GUIDANCE NOTE 32

MEDICAL GASES.
GOOD DISTRIBUTION PRACTICE.

REVISION 1: 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. This document replaces BCGA GN 32: 2016. It was approved for publication at BCGA Technical Committee 156. This document was first published on 05/05/2017. For comments on this document contact the Association via the website www.bcga.co.uk.

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TERMINOLOGY AND DEFINITIONS

May	Indicates an option available to the user of this Guidance Note.
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.

GUIDANCE NOTE 32

MEDICAL GASES. GOOD DISTRIBUTION PRACTICE.

1. INTRODUCTION

The distribution of medicinal products is an important activity in the integrated management of the supply chain. The quality and the integrity of medicinal products can be affected by a lack of adequate control. The Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA) have published guidance on Good Distribution Practice (GDP).

Companies who store and distribute medical gas products need to hold a Wholesale Distribution Authorisation (Human) (WDA(H)) (or for veterinary medicines a WDA(V)) issued by the MHRA. Holders of a WDA(H) shall comply with GDP.

GDP requires that medicines are obtained from the licensed supply chain and are consistently stored, transported and handled under suitable conditions, as required by the Marketing Authorisation or product specification.

This document interprets the specific GDP requirements for medical gas products and is intended to be used by the medical gas industry to ensure a consistent approach.

The MHRA carries out inspections to check if distribution sites comply with GDP. You will be inspected when you apply for a WDA(H) and then re-inspected periodically at a frequency based on the outcome from previous inspections (a risk based system). Manufacturing sites holding a Manufacturer's / Importer's Authorisation (MIA) will also be inspected for GDP during Good Manufacturing Practice (GMP) inspections in the event that gases are being distributed from these sites.

The procedures in this document specifically comply with the principles of GDP and meet the regulatory requirements for wholesale dealing as described in the European Commission Guidelines *of 5 November 2013 on Good Distribution Practice of medicinal products for human use* [2013/C 343/01] (3), as it applies to medical gas products.

2. SCOPE

This document applies to medical gas storage and distribution sites named on a company's WDA(H) (and WDA(V) as applicable), where medical gas products are supplied only to approved customers. These facilities could include:

- Company managed sites.
- Agent operated sites.

It covers sites where medical gas products are stored for:

- Direct supply to approved medical gas customers using company managed transport (where the cylinders are stored on site for more than 36 hours).

- Direct supply to company approved medical gas customers using Agent operated transport.

- Collection by medical gas customers, approved by the company.

Although this document does not specifically cover the storage and distribution requirements of those company sites where there is manufacturing and medical gas product filling activities on site, the basic principles of the procedure are applicable to the way in which these sites handle, store and distribute medical gas products.

The target audience for this document is all company and Agent-employed staff involved in the supply of medical gas products to customers from UK retail facilities, Agent operated stores and medical gas product manufacturing, distribution and storage locations.

3. LEGISLATIVE REQUIREMENTS

GDP is that part of the overall Quality Management System which covers the regulatory requirements for the storage, distribution and supply of medical gas products to company approved customers. It is also intended for the control of medical gas products supplied for veterinary use.

Following the changes to the 'Medicinal Products for Human Use' regulations, EU Directive 2001/83/EC (1), the European Medicines Agency reviewed their guidance on GDP and specifically the requirements for the control of falsified medicines. The revised guide also added a number of other initiatives applicable to wholesale distribution activities including the principles of Risk Management, Corrective and Preventative Actions (CAPA) and Change Management.

Risk Management is a fundamental principle and is an integral part of a Quality Management System. CAPA and Change Management utilise the principles of Risk Management.

The European Industrial Gases Association (EIGA) provide further information on change management in EIGA Document 51 (4), *The management of change*.

Where Agents are used to act on behalf of a company to manage the storage and distribution of medical gas products to their approved customers, part of their approval is to ensure that the Management Systems established by the Agents meet these requirements. To assist Agents to comply with company procedures when handling and supplying cylinders to approved customers, it is recommended they are provided with appropriate documents, such as an Agents Manual, covering the relevant procedures they are expected to follow to ensure that they meet the minimum requirements for GDP.

For Agent operated sites, it is necessary to formalise the rental of a section of the Agent's site in order to maintain the storage and distribution activities under their control, with the Agent's staff being responsible for the day to day running of the activity. Agent operated sites will

remain under the responsibility of the company Responsible Person (RP) named on the WDA(H) (and WDA(V) as applicable).

This procedure also takes into account the additional requirements detailed in the EU Directive 'Principles and Guidelines of Good Manufacturing Practice' [2003/94/EC] (2), Annex 6 (Manufacture of Medicinal Gases), which are applicable to the storage and distribution of medical gas products.

When changes are made to this procedure, all relevant personnel shall be notified of the change. As appropriate, Agents shall also be notified and provided with an updated copy of this procedure. Where appropriate, additional training shall be provided to the relevant Agent's staff.

3.1 Licence requirements

It is a requirement of GDP that the storage and distribution facilities for medical gas products should be covered by an appropriate licence issued by the MHRA.

The licensing of all medical gas product storage and distribution facilities within the UK are currently covered by the MIA and WDA(H) (and WDA(V) as applicable). These licences specify the sites approved by the MHRA where medical gas products can be stored and distributed to approved customers.

A Responsible Person is named on the WDA(H) (and WDA(V) as applicable) for each listed site (including those sites where an Agent's staff locally manage the medical gas product storage and distribution activities). The same named Responsible Person can be listed on multiple sites, but in this situation the day to day duties for each site are delegated to a nominated Authorised Person (refer to Section 3.4).

The Responsible Person is responsible for ensuring all storage and distribution sites (including those operated by Agent staff):

- Are compliant with the GDP requirements detailed in this procedure.
- Are routinely audited by an approved auditor to confirm compliance with the procedure.
- Take appropriate corrective and preventative actions when non-conformances are identified either from the routine audits or from self-inspections on site.
- Get approval for any changes to the operation or personnel on site that impacts on the storage and distribution of medical gas cylinders. Where appropriate these changes shall be notified to the MHRA by the Responsible Person.
- Appointing a person on each site to be the Authorised Person who will be responsible for the delegated duties of the day to day management of the GDP activities, including the self-inspection requirements detailed within this procedure.

Each company shall have a central department that will be responsible for maintaining a register of each site named on the WDA(H) (and WDA(V) as applicable), the Responsible Person or nominated Authorised Person named for the site and the names of the Nominated Deputies to ensure that there is always a trained person available on site to manage the supply of medical gas products to approved customers.

As the control and documentation of the medical gas products delivered to approved customers is likely to utilise standard company procedures and systems, then Agent operated sites would be considered as company controlled. In the event of these requirements changing, the company shall ensure that the new arrangements are implemented within an acceptable time frame.

3.2. Quality management system principles

The EU GDP Guidelines (3) require that the licence holder shall operate a Quality Management System, setting out the responsibilities of the key personnel and the procedures to be followed, based on risk management principles.

Where Agents do not have direct access to a company's Quality Management System, they shall be provided with controlled copies of the procedures.

For medical gas products, the Quality Management System is required to ensure that:

- Medical gas products are stored in a defined area and maintained in a condition that is suitable for their intended use.
- The responsibilities of key personnel are defined.
- Medical gas products are only supplied to approved customers.
- Appropriate records are maintained of the supply of medical gas products to approved customers.
- Distribution sites are audited against an audit schedule and that any non-conformances are documented, with the completion dates for any appropriate corrective and preventative actions identified.
- Any deviations from the approved procedures are documented and investigated.
- Appropriate corrective and preventative actions are taken to manage any non-conformance and to prevent reoccurrence.

The procedure shall be reviewed every two years by the Responsible Person to ensure that the procedure reflects any changes identified through the CAPA processes or any additional guidance detailed within the EU GDP Guidelines (3). As part of this review, a Gap Analysis shall be conducted between the EU GDP Guidelines (3) and any corresponding company procedures to ensure that all aspects of the Guide are covered as they apply to the storage and distribution of medical gas products.

3.3 Change management

Any significant changes that impact on the storage and distribution of medical gas products on any site shall be subject to the change management procedures.

Prior to any changes to the approved facilities being made, approval shall be obtained from the Responsible Person or his Nominated Deputy. Records of any approved changes shall be kept on site.

For any changes that will impact on the storage and distribution of medical gas products on licensed sites, then the change should be implemented by following an approved change management procedure. Guidance is available in EIGA Document 51 (4).

Whenever there are any changes to the range of medical gas products stored on any site, the Responsible Person shall determine if there is a need to carry out a Risk Assessment to assess whether there is a need to change any procedures or facilities relating to their storage and distribution.

3.4 Responsible Person and Nominated Deputies

Each site named on the WDA(H) (and WDA(V) as applicable) shall have a person named as the Responsible Person who has the overall responsibility for ensuring the effectiveness of the Quality Management System to meet the objectives of GDP.

The Responsible Person may delegate his duties, but not his responsibilities, to nominated deputies on site, often referred to as an Authorised Person. For companies with multiple sites, each site shall have an allocated person, from the company or Agent Manager, who shall act as the Responsible Person's Nominated Deputy for that site, refer to Figures 1 and 2.

The Responsible Person's Nominated Deputy is responsible for carrying out the routine audits on site to ensure that the GDP procedures used are in compliance with this procedure and the EU GDP Guidelines (3), as they apply to medical gas products. The Responsible Person's Nominated Deputy may be authorised to approve any corrective actions with the Authorised Person when any non-conformances are identified.

Where a company has multiple Agents sites, the Responsible Person shall ensure that all Agents are overseen by a Nominated Deputy. This Nominated Deputy shall be responsible for ensuring that all Agent employed staff are appropriately trained and carry out routine GDP audits. The Responsible Person shall be responsible for informing the Nominated Deputy about any changes to this procedure and for ensuring that any changes are circulated to the Authorised Person and any additional training conducted.

An Authorised Person should be appointed for each site to manage the delegated day to day activities associated with the storage and distribution of medial gas products. The Responsible Person shall be responsible for approving the Authorised Person, who shall have suitable experience to carry out the tasks and have been trained and assessed in the procedures detailed in this document.

In addition to managing the supply and distribution of medical gases to approved customers, the Authorised Person shall be responsible for notifying the Responsible Person of:

- Any non-conformance identified on site.

- The agreed corrective and preventative actions to address any non-conformances, including the timeframes, when appropriate (whether identified on site or following audits).

- Any changes to the approved storage and distribution facilities on site.

- Any changes to the Nominated Deputy list for the site, to ensure there is always a suitably approved and trained person on site to manage the supply of medical gas products to approved customers.

Each site shall have at least one such Nominated Deputy continuously available to ensure that the requirements of this procedure are met.

The site shall have documented arrangements in place to set up temporary cover by another approved Nominated Deputy, when the permanent Nominated Deputy is absent.

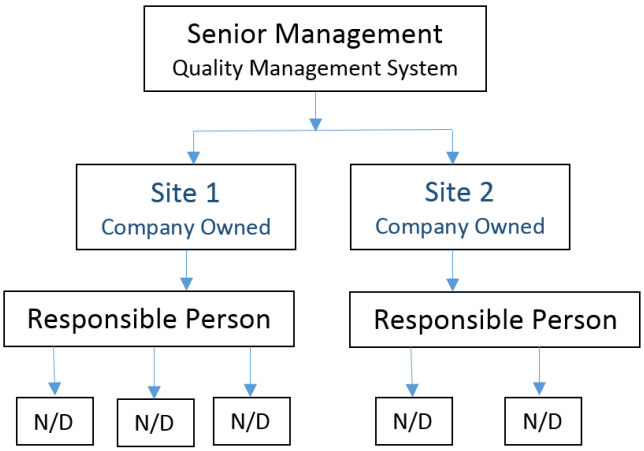

Figure 1: Each site under the responsibility of an individual Responsible Person

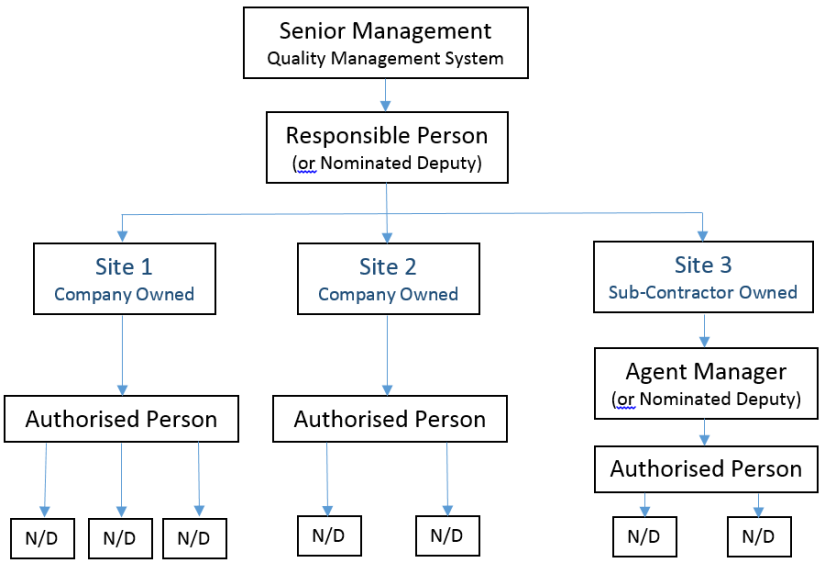

Figure 2: Multiple sites under the responsibility of a single Responsible Person

4. GDP RESPONSIBILITIES

4.1 Responsible Person key responsibilities

The Responsible Person shall be responsible for:

- Ensuring the company's storage and distribution processes is compliant against the requirements of the GDP guidelines.

- Ensuring that the Quality Management System (QMS) for GDP is implemented and maintained.

- Approving the authorisation of the Nominated Deputy named on each site, where required.

- Ensuring that regular self-inspections and audits are conducted, any findings and deficiencies are reviewed, and that any required corrective and preventive actions (CAPA) are completed, documented and reviewed to monitor their effectiveness.

- Coordinating and promptly performing any recall operations for medical gas products.

4.2 Nominated Deputy / Authorised Person key responsibilities

To comply with GDP guidance, the Nominated Deputy on each storage and distribution site is responsible, to the Responsible Person, for ensuring the following (to maintain continuity the following duties can sometimes be delegated to other members of staff, a nominated deputy to the Authorised Person, that are authorised to conduct these duties):

- Only the correct medical gas product/packages are supplied to approved customers.

- Sufficient records are maintained for the distribution and supply of medical gas products to approved customers so as to enable traceability of product in the event of a recall.

- Medical gas products are stored in dedicated storage areas with suitable segregation, refer to Section 6.1 (Premises, segregation and signage).

- Storage facilities are designed to prevent deterioration of the medical gas products so that they are kept in a condition suitable for their defined use, refer to Section 6.2 (Premises, protection).

- Cylinders are supplied on a 'First-Expired First-Out' (FEFO) basis.

- A record is kept of all medical gas products returned under complaint. As necessary, these products are suitably labelled and stored until an investigation is carried out.

- All personnel handling and controlling medical gas products receive the appropriate training.

- All training is recorded.

4.3 Compliance

To make sure that full compliance with GDP is observed, all licensed operated facilities and Agent operated facilities shall comply with the following standards and guidelines:

- Good Distribution Practice Guide - issued by the Regulatory Authority, as interpreted in this document.

- Company stock control procedures.

- Company commercial procedures.

For Agent operated sites, the relevant procedures shall be documented, such as in an Agent Manual.

4.4 Approved customers

There are legal restrictions as to who may purchase medical gas products covered by a Marketing Authorisation, dependant on the legal status of the gas.

Medical gas products shall only be supplied to approved customers holding a company account or directly to patients, where the supply is covered by a prescription.

When setting up a customer account, the company are responsible for obtaining the relevant information from the customers, in order to demonstrate that they meet the regulatory requirements.

Approval shall be given to customers for the specific medical gas products being requested.

A customer account is required even if a new customer requires immediate supply of medical gas products, such as in an emergency situation

For medical gas products collected by customers, the Responsible Person on site (or their Nominated Deputy) shall ensure that medical gas products are only supplied to customers holding a current account that has been approved for the supply of the medical gas product being requested.

Where a customer has a company account that has not previously been supplied with medical gas products, the account shall be approved before any medical gas products are supplied.

Where a customer with a company account has previously been supplied with medical gas products but not the medical gas product being requested, the account shall be approved before any new medical gas products are supplied.

5. PERSONNEL - TRAINING

All personnel involved in the supply of medical gas products to customers shall:

- Be trained in the requirements of GDP and have had their competence assessed.
- Have an on-going training programme to maintain their competence in GDP.

Periodic retraining of all personnel involved in the processes of storing and distributing medical gas products, including the Responsible Person(s), Authorised Person(s) and Nominated Deputy(s), shall be carried out every two years.

All training of personnel shall be recorded and records maintained.

The relevant GDP training of personnel involved in the storage and handling of medical gas products on sites operated by Agents shall be recorded in a suitable local system.

The Authorised Person is responsible for ensuring that any Nominated Deputies are trained, are competent to carry out their specific duties and that their training records are maintained.

The Authorised Person shall be responsible for the retraining of personnel identified by non-conformances raised through the system.

Any new personnel on a site shall be expected to have completed their training and have their training and competence assessment completed before they are allowed to handle medical gas products unsupervised. Once the training is complete, they should be added to the list of Nominated Deputy's for the site.

6. PREMISES

Premises used for the storage and distribution of medical gas products shall be secure and of sufficient capacity to allow for their safe handling and segregation.

The storage arrangements at the facility shall be designed to ensure that the product quality and medical gas product appearance standards are not compromised during storage.

Further information on the storage of gas cylinders is available in BCGA CP 44 (5), *The storage of gas cylinders.*

6.1 Segregation and signage

To prevent supply of the wrong medical gas product or empty medical gas cylinders, medical gas products shall be stored in designated areas that permit adequate segregation between:

- Medical and non-medical.
- Full and empty medical gas cylinders.
- Different medical gas products.

- Quarantine areas; for complaint and incident products and any non-conforming products, including those identified as being outside their supply or expiry date.

All storage areas shall be well defined and the exact requirement for marked areas will depend on the level of activity for the site and the agreed stock levels. In all cases, appropriate signs shall be used to make sure there is no confusion between different product stocks and the status of the medical gas products, refer to BCGA CP 44 (5).

6.2 Protection

Risk Management techniques shall be used when designing the storage areas for medical gases, which will be dependent on the number and sizes of the products being stored, the time that they are likely to be on site and the local environmental conditions.

Storage areas shall comply with BCGA CP 44 (5), and specifically for medical gas cylinders be designed so that:

- Medical gas products are secure and not liable to theft or misuse. Access to the storage area shall be restricted to authorised personnel.

NOTES:

1. To protect medical gas products from theft or tampering, they shall be stored away from site entrances and wherever the public has easy access.
2. Particular care should be taken to keep medical nitrous oxide cylinders secure.

- There is good ventilation throughout the store. This will prevent the accumulation of any gases, should a leak occur.

- There are no sources of excessive heat or ignition.

- Medical gas products are suitably protected to prevent contamination of the product and to maintain the external condition of the medical gas packages so that they remain suitable for their intended use.

NOTE: Where medical gas cylinders are to be used on cylinder manifolds supplying medical gas pipeline systems, there are less risks associated with patient safety than for those medical gas cylinders that are used locally to the patient.

- Product presentation standards can be maintained; this will help keep products clean and prevent the deterioration of product labels.

Medical gas products should be stored under cover so as to maintain them in a clean condition prior to supply to the customer, protected from adverse weather conditions.

Possible design options for the storage facility include:

- A fenced area with a canopy covering the storage area which provides protection to the medical gas products from the elements. Dependant on the prevailing winds, this area may need additional screening.

- A covered ventilated container.

- Covered pallets, for example, wine racks, used for the storage and distribution of medical gas cylinders up to 5 litre water capacity.

- Other approved covered pallets for 10 litre cylinders.

- Tarpaulin type covers designed to be fitted over a standard pallet to protect medical gas products. These tarpaulin covers should be fitted with a transparent screen to permit the contents to be easily identified without removal. For examples refer to Figure 3.

Figure 3: Typical tarpaulin type covers

The method of covered storage used should be appropriate to the scale of the medical gas operation on site. Where medical gas products are stored on site for a relatively short period of time (such as where cylinders are delivered overnight for onward delivery the next day) it is acceptable that they should be stored in the open without any permanent cover, provided they are intended for onward delivery to the customer.

6.3 Pest control

Consideration should be given to whether any form of pest control is necessary where medical gas products are stored, as it is unacceptable that rodents come into contact with the outer surfaces of the medical gas products.

Medical gas product storage areas shall be regularly cleaned and any evidence of pests being within the area noted. If there is evidence of pests in the area, bait boxes should be used as a means of deterrent. However, if there is no evidence of pests, care should be given to the use of bait boxes as they will attract rodents to the area.

7. OPERATIONS

Medical gas products and the information they carry regarding their identity and status shall not be adversely affected by transport and storage activities.

7.1 Receipt of medical gas products

On receipt of full medical gas product on site, a trained designated person shall examine them to make sure that:

- They correspond to delivery documentation.
- They appear clean and in good condition.
- The valve outlet caps / tamper evident seals are fitted correctly and are in good condition; this will ensure the valve outlets are kept clean and dry and are not contaminated.
- They are fitted with a batch label, fitted to the correct location and that the label is legible.
- They are fitted with a gas contents label and, as appropriate, have all the relevant transport and medical information displayed. For information on the labelling of medical gas cylinders refer to BCGA TIS 34 (6), *Medical Gases. Gas cylinder labelling requirements*.

Medical gas products that do not comply with the above requirements shall be suitably labelled, quarantined and returned to the supply site for further investigation.

Where medical gas products have been accepted on site into full stock and subsequently found to be in an unacceptable condition, they shall be treated as a complaint product, refer to Section 8. The product shall have a complaint label attached and the tamper evident seal removed.

7.2 Stock rotation

A stock rotation procedure shall be established to ensure that 'First Expired' products are supplied first (FEFO), with regular checks to check its effectiveness.

Medical gas product stock levels shall be reviewed at least annually to make sure that under normal conditions, products are supplied with an adequate remaining shelf life. Excess stocks shall be returned to the supplying branch or deliveries adjusted to reduce stock levels.

Routine stock checks shall be carried out twice a year and results recorded, confirming reconciliation of the site's medical gas product stocks. Any discrepancies or non-conforming product stored on site shall be documented on the stock check.

All medical gas products should be supplied with an appropriate shelf life remaining before the expiry date.

Medical gas products with less than the approved shelf life remaining shall:

- Have their tamper evident seal removed.
- Be segregated.
- Be returned to the filling branch as an empty.

7.3 Medical gas product supplied

All transactions involving medical gas product shall be recorded in the company commercial system against the approved customer account numbers.

Medical gas products supplied to approved customers shall be checked to ensure:

- They have product labels fitted, which are legible and in good condition.
- They have a batch label fitted, which is legible and in good condition.
- They have a tamper evident seal fitted, which shows no evidence of being tampered with.
- That for cylinders fitted with a permanent contents gauge, the gauge is reading in the 'Full' section.
- They have an appropriate shelf life remaining.
- They are in a clean condition.

It is the responsibility of the product loader/handler to make sure the products either loaded onto the delivery vehicle or supplied to caller customers are in an acceptable condition. Unacceptable products include those where there is evidence that cylinders are leaking.

NOTE: A leak can be identified, for example, by the valve making a noise or by the contents gauge (where fitted) not recording 'Full'.

Any product identified as being in an unsuitable condition shall not be loaded onto the vehicle and is to be placed immediately in the quarantine area and handled as a complaint product, refer to Section 8. The product shall have a complaint label attached and the tamper evident seal removed.

Before supplying any medical gas products to customers, the appropriate documentation shall be completed and the customer's signature obtained, confirming the correct products have been supplied against the order.

7.4 Returned empty medical gas product

Returned empty medical gas products (where the tamper evident seals have been removed) shall be segregated from the full product stock to prevent them being re-distributed to customers.

To minimise site holdings of empty product they shall be returned for refilling as soon as possible.

7.5 Returned full medical gas product

Where full products are returned to the site (which have not been delivered to customers), these may be returned to the full product stock providing that the tamper evident seals are still intact.

All other full medical gas products returned by customers shall not be placed in full product stock, even if their tamper evident seals are still intact. These products shall have their tamper evident seals removed by the person receiving the product from the customer and be placed in the empty product storage area for return to the supply branch.

7.6 Medical gas product belonging to other companies

Any medical gas products, not filled or owned by the company, discovered in the distribution network shall be separated from all other medical gas products. They shall be clearly labelled and arrangements made to return them to their owners. They shall not be supplied to customers.

8. COMPLAINTS AND RECALLS

8.1 Medical gas product returned under complaint

Complaints can be received from the customer, for example when:

- Placing an order for a replacement product.
- Returning a product to a storage site for replacement.
- Exchanging empty products when full products are being delivered.

For complaint product notified to the company when the customer is placing an order, a complaint label shall be attached to the product on collection, making sure that the relevant details have been recorded.

Where a customer returns a complaint product to the storage and distribution site or where a customer identifies a complaint product to the driver, the basic information concerning the complaint, the product barcode and batch number and any other relevant information shall be recorded.

All complaint products shall be labelled with an appropriate complaint label and placed in the quarantine area ready to be returned for investigation.

8.2 Product recalls

In the event of a recall, the MHRA will be informed via the Defective Medicines Report Centre (DMRC) and the specific requirements of the recall will be agreed. Where the recall involves a named storage and distribution site named on the WDA(H) (and WDA(V) as applicable), the Responsible Person will be required to ensure that any necessary actions associated to the recall are completed.

If a product recall is necessary, the recall procedure shall require that a report is produced to detail the location of all affected product requiring recall. The report will identify where medical gas products are being:

- Stored on a storage and distribution site.
- Held by a customer.

If any recalled medical gas products are reported as being on a licensed storage and distribution site, the Responsible Person shall send the relevant details to the Authorised Person on each affected site, who shall identify, label, quarantine and hold on site until follow-up instructions are given by the Responsible Person.

All recalled medical gas product shall be identified by the company and arrangements made to ensure that they are not supplied to customers.

If any recalled medical gas products are held by customers supplied by the storage and distribution site, the company shall contact the customer, request that the cylinders on the customer's site are identified and labelled as recall cylinders and to return them to the site so that they can be quarantined and stored until additional instructions are given.

Under normal circumstances individual sites should not be required to be actively involved in any product recall, other than to check stock on site. However, if the decision is made to collect cylinders from customer's sites, instructions shall be given to label them on collection and return them to site where they shall be quarantined and held on site until follow-up instructions are given by the Responsible Person.

The person responsible for managing the recall action on the site shall maintain all relevant records to allow for the actions being conducted and/or completed during the recall to be assessed and reported.

Recall exercises to test the efficacy of the recall procedure should be carried out. During these recall exercises, the Authorised Person on site shall follow any instructions given, allowing the overall efficacy of the recall procedure to be assessed.

9. SELF-INSPECTION AND AUDIT

Self-inspections and audits shall be conducted at regular intervals on medical gas product storage and distribution sites to verify that the facilities and processes used are in compliance with the requirements detailed in this document and in the EU GDP Guidelines (3).

Self-inspections shall be carried out by approved personnel for each site at the agreed interval, using an approved Self-Inspection Checklist. The Self-inspection Checklist should take account of any corrective and preventative actions that have been agreed to address identified non-conformances.

Independent audits of the site shall be carried out at the agreed frequency.

A schedule shall be maintained for the planned GDP audit dates.

9.1 Site self-inspection

The Authorised Person is responsible for carrying out self-inspections of the site's medical gas product storage and distribution activities. The self-inspections are to be recorded. For Agent operated sites, the self-inspection checklist shall be defined within their documentation. Should any identified non-conformances be identified (with associated corrective and/or preventative actions) the checklist used should be amended to include any additional actions as a means of demonstrating that the actions have been completed within the appropriate time frames.

The self-inspection programme shall be carried out monthly and the results documented and maintained on site for review.

The self-inspection reports shall be reviewed by the appropriate Manager(s) when they are carrying out their independent site audits.

9.2 Audit

The Responsible Person is responsible for agreeing the audit schedule for all medical gas product storage and distribution sites which should be at a frequency of at least once every 18 months.

The auditor shall utilise an audit checklist to ensure that at least the minimum requirements of this procedure are being complied with by every storage and distribution site to ensure that they are operating to the basic principles as defined in the EU GDP Guidelines (3).

Each auditor responsible for carrying out these inspections shall be suitably trained and authorised to carry out the audits.

The auditor shall produce a report and circulate it as a minimum to the Responsible Person, Site Manager, Area Manager and company Quality Manager. Records of the audit shall be retained at the site.

Any non-conformances identified at the audit shall be recorded, along with the proposed corrective and preventative actions. These actions shall be approved by the Responsible Person. Where appropriate, the Authorised Person shall inform the Responsible Person when all actions have been completed.

The Responsible Person will approve whether non-conformance reports may be closed in the Audit Management system or whether it needs to be closed only after the site has been audited, to confirm that the appropriate actions have been taken.

10. REFERENCES

	Document Number	Title
1.	European Directive 2001/83/EC	European 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.
2.	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
3.	European Commission Guideline 2013/C 343/01	European Commission Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use.
4.	EIGA IGC Document 51	The management of change.
5.	BCGA Code of Practice 44	The storage of gas cylinders.
6.	BCGA Technical Information Sheet 34	Medical Gases. Gas cylinder labelling requirements.

Further information can be obtained from:

UK Legislation	www.legislation.gov.uk
European Industrial Gases Association (EIGA)	www.eiga.eu
British Compressed Gases Association (BCGA)	www.bcga.co.uk
Medicines and Healthcare products Regulatory Agency (MHRA)	https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
European Medicines Agency (EMA)	www.ema.europa.eu

British Compressed Gases Association

www.bcga.co.uk