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1. INTRODUCTION

Although primarily applicable to the pharmaceutical industry, GMP defines good working practices that can be adopted to all of our activities.

Advanex Europe Ltd (AEU) has a quality management system based upon the international standard BS EN ISO9001. This standard is used as guideline for the higher level management of systems. GMP on the other hand is used to directly control and systemise processes and activities. The aim of GMP is to control processes and build quality into a product and / or service

2. SCOPE

This document is not intended to be a concise definition of GMP. It is designed to offer guidelines based on the *Rules and Guidance for Pharmaceutical Manufacturers and Distributors,* to enable the principles of GMP methods of working to be adopted by Advanex Europe Ltd, where practical and applicable.

3. TERMS & DEFINITIONS

GMP (Good Manufacturing Practice) cGMP (Current Good Manufacturing Practice)

"That part of Quality Assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the Marketing Authorisation or product specification".

Quality Assurance:
"The sum total of the organised arrangements made with the object of ensuring that medicinal products are of the quality required for their intended use".

Quality:
"The totality of features and characteristics of a product or service which bear on its ability to meet stated or implied needs".

Rules and Guidance for Pharmaceutical Manufacturers and
Distributors (often referred to as the Orange guide):
The part of the UK Medicines Act (1968) that defines GMP guidelines
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4. GMP REQUIREMENTS

The "Rules and Guidance for Pharmaceutical Manufacturers and Distributors" has nine chapters and annexes. The nine chapters are:

1. Quality Management
2. Personnel
3. Premises and Equipment
4. Documentation
5. Production
6. Quality Control
7. Contract Manufacture and Analysis
8. Complaints and Product Recall
9. Self-Inspection

The key points from each of the chapters, which are particularly relevant to the AEU, are listed below.

4.1 Quality Assurance & System Management

- Senior management is responsible for product quality and safety but the commitment of all staff is vital.
- There must be a comprehensive and effectively implemented documented Quality Assurance system, incorporating Good Manufacturing Practice and Quality Control.
- The system should be fully documented and its effectiveness monitored.

4.2 Personnel

- GMP ultimately depends on people. If a person is not confident in being able to perform a required task competently they must not perform the task and inform their line manager.
- There must be adequate resources provided to enable all parts of the Quality Assurance system to be effective.
  This includes competent personnel, suitable premises, equipment and facilities.
- There must be sufficient qualified / trained personnel to carry out all necessary tasks.
- The responsibilities of individuals should be clearly defined, understood and documented.
- All personnel should receive adequate and continuing training, relevant to the work they perform this should include the principles of cGMP

4.3 Premises and Equipment

- Premises and equipment must be built and maintained to suit the operations being carried out.
- Working areas must be designed to minimise the risk of errors & contamination and promote effective cleaning and maintenance.
- Premises and manufacturing equipment should be suitably maintained and relevant levels of cleaning performed.

- Measuring, weighing, recording and control equipment should be calibrated regularly.
- The entry of unauthorised / untrained people into manufacturing areas should be prevented.
- Defective equipment should be removed if possible or identified as defective if not.
- All chemicals must be approved before use.

4.4 Documentation

- Clear documentation facilitates goods communication, prevents errors and provides essential record keeping.
- Specifications, instructions, procedures and records must be free from errors and available to the person performing applicable operations.
- Documentation should be regularly reviewed and updated where necessary.

- Documents should be authorised for use, be unambiguous, have clear and concise contents, a title and purpose.
- Documents should be regularly reviewed and kept up to date.
- Documents should not be hand-written (except where necessary for the entry of data).
- Records should be completed in indelible ink, pencil must not be used.
- Any alteration of a record should be signed and dated with the original entry still visible.
- Where the reason for an alteration or addition isn't immediately obvious, explanatory notes must be added.
- All manual data entries must be signed and dated.
- Use the **dd/mmm/yy** or **dd/mmm/yyyy** date format
- Documents must be retained for a minimum of seven years

4.5 Production

- Production activities must follow clearly defined instructions and procedures and should only be performed competent people who have received applicable training.
- All materials and products should be stored under the appropriate conditions and in an orderly fashion to permit batch segregation and where required stock rotation.
- All products must be clearly identified at all stages of manufacture.
- Controls must be in place to control the content and quality of labels and other identifiers
- At each stage of processing, products and materials should be protected from contamination.
- No food, drink or medicines should be taken into manufacturing areas
- Any deviation from instructions or procedures should be avoided. However, changes may be approved in writing by a competent, authorised person.
- QA will decide on the level of approval and validation required. This may include customer approval
- Validation studies should be conducted to demonstrate that the process, equipment and/or activity actually leads to the expected results.

- As a minimum, all deviations & changes must be recorded.

4.6 Quality Control

- Quality Control must be involved in all decisions that may concern the quality of the product.
- The independence of Quality Control from Production is considered fundamental to the satisfactory operation of Quality Control.
- Sampling of product should take place in accordance with written procedures.
- Analytical methods should be validated and approved.

4.7 Contract Manufacture & Analysis

- GMP requirements must be considered and communicated as required for all sub-contract operations
- Clarity of customer requirements must be in place. This may take the form of a purchase specification or contractual agreement.
- No deviation from a contractual agreement can be made without approval of the customer.

4.8 Complaints and Product Recall

- A person should be designated as responsible for handling complaints / concerns & recalls.
- All complaints and other information concerning potentially defective products must be recorded.
- All concerns must be reviewed carefully according to written procedures.
- Quality Control should be involved in the analysis of product defects.
- Procedures should be in place to enable the effective recall of product if required
- Recall operations should be capable of being initiated promptly and at any time.

4.9 Self Inspection

- Internal Audits should be conducted in order to monitor and evaluate the effectiveness and compliance of the system including compliance with cGMP.
- Internal Audits should be conducted in an independent and detailed way by designated competent persons.

5 GMP Basics

- **ALWAYS** follow procedures & instructions!
- **DO NOT** carry out a task for which you have not been trained or in which you do not feel competent
- Actions **MUST** be documented!
- Everything documented **MUST** be signed and dated!
- **ALWAYS** use the dd/mmm/yy or dd/mmm/yyyy date format!
- Any changes to paperwork **MUST** not obliterate the original information.
- The reasons for any changes **MUST** be clear or explained!
- Always be on the look out for mistakes, defects and unusual events. Report them immediately.
- **NO** eating, drinking, smoking or personal medication in the manufacturing areas!
- If in doubt **ASK**!
- **EVERYBODY IS RESPONSIBLE FOR GMP**