oxygen Regulators Used for Medical and Emergency Applications* [10].

5.3 Filters

A filter represents a high risk of ignition in an oxygen or oxygen mixture VIPR as it creates an impingement zone for any free-flowing particles. The use of filters shall therefore be limited, and the materials of construction, filter mesh size, shape and location in the VIPR be part of the component risk assessment.

Where possible filters shall be limited to a position immediately upstream of the regulator inlet where they protect the regulator seat from particle damage and subsequent failure to operate as designed.

The selection of filter material is critical, typically a nickel, Monel or sintered bronze shall be selected whereas stainless steel or aluminium bronze shall be avoided. If a filter is dismountable the VIPR should be adiabatically tested with and without the filter.

Filters should be located such that they are not subjected to bi-directional flow because of the risk of particles collecting on the filter and then being pushed as a concentrated mass of material to an impingement site when the gas flow reverses.

The VIPR design should be such that it is not possible to trap particles between filters.

Use of a short anti-dust tube as an alternative to a filter in the VIPR to cylinder connection presents a reduced impingement and contamination trap whilst still offering protection from particles entering the VIPR from the cylinder.

NOTE: When using an anti-dust tube, the protection of the regulator seat by a filter remains necessary

5.4 VIPR to cylinder connection

VIPRs shall be installed using the defined torque in accordance with EN ISO 13341*, Gas cylinders -- Fitting of valves to gas cylinders* [11].

The gas tight connection on the cylinder valve /gas cylinder interface should be in accordance with EIGA Doc. 138 *PTFE used as a sealant for cylinder/valve connections* [12].

Incidents have been documented with cylinder valves and VIPRs having a parallel thread on the valve to cylinder connection. If a guard is mounted directly to the valve and when a parallel thread are used the following precautions shall be taken:

- apply the correct valving procedure to avoid:

- unscrewing of the VIPR from the cylinder;
- ignition at the VIPR to cylinder neck interface, if the package is dropped; and
- breaking of the connection thread in the VIPR due to overstressing.

- Use of the correct O-ring

By using a guard mounted to the valve the above criteria shall be checked by risk assessment study, which can result in additional requirements.

When valve guards are fitted they shall be designed and tested in accordance with EN ISO 11117, *Gas cylinders -- Valve protection caps and valve guards -- Design, construction and tests,* [13].

Formal procedures and training are required to ensure the above plus the correct thread matching, choice of O-ring seal size and materials.

Reference shall be made to EN ISO 15245-1, *Gas cylinders -- Parallel threads for connection of valves to gas cylinders. Specification* [14].

5.5 Pressure and content Indicator

5.5.1 General

The high-pressure indicator on a VIPR is used as a contents indicator and should not be considered as a calibrated measuring device.

The indicator should be designed to resist excessive moisture ingress and environmental operating conditions, see IP54 of EN 60529, *Degrees of protection provided by enclosures (IP Code*) for guidance [15].

Where a mechanical indicator is utilised, it shall have an inlet restrictor to protect the Bourdon tube from a sudden rush of pressure and to minimise the flow of gas release in case of failure. The inlet flow restrictor should remain part of VIPR body in case of indicator shear off.

The indicator, irrespective of type, should be protected from external impact damage.

The indicator may be active (upstream of the shut off valve) or passive (downstream of the shut off valve). An active indicator is preferred as this is subjected to constant pressure, rather than being subjected to a large pressure surge whenever the shut-off valve in the VIPR is opened. An additional benefit is that the user always sees the actual pressure/content. Using an active indicator, extra care shall be taken in the design and inspection to prevent leaks as this can lead to the depletion of the cylinder content.

5.5.2 Learnings from incidents

The content indicator is used by the user to assess if the content of the gas cylinder is sufficient for intended need such as for emergency intervention, treatment of a patient, transport or ambulatory use and back-up of other gas systems)

In case of a broken or blocked pointer the pressure indicator delivers wrong information, which can result in

- starting a procedure with an empty cylinder, but appearing to be full;
- interruption of gas delivery;
  - noticed, for example alarm of the ventilator;

  - unnoticed (patient left alone);
  - not understood, because the information looks good;

- assuming a cylinder is empty when it is full.

Oxygen cylinders are often used in emergency situations with a patient in critical condition. Any failure to supply oxygen or delay in the medical procedure in progress can have severe consequences for the patient including:

- death;
- serious deterioration in state of health; or
- loss of opportunity to treat the patient.

Table 1 Failure findings

Failure	Failure mode	Failure cause(s)
No or incorrect content information	broken pointer: pointer disconnected from Bourdon tube	Incorrect soldering process Humidity/corrosion Mechanical impact (e.g. drop) Vibrations (e.g. transport)
incorrect content information	blocked or deformed pointer: pointer indicating a wrong content.	Humidity/corrosion Scale plate deformation (displacement) Mechanical impact (e.g. drop)
incorrect content information	over-stretched Bourdon tube: after which the pointer never shows proper content	Bourdon tube material quality High pressure during filling
incorrect content information	misalignment of the scale to the pointer	Assembling Mechanical impact (e.g. drop) Vibrations (e.g. transport)

5.5.3 EIGA recommendations

EIGA recommendations include the following:

- To inform the VIPR manufacturer about the risks listed in Table 1. In addition, perform the corresponding risk analysis;

- The design shall cover operation conditions such as mechanical impact and transport;
- Manufacturing process of content indicator ensure proper quality and reliability;
- Ensure alignment of pointer and scale; and
- Prevent this by design, for example loose pointers should remain in a position where it is visible, that this is an incorrect indication. This is a fail- safe design.

In the event of a leak within the indicator, its casing should be designed such that the pressure is safely relieved to prevent a overpressure that could lead to a hazardous rupture of the casing.

Electronic indicators (pressure probe plus electronic) are a recent development, which open new users possibilities. All safety requirements for analogue indicators are also valid for electronic indicators. Expertise is developing with time; nevertheless, potential issues that should be considered in the risk assessment include:

- incorrect and/or not validated software;
- battery life;
- mechanical impact;
- vibrations;
- manufacture assembling issues;
- signal interference or distortion;
- false alarms;
- corrosion;
- temperature fluctuation impact on the indicator performance;
- complicated maintenance;
- gas compatibility; and
- readability of display.

5.6 Shut-off function

There are two options for this functionality;

- shut off valve; or
- on/off valve.

5.6.1 Shut off valve

The shut off valve isolates the low pressure (downstream of the regulator) from the high pressure (cylinder) side of the VIPR. This may be a separate valve or be operated together with the flow selector.

The shut off valve shall be designed for maximum cylinder developed pressure and to operate under a high differential pressure. The most common spindle seal has an O-ring outer spindle seal. The inner spindle can be either of non-rotating or rotating type.

The material of the valve seat is important to ensure a gas tight seal and is often a non-metallic insert in a metallic holder. The guidelines in 5.2 shall be considered.

The gland on the valve stem is a potential source of a leak of gas, which may be outwards under a high pressure or inwards when the cylinder is being vacuumed prior to filling. The number and type of O-rings in this area is an important design consideration.

The shut off valve shall have controlled slow opening characteristics to limit the opportunity for ignition through adiabatic compression. The required force to operate the valve shall be defined to ensure ease of operation for the end user.

5.6.2 On/Off Valve

The on/off valve isolates the cylinder content on the low-pressure side from the user outlet(s). This is typically a valve positioned after the pressure regulator and associated pressure relief devices

The on/off valve shall be designed for set pressure of the pressure relief device, typically 10 bar. The material of the valve seat is important to ensure a gas tight seal and is often a non-metallic insert in a metallic holder. Guidance on materials is given in 5.2.

The design of the regulator has to be considered when using an on/off valve, as it will be permanently loaded with cylinder pressure which may lead to creep and activation of the pressure relief device.

5.7 Filling port

The VIPR shall have a dedicated filling port. The filling port shall include an integral non-return valve that is opened when connected to the filling system by a filling adaptor. This non-return valve prevents the release of gas from the cylinder in customer service.

Filling ports are described as:

- passive;
- semi active; or
- active.

For further information and representation see EN ISO 10524-3 [4].

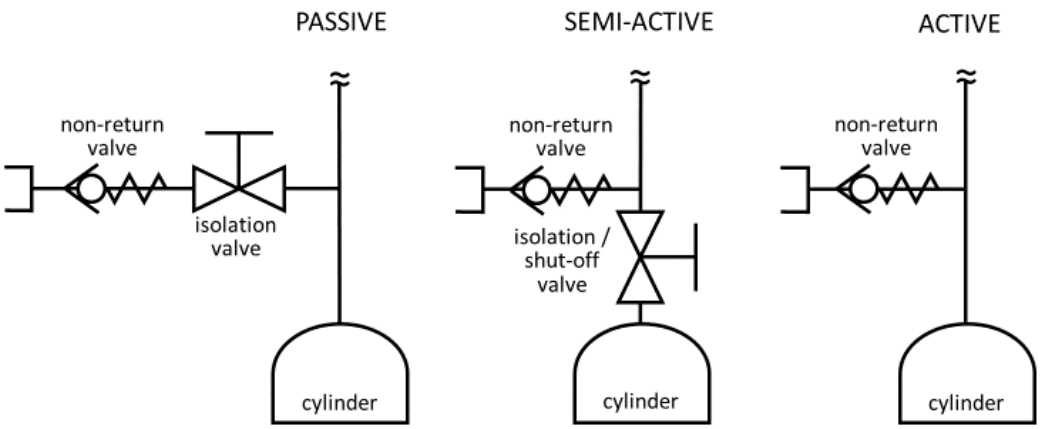

Figure 1 VIPR valve configurations

A passive port has an isolation valve that is designed only for the filling process. This valve would be closed at all other times.

A semi active port has an isolation/shut-off valve which is opened during use, exposing the non-return valve to cylinder pressure.

An active port does not have any form of isolation valve, and the non-return valve is therefore always exposed to the cylinder pressure.

Table 2 Comparison of filling ports

Filling port	Pros	Cons
Passive	Leak tight under all circumstances	High complexity Additional filling operation Risk of not filling cylinder
Semi active	Leak tight during transport	Additional filling operation Risk of not filling cylinder
Active	Easy to fill Simple design	Risk of uncontrolled leakage

The choice of the type of filling port the usability of the VIPR for the customer should also be considered.

The filling adaptor and valve combination shall be subjected to an adiabatic compression test as stipulated in 5.2.

It is required that the filling connector used to fill the package is designed by a manufacturer ensuring that all material dimensions are accurate. A poorly fitting filling adaptor is a high risk and multiple incidents have been linked to wrong fitting or excessively worn filling adaptors.

The filling connector design and manufacturing (including the push pin) shall prevent any misalignment.

Any design changes to the filling port of the VIPR or the fill connector shall result in testing of the combination.

Though the filling port is designed mainly for one directional flow, the effects of a backflow from the cylinder need to be tested, see the test in EN ISO 10524-3 [4]. There have been incidents where O-rings on the fill connector have become dislodged during backflow leading to an ignition. It is possible to depressurize the cylinder via the filling port prior to filling or testing using an appropriate tool to open the non-return valve. Therefore, the requirements generated by this reverse flow need to be considered in the design and material selection of the fill system and VIPR.

The filling port connection is not used by the customer so can be freely chosen from an accepted valve outlet standard or be a proprietary design assuming there are no mandatory national regulations.

The filling connector has to be designed and tested to maximum filling pressure. An interchangeability between high and a lower filling pressure, for example between 300 bar and 200 bar shall be prevented.

The filling port can be susceptible to the ingress of airborne particle if left unprotected in transport, storage or customer service. The use of a cap or shrink wrap to protect the port is an acceptable solution.

If pressure-tight plugs are used to meet the external leakage requirement, such plugs shall be designed for the cylinder pressure and require the use of a proprietary tool for removal. The risk of ejection in case of leak of the non-return valve when removing the plug shall be addressed to prevent any risk to the operator, for example by means of a vent hole.

5.8 Residual Pressure Valve (RPV)

An RPV shall be built in to the design of the VIPR to ensure a positive residual pressure is maintained in the cylinder. The RPV can have a dual function and be designed to prevent back flow from the customer. Maintaining a positive pressure and protecting from back flow prevents ingress of moisture and particles into the cylinder thereby reducing the risk of cylinder corrosion and out of specification product. The RPV should comply with the requirements of EN ISO 15996, *Gas cylinders -- Residual pressure valves -- General requirements and type testing*, [16].

5.9 Pressure regulator

The pressure regulator is designed to reduce the cylinder pressure, typically from between 200 bar to 300 bar) down to the user pressure (approximately 4,5 bar) which varies with national medical practices. More details see EN ISO 10524-3 [4].

The design of the regulator can be either a piston or diaphragm type, with a single or multiple stage.

The effect on the outlet pressure of decreasing inlet pressure (regulating characteristic) needs to be well understood during development of the VIPR to ensure that the outlet pressure remains within the required design tolerances.

The design of the regulator seat shall be such that if, the regulator seat burns, there is no direct gas path from the high-pressure side to the low-pressure side through the seat cavity.

The low-pressure side of the regulator shall be protected by a pressure relief device. This device shall activate if the low-pressure side is subjected to high pressure. The primary relief device is set to relieve the pressure to prevent a pressure higher than 10 bar in the low-pressure side.

When the activation of the relief device is due to an ignition of internal parts of the pressure regulator, the relief device itself may ignite or expel a flame that could impinge on to the cylinder guard. Consideration shall be given to the location and size of the relief device vent holes to ensure the most favourable direction of vent flow and to the materials of the guard, if fitted

The outlet(s) of any relief device need to be designed to minimise the risk of water ingress which, for example, if frozen may cause a blockage.

Care needs to be taken to mitigate any risk of a lubricant from the low-pressure side finding its way back into the high-pressure side, where its compatibility with the gas stream at the elevated pressures may be greatly reduced.

Where possible the low-pressure side should be designed to withstand the high-pressure conditions.

5.10 Flow selector

Two types of device are used to select the flowrate.

- Type 1: Flow selector device allowing the selection of one flowrate among a number of pre-set flowrates, via a series of fixed positions; and

- Type 2: Fully adjustable device where the flow is continuously controlled by adjusting the pressure upstream a fixed orifice

Type 1 is the most commonly used and should be preferred for usability reason. The flowrates are fixed by a rotating flow disc. The material of the disc, O-rings and its lubrication are important as any sticking or chemical reaction can affect the ability of the device to deliver the required flowrate.

The flow selector device should be designed to self-centre on a flow setting, that is to have no stable position between adjacent settings. If the design does not prevent a stable position between adjacent settings, a minimum flow rate should be ensured in the in between positions, for example 50% of higher flowrate.

5.11 Pressure outlet connection

The pressure outlet connection is usually a quick connector, designed in accordance with the acceptable medical regulations and/or standards in the country of operation. The type of connection is gas specific and is generally the same as that used on the medical gas pipeline system.

The pressure outlet connection typically incorporates a non-return valve which is opened by inserting the appropriate connector.

5.12 Flow outlet connection

The flow outlet connection should be designed as a male connection to accept a tubing (push-on hose) at atmospheric pressure. This type of design is often referred to as a nipple or hose barb or fir tree, see EN13544-2 *Respiratory therapy equipment. Tubing and connectors*, [17].

5.13 Tamper evident seal and outlet covers

Protection of the outlet connection ports needs to be considered, as with the filling port (5.7), as the other ports may also be susceptible to particulate ingress. There have also been documented incidents in the Industrial Gases industry of insects being found in these ports.

In addition to being used as protection, connection port caps and seals can be used to indicate the 'status of use' of the cylinder (commonly known as tamper evidence seals). This is seen most commonly immediately after filling when the addition of a cap/seal to the customer outlet designates a full cylinder.

Finally, caps may also be used to deter incorrect customer operation of the valve. Filling ports (which are only used by the gas supplier) are often sealed with a cap displaying a label or pictogram warning the customer not to connect anything to the port.

5.14 On/off handwheel and flow selector

The ergonomics of the on/off handwheel and of the selector shall be designed taking into consideration the maximum force that an end user can apply to enable them to open the VIPR. The direction for opening/closing valve and increasing/decreasing flow shall be clearly and durably marked.

5.15 Valve protection

Where a VIPR is fitted with a guard, it shall comply with the requirements of ISO 11117, *Gas cylinders -- Valve protection caps and valve guards -- Design, construction and tests* [13]. The guard can be made of plastic or metal and should be designed to assist with the correct handling of the cylinder package. The effects of environmental factors shall be considered, e.g. UV resistance for plastic and corrosion resistance for metal guards. Flame resistance should also be considered, such as using plastics classified V-1 according to EN 60695-11-10 *Fire hazard testing. Test flames. 50 W horizontal and vertical flame test methods* [18].

For the design of the guard, consideration should be given to the mode of use of the cylinder package, especially when small cylinders are directly attached to hospital beds or are placed adjacent to the patient.

The design of the valve guard shall be as open as possible, properly allowing the leak checks both from the valve components and from the cylinder thread.

The VIPR fitted with guard should be suitable for use on small diameter cylinders, typically with a diameter of 100 mm. If the guard external dimensions are greater than cylinder diameter operational risks, such as effective strapping need to be considered.

In the design of the valve guard, the valve guard should allow reading the VIPR information, such as batch number, valve serial number and manufacturing date, without disassembling the valve guard.

For VIPR with safety pressure relief devices with an indication of activation, the valve guard design should allow to see if these have activated without disassembling the valve guard itself.

If no guard is fitted, the appropriate impact test is required.

6 Filling activities

6.1 Safety considerations

It is required that a site-specific hazard review is completed to identify all potential hazards to the operators. The location of the filling area and the surrounding hazards may differ greatly depending on the site and give rise to requirements for protective barriers.

There are a number of generic recommendations that should be implemented for the protection of the operator via Personal Protective Equipment, see EIGA Doc 136, *Selection of Personal Protective Equipment,* [19]

6.2 Filling equipment design

The design and location of the filling equipment is as important as the design of the cylinder package and similar considerations need to be given to material selection and cleanliness.

Medical cylinders would usually be segregated from non-medical cylinders and in many cases the filling racks are dedicated to medical. The equipment used in medical filling racks may differ from non-medical practice due to the requirement to use polymers that are approved for medical use such as EPDM, (Ethylene Propylene Diene Monomer) instead of Viton® (Fluorocarbon) even though they may have a lower auto-ignition temperature in oxygen, see EIGA Doc 73, [8].

The necessity of filters or particle traps on filling installation equipment should be assessed. If used, they shall be designed with compatible materials and able to be easily maintained. The flow through the filter shall be unidirectional, never bidirectional. Any gas released from the cylinders shall not pass through a filter before being vented to the atmosphere.

The necessity for heat sinks on filling equipment such as flexible hoses, should also be considered as it limits the propagation of ignitions, see EIGA Doc 42, *Flexible Connections in High Pressure Gas Systems* [20].

6.3 Inspection prior to filling

In addition to the pre-fill inspection requirements required by EN ISO 24431 *Gas cylinders. Seamless, welded and composite cylinders for compressed and liquefied gases (excluding acetylene). Inspection at time of filling* [21], a specific visual pre-fill inspection shall be performed and include:

- Date for the next required refurbishment of the VIPR or removal from service;
- Inspection of valve for contamination especially the filling port and patient outlet connection(s);
- Absence of contamination from the patient or user (e.g. blood, body fluid, alcohol-based hand cleaner gel, etc.), see EIGA TB 03*, Handling and cleaning externally soiled medicinal gas containers,* [22];
- Condition of the valve especially the content indicator, flow selector knob and patient outlet connection(s) for any sign of damage, ignition or missing part;
- Where relevant, the condition of the electronic content indicator, e.g. low battery indication, display integrity;
- Inspection of the filling connector for absence of damage and contamination;
- Ensuring the filling connector is the appropriate type (including push-pin) for the VIPR filling port.

It is important to carry out a residual pressure test prior to filling to indicate that there has been no internal contamination of the cylinder.

The residual pressure check can be performed by:

- Checking content indicator;
- If no content indicated, open shut off valve, select flow and check for gas flowing; or
- If no flow, gently push (prod) non-return valve in filling port with an appropriate tool.

If no residual pressure is detected, send cylinder package for maintenance evacuation and/or purging.

Good Manufacturing Practice Annex 6, Manufacture of Medicinal Gases [23] requires that cylinders which have been returned for refilling should be prepared with care in order to minimise the risks of contamination, in line with the procedures defined in the Marketing Authorisation. See also EIGA Doc. 99 Part1 *Good Manufacturing Practice Guide Part I for Medical Gases* [24]. These procedures which should include evacuation and/or purging operations should be validated.

It is acceptable to vent the cylinder individually via the customer outlet (s) or to vent them via the filling port when connected to the filling manifold. In case of venting via the filling port line the following considerations need to be considered

- low temperature creating temperature gradient due to quick gas venting;
- high gas flow in case of oxygen or oxygen mixtures; and
- friction of non-metallics (e.g. O-rings).

Where the cylinder is vented via the filling manifold this shall only be done when the filling port has been designed and tested for bi-directional flow.

When the cylinder is empty this is an opportunity to check that the content indicator shows zero position.

6.4 Filling

On VIPR with semi active filling port to reduce the risk of deformation of the PIN of the filling connector and/or filling port (against high pressure) the following procedure is recommended:

Prior to connecting the filling connector ensure that the main shut off valve is closed and the VIPR downstream is vented, for example through the low-pressure outlet / flow selector. Depressurisation of the VIPR minimises the risk of damage to either filling connector pin or check valve (non-return valve).

The filling process can include a vacuum and/or purge step(s) depending on the local filling procedure and the marketing authorisation.

6.5 Filling inspection

The general process for checking for leaks during filling shall be conducted during the initial stages of the filling process as with any other oxygen cylinder. This ensures that there are no loose connections, damaged fill connectors or VIPR components.

If leaks are discovered

- The filling process shall be stopped, or
- The leaking cylinder package shall be isolated and identitied and at the end of the filling process shall be removed and quarantined for further investigation.

6.6 Post filling inspection

The cylinders shall be checked to ensure that they have been filled after the cylinders have been disconnected from the filling system. This is usually either via touching the cylinder shell, which, if filled, should have an elevated temperature or by checking the VIPR contents indicator (indication in line with filling pressure). Where cylinders are filled individually the process control system can render such checks unnecessary.

After filling, a leak check shall be completed on the VIPR including the filling and discharge connections and the cylinder to VIPR connection. If a leak detection fluid is used, it shall be approved for the application, see EIGA Doc 78, *Leak detection fluids - Gas Cylinder Packages* [25]. Where used it shall be ensured that this does not enter into the VIPR fill or discharge connections.

There is a specific medical requirement to check that the VIPR is functioning correctly. The procedure for this shall be documented. This could need to be agreed with the relevant authorities. For example, the operator could select a flow and confirm there is gas being released from the cylinder. For more details see EIGA Doc 218, *Medicinal VIPR Package: Lifetime Performance of Drug Delivery Device* [26].

7 Maintenance, handling and life cycle

7.1 Maintenance procedure

If the VIPR needs to be removed from the cylinder this shall be in accordance with EN ISO 25760 *Gas cylinders. Operational procedures for the safe removal of valves from gas cylinders* [27] Safety aspects shall be addressed along with specific tooling to avoid damage to the VIPR.

Procedures shall be in place to ensure that the VIPR is installed to the correct torque and that there is no possibility that the VIPR is hand tight in the cylinder, see EN ISO 13341 [11].

Only trained maintenance staff shall be used for repairs and refurbishments to VIPRs in accordance with written procedures approved by the VIPR manufacturer. This can require the original manufacturer to be engaged to obtain approval for the location and personnel approved for the work.

When maintaining the VIPR only spare parts approved by the original manufacturers shall be used.

7.2 Life time and periodicity of maintenance

The Medical Device Directive [2] requires in Annex I that the characteristics and performance of the VIPR must not be affected to such a degree that the clinical condition and safety of the patients are compromised during the lifetime of the VIPR as indicated by the manufacturer in the instructions of use.

The service life as defined in EN ISO 10524-3:2019 [4] is the time period during which a VIPR can be used to refill a cylinder. Such requirements are not described in the EN ISO 10524-3:2005 [28], which resulted in different interpretation in the instruction of use. Further information see TB 29, *Service life of Valves with Integrated Pressure Regulator (VIPRs) Fitted to Medical Gas Cylinders*, [29].

The VIPR manufacturer shall advise the type and frequency of the maintenance and/or inspection of the device and subsequent testing as required in the user instructions.

7.3 General cylinder package handling

Experience from the field shows how improper cylinder handling has been identified as one of the root causes of VIPR breakdown or malfunctioning. Most frequent damage, and consequent failures, involve pressure indicators, flow outlet and in particular the pressure outlet (quick connector) .

The different supply chain phases can comprise:

- Cylinder handling at production sites, distribution hubs and platforms and customer and patient storage location;
- Cylinder transport to take into account actions such as acceleration, vibration; and
- Cylinder fixing at point of use including cylinder clamps on ambulances or helicopters.

Gas companies, caregiver personnel and end users should ensure that when handling the cylinders, they avoid damage to the VIPR. Potential for damage to the VIPR includes dropping of th cylinder packages and shocks and mechanical stress applied by external factors such as strapping.

This can be by training and adequate VIPR protection including the selection of cylinder containers such as boxes, tubes, first aid bags and backpacks.

7.4 Cleaning of cylinder packages

As there is a risk of damage to the VIPR and cylinder due to the incorrect selection of cleaning materials, only those recommended by the gas supplier should be used. For more information and guidance see EIGA Technical Bulletin TB 03, *Handling and Cleaning Externally Soiled Medicinal Gas Containers* [22]

7.5 Further considerations for the safe use of VIPRs

This publication gives recommendation mainly to the design and operation of the VIPR packages. Other aspects that shall be considered for the VIPR include:

- manufacturing process (including cleaning) and quality assurance;
- packaging for delivery;
- fitting on the cylinder;
- removal from cylinder (devalving); and
- efficient communication with the manufacturer about VIPR performance, failures and incidents.

8 Additional recommendations to the user

Care shall be taken when operating a medical gas package incorporating a VIPR.

The user shall be familiar with the operating instructions and the functionality of the VIPR including:

- shut off function;
  - shut off valve;
  - on/off valve;
- flow selector function;
  - checking for gas flow when the cylinder is being used;
  - autonomy of cylinder depending on initial pressure and flow rates.

It is recommended, that the gas company records the instructions and training provided by them to the user of VIPRs

The location of the cylinder, whilst in use shall be considered, and sources of ignition and storage of consumable materials minimised. The operating instructions shall require the user to contact the gas supplier if there is any doubt about the correct operation and storage of the VIPR package.

When the cylinder is not in use, ensure the main shut off function is in the closed position. If there is a separate flow selector, this should be reduced to the lowest flow possible to avoid incidents on start up with high initial flow after the shut off function is opened.

The general conditions for cylinder storage require careful consideration; it is advised to keep medical cylinders inside a purpose designed cylinder storage area, clean, with adequate ventilation, and protection from the elements and extreme temperatures. These precautions are particularly important for a VIPR due to the additional components and functionality.

9 References

Unless otherwise stated the latest edition shall apply.

[1] EIGA Doc 104, *Safety Principles for Pressure Regulators for Medical Oxygen Cylinders* www.eiga.eu

[2] Directive 2010/35/EU *of the European Parliament and of the Council of 16 June 2010 on transportable pressure equipment* www.europa.eu

[3] Directive 93/42/EEC *of the European parliament and of the Council for Medical Devices* www.europa.eu

[4] EN ISO 10524-3;2019, *Pressure regulators for use with medical gases. Pressure regulators integrated with cylinder valves-- Part 3* www.cen.eu

[5] EIGA Safety Information, SI 21 *Cylinder Valves - Design Considerations* www.eiga.eu

[6] EN ISO 15001, *Anaesthetic and respiratory equipment -- Compatibility with oxygen* www.cen.eu

[7] EIGA Doc 13, *Oxygen pipeline and piping system* www.eiga.eu

[8] EIGA Doc 73, *Design Considerations to Mitigate the Potential Risks of Toxicity when using Non-Metallic Materials in High Pressure Oxygen Breathing Gas Systems* www.eiga.eu

[9] EN ISO 11114-1, *Gas cylinders. Compatibility of cylinder and valve materials with gas contents. Metallic materials* www.cen.eu

[10] ASTM G175, *Standard Test Method for Evaluating the Ignition Sensitivity and Fault Tolerance of Oxygen Regulators Used for Medical and Emergency Applications* www.astm.org

[11] EN ISO 13341, *Gas cylinders -- Fitting of valves to gas cylinders* www.cen.eu

[12] EIGA Doc. 138, *PTFE used as a sealant for cylinder/valve connections* www.eiga.eu

[13] EN ISO 11117, *Gas cylinders -- Valve protection caps and valve guards -- Design, construction and tests* www.cen.eu

[14] EN ISO 15245-1, *Gas cylinders -- Parallel threads for connection of valves to gas cylinders. Specification* www.cen.eu

[15] EN 60529, *Degrees of protection provided by enclosures (IP Code)* www.cen.eu

[16] EN ISO 15996, *Gas cylinders. Residual pressure valves; General requirements and type testing* www.cen.eu

[17] EN13544-2, *Respiratory therapy equipment. Tubing and connectors,* www.cen.eu ,

[18] EN 60695-11-10, *Fire hazard testing. Test flames. 50 W horizontal and vertical flame test methods* www.cen.eu

[19] EIGA Doc 136, *Selection of Personal Protective Equipment,* www.eiga.eu

[20] EIGA Doc 42, *Flexible Connections in High Pressure Gas Systems* www.eiga.eu

[21] EN ISO 24431, *Gas cylinders. Seamless, welded and composite cylinders for compressed and liquefied gases (excluding acetylene). Inspection at time of filling* www.cen.eu

[22] EIGA TB 03, Handling and cleaning externally soiled medicinal gas containers www.eiga.eu

[23] Good Manufacturing Practice GMP *Annex 6, Manufacture of Medicinal Gases* www.europa.eu

[24] EIGA Doc. 99, Part1 *Good Manufacturing Practice Guide Part I for Medical Gases* www.eiga.eu

[25] EIGA Doc 78; *Leak detection fluids - Gas Cylinder Packages* www.eiga.eu

[26] EIGA Doc 218, *Medicinal VIPR Package: Lifetime Performance of Drug Delivery Device www.eiga.eu)*

[27] EN ISO 25760, *Gas cylinders. Operational procedures for the safe removal of valves from gas cylinders* www.cen.eu

[28] EN ISO 10524-3:2005, *Pressure regulators for use with medical gases. Pressure regulators integrated with cylinder valves-- Part 3* www.cen.eu

[29] EIGA Technical Bulletin TB 28, *Service life of Valves with Integrated Pressure Regulator (VIPRs) Fitted to Medical Gas Cylinders* www.eiga.eu