GUIDANCE NOTE 40

MEDICAL GASES
QUALITY MANAGEMENT SYSTEMS
CORRECTIVE AND PREVENTATIVE ACTIONS

2019

British Compressed Gases Association

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ISSN 2398-936X

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 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 160. This document was first published on 01/05/2019. For comments on this document contact the Association via the website www.bcga.co.uk.

CONTENTS

* Throughout this publication the numbers in [ ] brackets refer to references in Section 7. Documents referenced are the edition current at the time of publication, unless otherwise stated.

TERMINOLOGY AND DEFINITIONS

Correction	An action to eliminate a detected non-conformity.
Corrective action	An action to eliminate the cause of a non-conformity and prevent recurrence.
Cylinder	A transportable pressure receptacle of a water capacity not exceeding 150 litres.
May	An option available to the user of this Guidance Note.
Non-conformity	Non-fulfilment of a requirement
Preventive action	An action to eliminate the cause of a potential non-conformity or other potential undesirable situation.
Quality function deployment	Quality Function Deployment (QFD) is a structured approach to defining customer needs or requirements and translating them into specific plans to produce products to meet those needs. The "voice of the customer" is the term to describe these stated and unstated customer needs or requirements.
Shall	Indicates a mandatory requirement for compliance with this Guidance Note and may also indicate a mandatory requirement within UK law.
Should	Indicates the preferred requirement but is not mandatory for compliance with this Guidance Note.

NOTE: Definitions for corrective and preventative actions are in-line with BS EN ISO 9000 [2], *Quality management system. Fundamentals and vocabulary.*

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1. INTRODUCTION

Good distribution practice (GDP) is that part of the overall Quality Management System (QMS) 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 good distribution practice 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 and Change Management.

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

For detailed information on good distribution practice for medical gases refer to BCGA Guidance Note 32 [4], *Medical gases. Good distribution practice.*

Any organisation that wishes to manufacture medical gases is required to comply with the basic principles and practices of Good Manufacturing Practice (GMP). This guidance specifically provides information on corrective and preventative actions for manufacturers of medicinal and medical device gases.

NOTE: In GHTF/SG3/N18: 2010 [3] it states that "*The acronym 'CAPA' will not be used in the document because the concept of corrective action and preventive action has been incorrectly interpreted to assume that a preventive action is required for every corrective action*." This Guidance Note will follow the same policy.

2. SCOPE

Manufacturers of medicinal and medical device gases will comply with the requirements of good distribution practice and, as such, will have a quality management system in place. This document provides guidance on incorporating the principles of corrective and preventative actions into their risk management process.

3. BACKGROUND

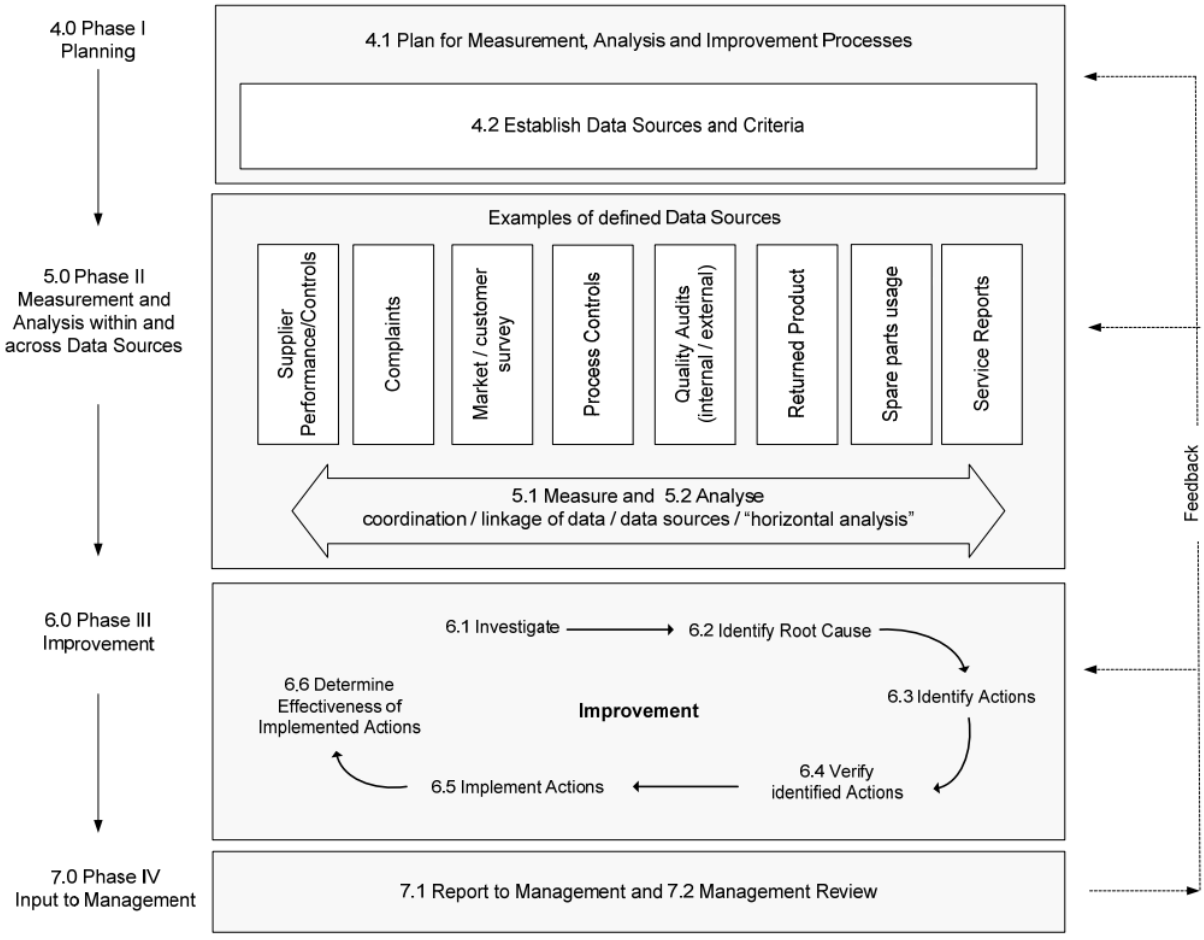
The manufacturer is responsible for the implementation and maintenance of a quality management system which enables their organization to provide safe and effective medicinal and medical device gases which meet customer and regulatory requirements.

A non-conformity is a non-fulfilment of a requirement defined in the quality management system.

When a non-conformity is identified, the manufacturer will determine the significance, the associated risk and the potential for recurrence.

The manufacturer may encounter situations that have not actually caused a non-conformity, but may do so in the future. Such situations may call for preventive action. For example, the identification of potential out of trend results from product analysis.

Figure 1 shows the typical phases that should be considered when planning, implementing and maintaining effective processes for measurement, analysis, improvement and providing input to management.



Source: GHTF/SG3/N18: 2010 (Figure 1) [3]

FIGURE 1: Typical phases for consideration

The manufacturer should maintain documented procedures, requirements and records to ensure and demonstrate the effective planning, operation and control of processes. Records of the evidence of decisions and actions taken should be part of the quality management system.

For further information regarding the planning operation and control, refer to GHTF/SG3/N18: 2010 [3].

4. CORRECTIVE ACTIONS

4.1 Identifying corrective actions

Within the medicinal and medical device gases industry there are three main ways of identifying the need for a corrective action:

- Customer complaints, refer to Section 4.2;
- Audit / self-assessment / inspections, refer to Section 4.3;
- Internal non-conformances raised by personnel, refer to Section 4.4.

4.2 Customer complaints

For medical and medical device gases, these normally relate to:

- Valves (unable to open, leaking, flow rate, etc.);
- Condition of package (painting, labelling, cleanliness, etc.);
- Documentation (certificates, patient information leaflets, etc.);
- Quantity (insufficient pressure);
- Adverse product reactions.

Table 1 suggests the necessary corrective actions.

Complaint issue	Suggestion for corrective action
Valves (unable to open, leaking, flow rate, etc.)	Return cylinder to manufacturer for investigation. If the need for corrective action is identified, then coordinate possible improvements with valve manufacturer.
Condition of package (painting, labelling, cleanliness, etc.)	Return cylinder to manufacturer for investigation. Internal review of work process and controls to identify potential gaps and opportunities for improvement. Any new requirements should be documented and personnel trained.
Documentation (certificates, patient information leaflets, etc.)	If documentation is required, coordinate with the customer to ensure that the necessary information is provided. If there is a systemic issue in providing the correct information, then an appropriate corrective action should be implemented.
Quantity (insufficient pressure)	Return cylinder to manufacturer for investigation. Internal review of work process and controls to identify potential gaps and opportunities for improvement. Any new requirements should be documented and personnel trained.
Adverse product reactions	Follow pharmacovigilance or materiovigilance procedures to identify and contain product that could be impacted. Qualified Person for Pharmacovigilance (QPPV) to coordinate evaluation and requirements for reporting to medical authorities.

TABLE 1: Types of complaints and corrective actions

4.3 Audit / self-assessment / inspection

During internal or external audits, self-assessments or inspections, deficiencies may be identified that require corrective actions to be taken.

Deficiencies that were raised in previous audits, self-assessments or inspections will also be reviewed to ensure that appropriate corrective actions have been taken and are effective. Failure to address a previous concern usually results in the seriousness of the deficiency being raised (for example, minor to major deficiency).

For medical and medical device gases, these normally relate to:

- Documentation;
- Not following procedures / processes;
- Recording of data (for example, non-GMP compliant corrections);
- Competence of personnel.

In selecting appropriate corrective actions, it is important to ensure that the corrective action should address any systemic problems, for example, changing the procedure and training of personnel to the revised procedure may not, by itself, be appropriate or sufficient to address the systemic cause(s).

Table 2 suggests the necessary corrective actions.

Deficiency	Suggestion for corrective action
Documentation found not to be in correct revision.	Issue all areas with correct revision of the document. Review process for document control.
Documentation does not reflect current practice.	Review of the procedure and requirements for the process with the relevant personnel. Identify any differences between current practice and the documented process. Agree and document process using an appropriate management of change system.
Personnel not following correct procedures.	Review the competence of the relevant personnel and, where appropriate, provide additional training or re-assign responsibilities.
Recording of data (non-GMP compliant corrections).	Review the competence of the relevant personnel and, where appropriate, provide additional training or re-assign responsibilities.
Recording of data (wrong values entered).	Review data integrity assessment to determine whether automation of process could be performed. Where appropriate, provide additional training or re-assign responsibilities.
Maintenance and calibration tasks not done.	Review the resources required to perform maintenance and calibration tasks. Escalate to senior management should there be insufficient resources available.
Calibration not performed correctly.	Review potential impact on finished product from the time the calibration error occurred to the detection of the error. Corrective action may involve recall of product and notification to the medical authorities.
Competence of personnel.	Review the requirements for the particular role and insure that the person is provided with the appropriate training/experience.

TABLE 2: Types of deficiencies and suggested corrective actions

4.4 Internal non-conformities raised by personnel

Personnel performing their normal duties may identify defects or deficiencies in products or processes. These deficiencies should be highlighted to their supervisors who may request for this to be recorded as a non-conformity.

Internal non-conformities which are raised are investigated to identify the causes and where appropriate determine corrective actions to prevent recurrence.

For medical and medical device gases, these normally relate to:

- Valves (unable to open, leaking, flow rate, etc.);
- Condition of package (painting, labelling, cleanliness, etc.);
- Documentation (incorrect certificates, failure of certificate system, etc.);
- Quantity (overfill / underfill);
- Failed batches of final product.

5. IDENTIFYING PREVENTIVE ACTIONS

The purpose of a preventive action is to eliminate the cause of a potential non-conformity or other potential undesirable situation. The need for preventive actions for medicinal and medical device gases are often identified through the activities identified in Table 3.

Activity	Description
Identification of out of trend (OOT) results	Purity or component impurities for product may be found to be out of trend in comparison with other manufactured batches. This is often identified during the Quality Control testing of the product or release approval process by the Qualified Person.
Risk assessments	Systematic reviews of potential failures, impact and controls may identify risk and opportunities for improvement.
Product quality reviews	During periodic product quality reviews, trends may be identified that may indicate that there is a potential for failure or an opportunity for improvement.
Scenario planning / testing	These are proactive activities to evaluate the efficiency and effectiveness of the defined processes, for example: • Business continuity planning • Emergency planning and response exercises • Product recall simulation exercises
Design review and Management of Change	Systematic review of the suitability for purpose and risks associated with the initial design or changes to equipment, processes and procedures.
Valve testing	Mechanical and chemical testing (as appropriate) of valve components to ensure suitability for the intended use of the valve.
Continuous improvement projects	Specific improvement projects may use various quality tools to identify opportunities to improve products and processes, for example: • Lean manufacturing • Six sigma • Value stream and process mapping • Design of experiment (DOE) • House of quality (QFD) • Mistake proofing • Benchmarking

TABLE 3: Activities to identify preventive actions

6. CORRECTIVE AND PREVENTIVE ACTION PLAN

In order to communicate and manage the follow-up of corrective actions that prevent recurrence, the actions may be organised within a corrective and preventive action plan. This plan should detail the following:

- Date, location and name of person raising the deficiencies;
- Description of the deficiencies identified;
- Category of deficiencies (e.g., minor, major, critical);
- Description of proposed corrective actions;
- Target date for completion of actions.

Normally, each corrective action would be assigned an action owner who is responsible for the completion and evaluation of the effectiveness of the proposed action.

7. 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.	BS EN ISO 9000	Quality management system. Fundamentals and vocabulary.
3.	GHTF/SG3/N18: 2010	Global Harmonization Task Force (GHTF). Quality management system. Medical devices. Guidance on corrective action and preventive action and related QMS processes.
4.	BCGA Guidance Note 32	Medical gases. Good distribution practice.

Further information can be obtained from:

British Standards Institute (BSI)	www.bsigroup.co.uk
European Medicines Agency (EMA)	www.ema.europa.eu
British Compressed Gases Association (BCGA)	www.bcga.co.uk

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