



Australian Government
Department of Health and Ageing
Therapeutic Goods Administration



MEDICINES MANUFACTURING PRINCIPLES

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Scope

These Manufacturing Principles apply to manufacturers of medicines (including sunscreens and products for use in clinical trials), active pharmaceutical ingredients, blood, tissues, cellular therapies for human use, for which a manufacturing licence is required.

Definitions

For the purposes of these Manufacturing Principles, good manufacturing practice means that part of quality assurance which ensures that products are consistently produced and controlled in accordance with quality standards appropriate to their intended use and as required by the product licence or product specification. In particular, good manufacturing practice relates to quality management, personnel, premises and equipment, documentation, production, quality control, contract manufacture and analysis, complaints and product recall, and self inspection.

Manufacturing Principles

1. Compliance with product licensing (marketing authorisation)

All manufacturing operations for products subject to product licensing, must be carried out in accordance with the information provided in the product licence application and any conditions attached to the product licence.

2. Quality management system

An effective quality management system, involving the active participation of management and personnel, must be established and implemented.

3. Personnel

- 3.1 There must be a sufficient number of competent and appropriately qualified personnel to achieve the quality assurance objective.
- 3.2 The duties of managerial and supervisory staff must be defined in approved job descriptions. Their hierarchical relationships must be defined in an approved organisation chart.
- 3.3 Managerial and supervisory staff must be given sufficient authority to discharge their responsibilities.
- 3.4 Personnel must receive initial and ongoing training, the effectiveness of which must be verified, covering in particular the theory and application of good manufacturing practice.
- 3.5 Hygiene programmes appropriate to the activities carried out must be established and implemented. In particular, these programmes must include procedures relating to health, hygiene practice and clothing of personnel.

4. Premises and equipment

- 4.1 Premises and manufacturing equipment must be located, designed, constructed, adapted and maintained to suit the intended operations.
- 4.2 Premises and manufacturing equipment must be laid out, designed and operated in such a way as to minimise the risk of error, and to permit effective cleaning and maintenance, in order to avoid contamination, cross contamination and any adverse effect on the quality of the product.
- 4.3 Premises and equipment which are critical to the quality of the products must be subjected to appropriate qualification and validation.

5. Documentation

- 5.1 A system of controlled documentation must be established and maintained. This documentation should include specifications, manufacturing formulae and processing and packaging instructions, procedures and records, covering the various manufacturing operations performed.
- 5.2 Documents must be clear, free from error and kept up to date. Pre-established procedures for general manufacturing operations must be available, together with specific documents for the manufacture of each batch. Documentation must enable the history of the manufacture of each batch to be traced.
- 5.3 When electronic, photographic or other data processing systems are used instead of written documents, the system must be validated to verify that the data will be appropriately stored for the required period. Data stored by these systems must be readily available in legible form. Electronically stored data must be protected against loss or damage of data. Audit trails must be maintained.

6. Production

- 6.1 Production operations must be carried out in accordance with pre-established instructions and procedures and in accordance with good manufacturing practice. All process deviations and product defects must be documented and thoroughly investigated.
- 6.2 Appropriate measures must be taken to avoid cross contamination and mix-ups.
- 6.3 Critical manufacturing processes must be validated and regularly re-validated. Changes to manufacturing processes must be controlled. Any new manufacturing process, or major modification of a manufacturing process, must be validated.

7. Quality control

- 7.1 A quality control system under the responsibility of a person who has appropriate qualifications and is independent of production, must be established and maintained. That person must have at his/her disposal, or must have access to, one or more quality control laboratories appropriately staffed and equipped to carry out the examination and testing of starting materials and packaging materials, and the testing of intermediate and

finished products.

- 7.2 During the final control of the finished product before release for supply, the quality control system must take into account, in addition to analytical results, essential information such as the production conditions, the results of in-process controls, the examination of the manufacturing documents and the conformity of the product to its specifications, including the final finished pack.
- 7.3 Release for supply procedures must ensure that product is not released unless it complies with the relevant product licence (marketing authorisation).
- 7.4 Samples of each batch of product must be retained under appropriate storage conditions for at least one year after the expiry date. Samples of starting materials, other than solvents, gases or water, used in the manufacturing process, must be retained for at least two years after the release of the batch of product in which they were used. Other arrangements may be acceptable, by agreement with the ANZTPA, for the sampling and retention of starting materials and certain products manufactured individually or in small quantities, or when their storage could raise special problems.

8. *Work contracted out*

- 8.1 Any manufacturing operation, including testing, which is carried out under contract, must be the subject of a written contract.
- 8.2 The contract must clearly define the responsibilities of each party and must define, in particular, the observance of good manufacturing practice by the contract acceptor and the manner in which the release for supply of each batch will be conducted.
- 8.3 The contract-acceptor must not subcontract any of the work entrusted to him under the contract without written authorisation from the contract-giver.

9. *Complaints and product recall*

The manufacturer must implement a system for recording and reviewing complaints, together with an effective system for recalling, promptly and at any time, medicines in the distribution network. Any complaint concerning a defect must be recorded and investigated by the manufacturer. If appropriate, action must be taken to correct the cause of the complaint or recall, so as to minimise the possibility of recurrence.

10. *Self-inspection*

The manufacturer must conduct regular self-inspections as part of the quality management system in order to monitor the implementation and compliance with good manufacturing practice requirements. Any necessary corrective actions must be taken. Records must be maintained of such self-inspections and any corrective action subsequently taken.

Codes of Good Manufacturing Practice

Unless exempt from manufacturer licensing, therapeutic products manufactured in Australia or New Zealand must be manufactured in accordance with the principles set out above.