GUIDANCE NOTE 42

MEDICAL GASES
INCIDENT REPORTING

2021

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 164. This document was first published on 20/04/2021. 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 7. 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.
Marketing Authorisation	Approval from the relevant National Regulatory Authority necessary to market and sell a medicinal product in that country. In the UK this is the *Medicines and Healthcare products Regulatory Agency*.
Medicinal product	As defined in *The Human Medicines Regulations* [2]: (a) any substance or combination of substances presented as having properties of preventing or treating disease in human beings; or (b) any substance or combination of substances that may be used by or administered to human beings with a view to: (i) restoring, correcting or modifying a physiological function by exerting a pharmacological, immunological or metabolic action, or (ii) making a medical diagnosis.
Medicinal gas	Any gas or mixture of gases classified as a medicinal product. 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.
Pharmacovigilance	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.
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.
Summary of Product Characteristics (SmPC)	A document required as part of the Marketing Authorisation for each medicine. It provides information for a healthcare professional on how to use the medicine. It includes details of the specification of the product.

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MEDICAL GASES. INCIDENT REPORTING

1. INTRODUCTION

Medicinal Gases and their associated equipment are widely used for treating patients in hospitals, at home and by the emergency services.

Many BCGA member companies are licensed by the *Medicines and Healthcare products Regulatory Agency* (MHRA) to manufacture and distribute medicinal gases used within the UK. They also provide a range of associated equipment and services (which are not licensed by the relevant Regulators), these are marked for conformity to the appropriate medical Regulations following a conformity assessment by an Approved Body for medical devices.

All medicinal gases and some of the associated equipment used are highly regulated by UK legislation. The gases and their primary packaging (container, including the valve) are classified as medicinal products and require a Marketing Authorisation (MA). The associated equipment is classified as a medical device when used to administer the gas.

Public health and patient safety are paramount and the relevant Regulators, the Gas Suppliers and the Equipment Manufacturers constantly strive to ensure that medicinal gases and their associated equipment meet appropriate standards of safety, quality, performance and effectiveness.

As such, if there is an incident with, or a problem is identified with, a medicinal gas or a medical device, there are reporting systems available. This document sets out the reporting systems which are in-place in the UK. Generally, the relevant Regulators focus on reporting adverse incidents. However, concerns about documentation, product design and usability should also be reported. There does not have to have been an adverse incident in order to make a report!

All parties should ensure they have adequate insurance to cover their activities and that they use their gases and look after their gas cylinders and associated equipment in a safe and responsible way.

2. SCOPE

This document applies to medicinal gases and their associated medical devices.

This document provides information on the reporting systems available in the UK if there is an incident with, or a problem is identified with, a medicinal gas or its associated medical device.

This information will assist those making a report to the relevant Regulators, the gas suppliers and the equipment manufacturers.

3. LEGISLATIVE REQUIREMENTS

In the UK compliance is required with *The Human Medicines Regulations* [2].

The MHRA regulates medicines and medical devices in the UK and is responsible for ensuring their safety, quality and effectiveness. The MHRA is an executive agency, sponsored by the *Department of Health and Social Care* (DHSC). Contact information for MHRA services is available at: https://www.gov.uk/guidance/contact-mhra

An Approved Body is an organisation that has been designated by the MHRA to assess whether manufacturers and their medical devices conform with the requirements set out in the *Medical Devices Regulations* [1] (as amended). For information on Approved Bodies for medical devices: https://www.gov.uk/government/publications/approved-bodies-for-medical-devices

NOTE: Conformity assessment marks. Although the UK conformity assessed certification mark, 'UKCA', has been available for use in Great Britain since 1 January 2021, a European Union (EU) conformity mark, 'CE' and a UK certification mark applicable to Northern Ireland (a 'UKNI' mark) is required for devices placed on the Northern Ireland market. Existing EU 'CE' marked devices will continue to be accepted on the Great Britain market until 30 June 2023.

The MHRA set out guidance for good manufacturing practice (GMP) and good distribution practice (GDP):
https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice

The MHRA participates with the European Medicines Agency (EMA) and references the EudraLex, Volume 4 [3], *Good Manufacturing Practice (GMP) guidelines*, which sets out the rules governing medicinal products in the European Union and contains guidance for the interpretation of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use.
https://ec.europa.eu/health/documents/eudralex/vol-4_en

Specifically, Annex 6, *Manufacture of medicinal gases*
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2009_07_annex6.pdf

For medical devices the *Medical Devices Regulations* [1] (as amended), requires vigilance and the reporting of serious incidents and field safety corrective actions.

4. REPORTING SYSTEMS

Guidance for the reporting of problems with a medicine or a medical device in the UK is available at: https://www.gov.uk/report-problem-medicine-medical-device

A similar reporting system is available for reporting incidents in the Republic of Ireland:
https://www.hpra.ie/homepage/about-us/report-an-issue

The *Defective Medicines Report Centre* (DMRC), refer to Section 4.2, provide guidance for reporting, investigating and recalling suspected defective medicinal products in the UK. This

will also include associated medical devices which are a part of the primary packaging for the medicinal product included in the Marketing Authorisation.

Adverse incidents involving other medical devices that occur in the UK shall be reported to the MHRA and the manufacturer. The notification and evaluation of adverse incidents and field safety corrective actions involving medical devices is known as the medical device vigilance system. Once a medical device has been placed on the UK market, the manufacturer shall submit vigilance reports to the MHRA and take any appropriate safety action when certain types of incidents that involve their device occur in the UK. The requirement to report falls to:

- the Manufacturer;

- the UK Responsible Person. Each medicinal gas and medical device supplier should appoint a Responsible Person to report any adverse incidents. For a medicinal product this is typically the Qualified Person (QP) named on the Manufacturer / Importer's Authorisation (MIA), commonly referred to as the manufacturer's licence. The QP can delegate their responsibility to an individual for the purpose of reporting incidents;

- the European Authorised Representative or the Authorised Representative based in Northern Ireland.

Guidance for manufacturers is available at:
https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance

Manufacturers are required to report direct to the MHRA (as the lead Competent Authority), however, for users the devolved administrations in the UK have their own reporting systems:

- Wales:
http://www.wales.nhs.uk/governance-emanual/reporting-adverse-incidents-and-dissemin

- Scotland:
https://www.nss.nhs.scot/health-facilities/incidents-and-alerts/report-an-incident/

- Northern Ireland:
https://www.health-ni.gov.uk/articles/reporting-adverse-incident

Members of the public can report direct to the MHRA.

There are specific requirements for the reporting of problems with a medicine or a medical device in the UK, depending on your involvement. These include:

- **Medicinal gas manufacturer / Marketing Authorisation holder**
Reports of safety concerns or incidents are to be made to the DMRC, refer to Section 4.2.

  It is recommended that the lead good manufacturing and distribution practice (GMDP) Inspector for medicinal gases at the MHRA is kept informed of any serious incidents, for example, ignitions involving cylinders containing medical oxygen (O_2).

- **Medical device manufacturer / Conformity Assessment mark holder**

For guidance on incident reporting obligations and the reporting systems available for manufacturers using the medical device manufacturer's vigilance reporting system, refer to Section 4.3.

To enable a process of continuous improvement for the safety and quality of the product, safety concerns or incidents should be reported to the medical device supplier.

When deemed necessary, safety concerns or incidents should be reported to existing customers of the medical devices, for example, in the form of a Field Safety Notice (after consultation with the relevant Regulator).

- **Medical device supplier**

Reports of safety concerns or incidents are to be made using medical device manufacturer's vigilance reporting system, refer to Section 4.3.

When deemed necessary, safety concerns or incidents should be reported to existing customers of the medical devices, for example, in the form of a Field Safety Notice (after consultation with the relevant Regulator).

- **Healthcare professionals**

Reports of safety concerns or incidents are to be made:

  - if relating to a medicinal gas, to the Marketing Authorisation holder (the Gas Supplier, using the information on the gas cylinder label). This allows the healthcare professional to complete their duty of care to comply with their pharmacovigilance duties. The Gas Supplier shall ensure the Marketing Authorisation holder is informed.

  - if relating to a medical device, to the medical device manufacturer. The named manufacturer of the device will inform the Approved Body (who has been responsible for conformity assessment of the medical device). Contact information will be within the 'Instructions for Use' and may be on the medical device.

  - to the MHRA using the Yellow Card Scheme, refer to Section 4.1.

NOTE: Healthcare professionals include Pharmacists, Clinicians, Nurses, electrical and biomedical engineering (EBME) personnel, etc.

- **Patient**

Patients who are prescribed domiciliary oxygen may report any safety concerns or incidents to their Homecare Service Provider. The process for making a report is detailed within the 'handbook' provided by the Homecare Service Provider for the safe use of the medical oxygen, refer to BCGA GN 29 [5], *Medical gases. The management of medical oxygen in domiciliary use.*

In addition, reports of safety concerns or incidents may be made using the Yellow Card Scheme, refer to Section 4.1.

NOTE: This includes all incidents involving a medicinal gas or a medical device.

- **Regulatory Authorities**

The Regulatory Authorities shall share reported information with each other to ensure safety.

4.1 Yellow Card Scheme

The Yellow Card Scheme is the UK system for collecting and monitoring information on suspected safety concerns or incidents involving medicines and medical devices reported by users. The Scheme is operated by the MHRA and currently relies on voluntary reporting of suspected adverse drug reactions by health professionals and patients. The purpose of the Scheme is to provide an early warning that the safety of a product may require further investigation. Reports can be made for all medicines and all medical devices available on the UK market. https://yellowcard.mhra.gov.uk/

The Yellow Card Scheme requires the following types of incidents to be reported as soon as possible:

- if a medicine causes side effects;
- someone's injured (or could have been injured) by a medical device, either because its labelling or instructions aren't clear, it's broken or has been misused;
- a patient's treatment is interrupted because of a faulty device;
- someone receives the wrong diagnosis because of a medical device;
- a medicine doesn't work properly;
- a medicine is of a poor quality;
- you think a medicine or medical device is fake or counterfeit.

NOTE: Medicinal gases are excluded from having specified safety features to prevent the supply of falsified medicines. Refer to EIGA BN 20 [7], *Falsified medicines regulations and medicinal gases*.

4.2 Defective Medicines Report Centre

The DMRC is a unit of the *Inspection, Enforcement & Standards Division* of the MHRA. The role of the DMRC is to minimise the hazard to patients arising from the distribution of defective medicines by providing an emergency assessment and communication system between manufacturers, distributors, the relevant Regulators and users. The DMRC produce a guide which is available at:
https://www.gov.uk/government/publications/a-guide-to-defective-medicinal-products

4.3 Medical device manufacturer's vigilance reporting system

Manufacturers of medical devices shall provide post-market vigilance reports to the MHRA. Guidance on incident reporting obligations and the systems available for manufacturers to report is available at:
https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance

Medical device vigilance identifies devices that may not be working correctly. It enables dangerous devices to be withdrawn from the market and to eliminate faults in medical devices with the intention of constantly improving the quality of devices and providing patients and users with increased safety.

Any event which meets all three reporting criteria below is considered an adverse incident and shall be reported to the MHRA:

- an event has occurred. This includes situations where testing performed on the device, examination of the information supplied with the device, or any scientific information indicates some factor that could lead, or has led, to an event;

- the manufacturer's device is suspected to be a contributory cause of the incident;

- the event resulted in, or might have resulted, in death or a serious deterioration in state of health of a patient, user or other person.

Not all adverse incidents result in death or a serious deterioration in health. These may have been prevented because of other circumstances, or because of intervention. Therefore, manufacturers shall still provide a report if:

- an incident associated with a device happened; and

- if it occurred again, it might lead to death or serious deterioration in health.

5. TYPES OF INCIDENTS

The types of incidents that may occur with medicines and medical devices are generally covered by the following topics:

- Medicinal gas, refer to Section 5.1;

- Cylinders and valves, refer to Section 5.2;

- Bulk containers, refer to Section 5.3;

- Adverse reactions, refer to Section 5.4;

- Theft, refer to Section 6.

5.1 Medicinal gas

Incidents with medicinal gas may include:

- Purity: Total assay of product is less than the specification (for example, O_2 / nitrous oxide (N_2O) mixtures where the medical oxygen content is less than as specified in the Summary of Product Characteristics (SmPC) document);

- Impurity: Minor component of product is greater than the specification (for example, nitric oxide (NO) / nitrogen dioxide (NO_2) in N_2O > 2 ppm);

- Contamination: Presence of a substance not in the specification that could be harmful to patient health (for example, solvents, hydrocarbons, oils, etc.);

- Content. Cylinders which do not have the required content of gas, or are empty, when required to be full, for example, when being prepared for use by a patient.

5.2 Cylinders and valves

Incidents with cylinders and valves include:

- ignitions involving cylinders containing O_2;

- inability to open or close the valve;

- leaks from cylinders and / or valves: resulting in an unintentional release of the product from the cylinder;

- connection problems between cylinders and associated devices;

- incorrect flow: malfunction of a valve and / or regulator, resulting in an incorrect flow of product;

- incorrect identification of a product. Including:

    - incorrect product label. It is a mandatory requirement to correctly identify the product a cylinder contains with a label which complies with the legislative requirement for the supply of pharmaceutical products as well as the carriage of dangerous goods.

    - incorrect colour schemes. Medical gas cylinders are allocated a specific colour scheme to help identify the product a cylinder contains. Refer to BCGA TIS 20 [6], *Medical gases. BCGA policy on colour coding*.

- unclear instructions for use;

- condition of package: package presenting signs of damage, debris, corrosion, contamination, etc.

NOTE: It is a requirement that medical gas cylinders are stored and managed in a manner that ensures that they will be delivered in a clean state, compatible with the environment in which they will be used.

5.3 Bulk containers

Incidents with bulk containers include:

- leaks: leaks in the container resulting in a visible gas cloud;

- safety relief devices: failure;
- mechanical failure: mechanical failure of oxygen vessels and vaporisers.

5.4 Adverse reactions

Adverse reactions are unwanted symptoms caused by medical treatment. They are also called ‘side effects’ or ‘adverse effects’.

Under pharmacovigilance, an adverse drug reaction is an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs under normal conditions of use, which is suspected to be related to the drug. The reaction may be a known side effect of the drug or it may be new and previously unrecognised.

6. SECURITY

Medical gas cylinders and associated medical equipment contain hazardous products.

Medical gas cylinders and their contents are attractive items for thieves.

In the event of theft or intentional damage, then each incident should be assessed to determine who and what needs to be communicated to the relevant interested parties, for example, local management, local security teams, the owner of the gas cylinders (the Gas Supplier), the Police, etc.

Fake or counterfeit medicines or medical devices shall be reported through the Yellow Card System, refer to Section 4.1.

When not in use, medical gas cylinders and associated equipment should be kept in a safe and secure location, which is well ventilated, where there are no sources of ignition. They should be maintained in a clean condition, suitable for use in a medical environment, refer to BCGA CP 44 [4], *The storage of gas cylinders*.

7. REFERENCES

	Document Number	Title
1.	SI 2002 No. 618	The Medical Devices Regulations 2002 (as amended).
2.	SI 2012 No. 1916	The Human Medicines Regulations 2012 (as amended).
3.	EudraLex	Volume 4. Good Manufacturing Practice (GMP) guidelines.
4.	BCGA Code of Practice 44	The storage of gas cylinders.
5.	BCGA Guidance Note 29	Medical gases. The management of medical oxygen in domiciliary use.
6.	BCGA Technical Information Sheet 20	Medical gases. BCGA policy on colour coding.
7.	EIGA Briefing Note 20	Falsified medicines regulations and medicinal gases.

Further information can be obtained from:

UK Legislation	www.legislation.gov.uk
Department of Health and Social Care (DHSC)	www.gov.uk/government/organisations/department-of-health-and-social-care
Medicines and Healthcare products Regulatory Agency (MHRA)	www.mhra.gov.uk
European Industrial Gases Association (EIGA)	www.eiga.eu
British Compressed Gases Association (BCGA)	www.bcga.co.uk

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