GUIDANCE NOTE 39

MEDICAL GASES

RESPONSIBLE PERSON

2020

British Compressed Gases Association

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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 promote safe practice and to prioritise environmental protection in the supply, use, storage, transportation and handling 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 161. This document was first published on 09/01/2020. For comments on this document contact the Association via the website www.bcga.co.uk.

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* Throughout this publication the numbers in [ ] brackets refer to references in Section 5. 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.
Medicinal gas	Any gas or mixture of gases classified as a medicinal product (as defined in European Directives 2001/83/EC [2] and European Directive 2001/82/EC [1]). Throughout this document the term 'Medicinal Gas' is used to describe the products that are supplied in accordance with the Marketing Authorisation for medicinal use.
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.
Responsible Person	Indicates person named on Wholesale Distribution Authorisation (Human) (WDA(H)) (or for veterinary medicines a WDA(V)) with primary responsibility for ensuring compliance with good distribution practice (GDP).
Agent Manager	Indicates person named within company documentation for conducting the duties delegated to them by the Responsible Person for a specific sub-contractor owned site named on the WDA(H) (or for veterinary medicines a WDA(V)).
Authorised Person	Indicates person named within company documentation for conducting the duties delegated to them by the Responsible Person or Agent Manager for a specific site named on the WDA(H) (or for veterinary medicines a WDA(V)). This person shall be authorised to conduct this role by the Responsible Person only.
Nominated Deputy	Indicates person named within company documentation for conducting the duties delegated to them by the Responsible Person or Authorised person for a specific site named on the WDA(H) (or for veterinary medicines a WDA(V)). This person shall be authorised to conduct this role by the Responsible Person or Authorised Person, as applicable.

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MEDICAL GASES. RESPONSIBLE PERSON.

1. INTRODUCTION

Medicinal Gases are licensed pharmaceutical products, which are highly regulated by European Directives and UK legislation.

The Medicines and Healthcare products Regulatory Agency (MHRA) is the Executive Agency of the Department of Health which protects and promotes public health and patient safety by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and are used safely.

Any organisation that wishes to manufacture medicinal gases shall have a Manufacturer's Authorisation for the manufacture of medicinal gases. Any organisation that does not hold a Manufacturer's Authorisation or wishes to provide and distribute medicinal gases that they have not manufactured shall have a Wholesale Dealer's Authorisation. These are issued by the MHRA.

Any site that distributes licensed pharmaceutical products to persons other than the end user (patient) shall be licensed to act as a Wholesale Distributor. The regulatory authorities refer to this activity as supply. This includes loans of medicines to a neighbouring suppliers as well as supply free of charge. The license specifies addresses of each site, what activities can be carried out on that site, what products can be handled on the site and names specific people.

Any licensed distributor of pharmaceutical products shall have at least one Responsible Person (RP) named for every site that either procures, handles, stores or supplies licensed medicines. The role of the Responsible Person is defined in European Directives and is transferred into UK law via the Human Medicines Legislation. Details of the regulatory requirements and further guidance are published in the '*Green Guide*' [5] which is produced periodically by the MHRA and published by the Pharmaceutical Press.

The license holder will usually be a company with a named person as the contact. The licence holder shall not permit any person to act as a Responsible Person other than the person named in the licence or another person notified to the licensing authority.

This document gives additional guidance to the medical gas industry and should be read in conjunction with the following documents:

- EC 2013/C 343/01 [3], *Good Distribution Practice of medicinal products for human use*.
- The Cogent Gold standard for Responsible Persons for Medicinal Products [6].
- The Green Guide Rules and Guidance for Pharmaceutical Distributors [5].
- Eudralex: https://ec.europa.eu/health/documents/eudralex/vol-4_en

- Eudralex, GDP Regulations: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XC0321(01)&from=EN

- British Compressed Gases Association (BCGA) Guidance Note 32 [7], *Medical Gases. Good Distribution Practice*.

2. SCOPE

Sets out the duties, roles and responsibilities of a Responsible Person within an organisation that distributes medicinal gases.

3. RESPONSIBLE PERSON

The principle document setting out the duties for the Responsible Person is EC 2013/C 343/01 [3] (Chapter 2.2) and its transfer into UK law via the Human Medicines Legislation. These shall be followed at all times. The MHRA may interview new Responsible Persons and inspect sites against this legislation. In support of the legislation, there are guidance documents. The *Green Guide* [5] is a comprehensive document which encompasses all of these documents. BCGA documents give further guidance for the gas industry.

3.1 New Responsible Person

A prospective Responsible Person shall be nominated and an application made to be named on the Wholesale Distributors Authorisation issued by the MHRA.

Before they are named on the license, the prospective Responsible Person will be assessed for their knowledge and experience. There is at present no specific qualification to become a Responsible Person, however, the *Cogent Gold Standard* [6] defines the knowledge that a prospective Responsible Person needs before they will be approved by the MHRA. A number of training organisations carry out training against this standard, which can also be carried out in-house. As part of the assessment process, a prospective Responsible Person may be interviewed by the MHRA to ensure that they have the necessary knowledge and experience. This assessment will use the *Cogent Gold Standard* [6] to define their expectations.

A Responsible Person can also be accepted on a license if they are eligible to act as a Qualified Person (QP) or are qualified as a Pharmacist. Persons with such qualifications will still be expected to cover the requirements of the *Cogent Gold Standard* [6].

The MHRA will take into account the type of products the Responsible Person will handle. At its simplest this may be a site that only handles oxygen (a General Sales List (GSL) gas). Further knowledge is required for handling Pharmacy (P) products such as those containing nitrous oxide and further information still for those handling Prescription Only Medicine (POM) gases. It is unlikely that a gas site will handle more complex products such as controlled drugs or cold chain drugs which require extra facilities and controls.

In most cases, the MHRA will expect to see at least one year's experience working in pharmaceutical distribution prior to being named on a license.

3.2 Expectations of a Responsible Person

The licence holder shall ensure that there is available, at all times, at least one person (referred to in the Regulations as the '*Responsible Person'*) who in the opinion of the licensing authority:

- has knowledge of the activities to be carried out and of the procedures to be performed under the licence. If the scope of the activities on site change from handling 'GSL' products only to 'P' or 'POM' products, the Responsible Person may require additional training to cover their new responsibilities;

- has adequate experience relating to those activities and procedures;

- understands the role of the MHRA in regulating and enforcing licensed medicine distribution.

The licence holder shall ensure:

- that the conditions under which the licence was granted have been, and are being, complied with;

- that the quality of medicinal products handled by the licence holder is being maintained in accordance with the requirements of all Marketing Authorisations.

The licence holder shall notify the licensing authority of:

- any change of the Responsible Person;

- the name, address, qualifications and experience of the Responsible Person.

Further details about the MHRA and their expectations with respect to Good Distribution Practice (GDP) are given on the MHRA website.
https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice

3.3 Duties of the Responsible Person

The Responsible Person is responsible for ensuring that the quality of the product is maintained throughout the distribution process, therefore safeguarding product users against potential hazards arising from poor distribution practices.

The Responsible Person at a gas distribution site should be aware of the following, which include but are not limited to:

- the conditions of the license for the site(s) where they are named on the license as a Responsible Person. The Responsible Person does not necessarily have to be based on any site for which they are a named Responsible Person. The Responsible Person can only act on sites where they are named on the license as a Responsible Person for that site;

- an understanding of the difference between the legal categories of medicine and any restrictions stated on the license. The license could restrict types of products that can be handled on a site such as 'GSL' only (for example, oxygen only) or 'GSL' and 'P' gases (oxygen and nitrous oxide mixtures). Some gases that are used in hospitals are 'POM' and this must be specified on the site details to handle these gases. Other restrictions may include storage and supply, but exclude procurement;

NOTE: A license that is restricted to medical gases cannot be used to handle other medicines such as tablets.

- the conditions of the wholesale dealer's license (WDA), ensuring they are met and that the guide lines on Good Distribution Practice (GDP) are complied with;

- understanding the requirements for an effective pharmaceutical quality management system and how it can be implemented, developed and maintained, complete with the importance of effective record keeping. This should include risk management and handling non-conformance;

- the requirement to develop a self-inspection programme and then to perform them accordingly;

- verifing that procurement operations establish the *bona fides* of all suppliers before procurement. This includes routine purchase and borrowing / loan of stock from other sites or suppliers even if these are a free of charge loan;

- the *bone fides* of customers. This is particularly important for 'P' and 'POM' products. The Responsible Person should understand the circumstances where each class of product can be sold to different types of customer (for example, hospital, pharmacy, distributor etc.);

- the relevant storage conditions for the products, which are to be complied with. In the case of gases, which are stored under cover and frequently stored in open or ventilated facilities, the Responsible Person should ensure themselves that suitable controls are met. Typical issues include pest control, such as the control of vermin and birds to prevent contamination of cylinders and their valves;

- that medicinal gases are stored separately from other gases, including non-medical cylinders of the same gas (for example, medical and industrial oxygen);

- good housekeeping is complied with around cylinders, including prevention of eating, drinking and smoking in the cylinder storage area;

Good housekeeping should also include prevention of accumulation of rubbish, vegetation and appropriate pest control.

- that regular reviews and monitoring of all areas and sites under their control are carried out. Where responsibilities have delegated, these should be defined in writing and they should receive written reports that such actions have been carried out on their behalf. Where arrangements are delegated, the Responsible Person remains responsible and he should personally carry out the delegated functions at least once a year;

- that all records relating to distribution of medicinal products are contemporaneous, accurate and available for the duration of their retention period. The Responsible Person should also verify that any document retention periods comply with legislation;

- understanding storage and transport conditions, including the 36 hour rule, where a site does not have to be named on a licence where ambient products are stored for less than 36 hours during transportation and prior to onward shipment. http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con446014.pdf

- ensuring that all persons involved with medicinal gases on-site are appropriately trained and that initial and continuous training programmes are implemented and maintained;

- co-ordinating and performing recall operations and recall simulation exercises (mock recalls), ensuring mock recalls have been carried out and any corrective action has been implemented and verified to be effective;

- that an appropriate complaints procedure is in place, ensuring that relevant customer complaints are dealt with effectively.

- where they can find information on defective and/or falsified medicines. https://ec.europa.eu/health/human-use/falsified_medicines_en

- how to report suspected defective or falsified medicines. https://yellowcard.mhra.gov.uk/

- keeping up to date with legislation and the expectations of the MHRA.

3.4 Management responsibilities of the Responsible Person

To carry out their responsibilities the Responsible Person should have:

- a clear reporting line to either the license holder or the Chief Executive;

- access to all areas, sites, stores and records which relate to the licensable activities being carried out;

- access to appropriate records relating to the discharge of their responsibilities.

Where the Responsible Person is not based on site and where the license covers a number of sites, the Responsible Person may have a nominated deputy with appropriate reporting and delegating arrangements. However, the Responsible Person should assure himself and the licensing authority that the necessary controls and checks are in place. The hierarchy of Responsible Persons should be defined to clarify which Responsible Person has primacy for any individual site.

Where a company has more than one Responsible Person and an individual site has a Responsible Person based at the site, the site based Responsible Person will usually be responsible for any activity on that site. In their absence, they can delegate Responsible Person responsibilities to any other Responsible Person. Delegation in the absence of the usual site Responsible Person should be clearly defined.

The Responsible Person should keep records of any formal inspections carried out in accordance with the requirements of the Pharmaceutical Quality Management System.

4. SPECIFIC REQUIREMENTS AND EXEMPTIONS RELATED TO THE MEDICAL GAS INDUSTRY

4.1 Specific requirements

The responsibilities of the Responsible Person will include:

- all medical gas packages;
- control over returned containers;
- maintaining the quality of the inside of gas containers, especially by minimising risk of moisture ingress, for example, through good management of storage sites and procedures to keep valves in the closed position when not in use;

4.2 Exemptions

Medicinal gases are exempt from the requirements within European Directive 2001/83/EC [3] and subsequent legislation for:

- safety features appearing on the packaging of medicinal products for human use;
- braille labelling requirements.

5. REFERENCES

	Document Number	Title
1.	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.
2.	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.
3.	European Commission 2013/C 343/01	Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013XC1123(01)&from=EN
4.	European Commission Regulation 2016/161	Commission Delegated Regulation (EU) 2016/161 of 2nd October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use.
5.	MHRA	The Green Guide Rules and Guidance for Pharmaceutical Distributors 2017 http://www.pharmpress.com/product/9780857112866/green
6.	Cogent Gold standard	The Cogent Gold standard for Responsible Persons for Medicinal Products http://www.thegold-standard.co.uk/job-details/?jobid=297
7.	BCGA Guidance Note 32	Medical gases. Good distribution practice.

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 Compressed Gases Association (BCGA)	www.bcga.co.uk

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