CODEX
BEAUTY LABS

Chapter: cGMP Manufacturing

Sections

I. MANUFACTURING AND QUALITY

2.1 INTRODUCTION

All cosmetic products sold on the market are required to be safe for the consumer. A fundamental part of establishing product safety is producing the product(s) according to good manufacturing practices.

Good Manufacturing Practices (GMP, also referred to as "cGMP" or "current Good Manufacturing Practices") ensures that products are consistently produced and have quality standards in line with their intended use and specifications.

GMP defines measures for both production and quality control; it also dictates that general measures for production and testing are clearly defined, validated, reviewed, and documented, and that the personnel, premises and materials are suitable for the production of cosmetics. GMP also has legal components, covering responsibilities for distribution, contract manufacturing and testing, and responses to product defects and complaints.

2.2 QUALITY MANAGEMENT

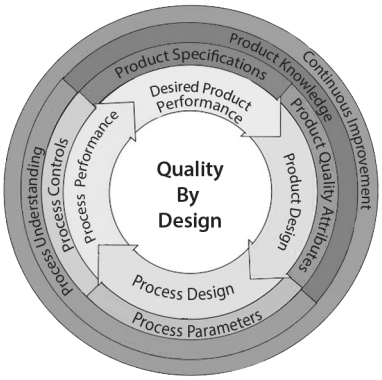
Cosmetic products must be manufactured in such a way as to ensure that they are fit for their intended use and do not place consumers at risk due to inadequate safety or quality. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment by staff at all levels across all departments within the company, and extends to the company's suppliers and distributors. To effectively achieve this quality objective, there must be a comprehensively designed and correctly implemented quality management system (QMS) in place.
Quality management ensures that the manufacture of a cosmetic product is consistent. Quality management for manufacture of cosmetic products consists of current GMP (cGMP) and quality risk management (QRM), which are interdependent practices. cGMPs fulfil the minimum requirements that a cosmetic manufacturer must meet to assure that their products are of high quality and do not pose any risk to the consumer. This is done through the description of production facility (where manufacturing process takes place) that are based on sound scientific judgement and risk assessments. QRM is the identification, assessment and prioritization of risks to the quality of a cosmetic product followed by coordinated and economical application of resources to minimize, monitor, and control the probability and/or impact of compromised quality.
The QMS should be fully documented and its effectiveness monitored. All parts of the system should be adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities.

The inter-relation between quality management, cGMP and QRM is fundamental to the production and control of cosmetic products. cGMP cannot be performed effectively without the application of QRM and a QMS in place. Quality by design embraces an integrated science and risk-based approach with continuous improvement for the entire life-cycle of the product.

GOOD MANUFACTURING PRACTISE (CGMP) AND PRODUCT LIFE-CYCLE

Management Responsibilities	
Quality Management System Elements	• Process performance and product quality monitoring system • Corrective action/preventive action (CAPA) system • Change management system; management review
Enablers	Knowledge Management Quality Risk Management

A QMS appropriate for the manufacture of cosmetic products should ensure that:



(i) Product realization is achieved by designing, planning, implementing, maintaining and continuously improving a system that allows for the consistent delivery of products with appropriate quality standards.

(ii) Cosmetic products are designed and developed in a way that complies with the requirements of cGMP.

(iii) Production and control operations are clearly specified and cGMP adopted and implemented.

(iv) All roles and responsibilities are clearly specified and documented, including managerial staff.

(v) Procedures are in place for the manufacture, supply and use of the correct starting and packaging materials and the selection and monitoring of suppliers.

(vi) Processes are in place to assure the appropriate management of subcontracted activities (including comprehensive technical agreements).

(vii) A state of control is established and maintained by developing and using effective monitoring and control systems for process performance and product quality.

(viii) The results of product and processes monitoring are taken into account in batch release, in the investigation of deviations, and, with a view to taking preventive action to avoid potential deviations occurring in the future.

(ix) All necessary controls on intermediate products, and any other in-process controls and validations are carried out.

(x) Continual improvement is facilitated through the implementation of quality improvements appropriate to the current level of process and product knowledge.

(xi) Arrangements are in place for the prospective evaluation of planned changes and their approval prior to implementation taking into account updates to the product information file, where required.

(xii) After implementation of any change, an evaluation is undertaken to confirm that the quality objectives were achieved and that no unintended deleterious effects impacted product quality.

(xiii) An appropriate level of root cause analysis should be applied during the investigation of deviations, suspected product defects and other problems. This can be determined using QRM principles. In cases where the true root cause(s) of the issue cannot be determined, consideration should be given to identifying the most likely root cause(s) and to addressing those. Where human error is suspected or identified as the cause, this should be justified having taken care to ensure that process, procedural or system-based errors or problems have not been overlooked, if present. Appropriate corrective actions and/or preventative actions (CAPAs) should be identified and taken in response to investigations. The effectiveness of such actions should be monitored and assessed, in line with QRM principles.

(xiv) Satisfactory arrangements exist to ensure, as far as possible, that the cosmetic products are stored, distributed and subsequently handled so that quality is maintained throughout their shelf life.

(xv) There is a process for internal audit, which regularly appraises the effectiveness and applicability of the quality system.

Senior management has the ultimate responsibility to ensure an effective QMS is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organization. Senior management's leadership and active participation in the QMS is essential. This leadership should ensure the support and commitment of staff at all levels and sites within the organization to maintaining the quality system.

There should be periodic management review, with the involvement of senior management, of the operation of the quality system to identify opportunities for continual improvement of products, processes and the system itself.

The quality system should be defined and documented. A quality manual or equivalent documentation should contain a description of the QMS including management responsibilities.

A) GOOD MANUFACTURING PRACTICE (GMP)

GMP is that part of quality management which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use. GMP is concerned with both production and quality control. The basic requirements of GMP are that:

(i) All manufacturing processes are clearly defined, systematically reviewed in light of experience and shown to be capable of consistently manufacturing cosmetic products of the required quality and complying with their specifications.

(ii) Critical steps of manufacturing processes and significant changes to the process are validated.

(iii) All necessary facilities for GMP are provided including (refer to cGMP attributes and corresponding principles below for further details):

a. appropriately qualified and trained personnel
b. adequate premises and space
c. suitable equipment and services
d. correct materials, containers and labels
e. approved procedures and instructions, in accordance with the quality system
f. suitable storage and transport

(iv) Instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided.

(v) Procedures are carried out correctly and operators are trained appropriately in these procedures.

(vi) Records are made, manually and/or by recording instruments, during manufacture, which demonstrate that all the steps required by the defined procedures and instructions were, in fact, taken and that the quantity and quality of the product was as expected.

(vii) Any significant deviations are fully recorded, investigated with the objective of determining the root cause and appropriate corrective and preventive action implemented.

(viii) Records of manufacture, including distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form.

(ix) The distribution of the products minimizes any risk to their quality.

(x) A system is available to recall any batch of product, from sale or supply.

(xi) Complaints about products are examined, the causes of quality defects investigated, and appropriate measures are taken in respect of the defective products and to prevent reoccurrence.

B) QUALITY CONTROL (QC)

Quality control (QC) is that part of GMP that is concerned with sampling, specifications and testing as well as the organization, documentation and release procedures, which ensure that the necessary and relevant tests are carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory. The basic requirements of quality control are that:

(i) Adequate facilities, trained personnel and approved procedures are available for sampling and testing starting materials, packaging materials, intermediate, bulk, and finished products, and, where appropriate, for monitoring environmental conditions for GMP purposes.

(ii) Samples of starting materials, packaging materials, intermediate products, bulk products and finished products are taken by approved personnel and methods.

(iii) Test methods are validated.

(iv) Records are made, manually and/or by recording instruments, which demonstrate that all the required sampling, inspecting and testing procedures were actually carried out. Any deviations are fully recorded and investigated.

(v) The finished products contain ingredients complying with the qualitative and quantitative composition of the product formulation as detailed in the product information file, are of the purity required, and are enclosed within their proper containers and correctly labeled.

(vi) Records are made of the results of inspection, and testing of materials, in intermediate, bulk, and finished products, is formally assessed against specification. Product assessment includes a review and evaluation of relevant production documentation and an assessment of deviations from specified procedures.

Product Stability Evaluation is an extremely important part of the overall product quality and conformity during shelf life. Stability testing is conducted on the dosage form packed in the container closure system proposed for marketing. Stability testing should be designed to take into account conditions expected on respective climatic zones (territories) where the product is anticipated to be marketed. Tests should be done to assure: 1) Stability and physical integrity of the cosmetic product under appropriate conditions of storage, transport and use; 2) Chemical stability; 3) Microbiological stability; 4) Compatibility between the contents and the container. The stability program usually consists of several attributes, which are used together in a synergistic way in order to determine product shelf life and consistency:

1. Microbial Testing: During development of cosmetics, efficacy of antimicrobial preservation must be demonstrated to prevent proliferation of or limit microbial contamination, which could occur during normal storage and usage of the product and create a hazard to the consumer through the product's infection or spoilage. The efficacy of the antimicrobial activity of a formulation is usually demonstrated by challenge testing or preservative efficacy testing (PET).

2. Accelerated stability testing: Accelerated tests, developed because of the relatively short development cycle for cosmetic products, enable the prediction of longer-term stability. A commonly accepted practice is to support the forecasts obtained from accelerated stability testing by carrying out periodic post-launch monitoring of retained samples stored at ambient temperatures. The resultant information can also be useful in further improving the product and in refining the methodology used for accelerated stability testing.

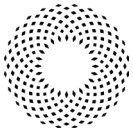
3. Long-term stability program, or real-time studies, are often used to ensure and support the product's defined shelf life.

4. Stress condition (freeze/thaw cycling) testing: As products can be expected to encounter temperature and pressure extremes during transport and storage, stability testing at these extremes should be considered (low-temperature testing, as well as freeze/thaw testing, and high-temperature testing).

5. Photostability: Cosmetics whose packaging may allow the product to be exposed to light should undergo photostability testing. The lighting used in testing should simulate the intensity to which the cosmetic will likely be exposed.

6. Extractables and leachable studies are performed during development when selecting an appropriate packaging material. These studies can be considered important specifically when changing to, or for new development of, novel packaging materials in direct contact with the finished product.

7. Bulk holding stability is studied to understand the consistency of the finished product and suitability of the respective container when stored in-house at the manufacturing site after compounding/mixing, but before entering the filling line. This is important to bring flexibility to the planning of operations and to allow products to be stored for defined amounts of time in the facility warehouse.



The **cGMP attributes and corresponding principles** involved in cosmetic production are as follows:

1. Personnel involved in the implementation of activities described in GMP guidelines should have appropriate training to produce, control, and store products with a defined quality.

2. Premises should be located, designed, constructed and utilized (1) to ensure protection of the product; (2) permit efficient cleaning and sanitizing and maintenance; (3) to minimize the risk of mix-up of products, raw and packaging materials, clean rooms-designed to control the environment from dust, airborne microbes, aerosol particles, and chemical vapors-should be used when small particles can adversely affect the manufacturing process.

3. Utilities: Where applicable, critical utilities like water systems or HVAC (heating, ventilation and air conditioning) systems are treated as raw materials as they need to meet the quality standards in the manufacturing process.

4. Equipment should be suitable for intended purpose and capable of being cleaned and sanitized and maintained.

5. Raw and packaging materials that are purchased should meet defined acceptance criteria relevant to the quality of finished products.

6. Production: At each stage of manufacturing and packaging operations, measurements and data should be taken to produce a finished product that meets the defined characteristics.

7. Finished products should meet the defined acceptance criteria. Storage, shipment and returns should be managed in a manner so as to maintain the quality of finished products.

8. Quality control laboratory is responsible for ensuring that the necessary and relevant controls, within its activity, are carried out for sampling and testing so that materials are released for use and products are released for shipment, only if their quality fulfils the required acceptance criteria.

9. Wastes should be disposed of in a timely and sanitary manner.

10. Subcontracting: A written contract or agreement should be established, mutually confirmed and controlled between the contract giver and the contract acceptor covering subcontracted activities, ultimately with the objective to obtain a product or service that complies with the defined contract giver requirements.

11. Complaints and recalls: All complaints that are communicated to the plant should be reviewed, investigated and followed-up on. When a product recall is made, corrective action must be implemented.

12. Batch deviation: Deviations from the specified requirements (specifications) should be authorized with sufficient data to support any decision made. Corrective actions should be made and documented to prevent recurrence of the deviation.

13. Change control: All changes that could affect the quality of product should be approved and performed by authorized personal. All change controls should be documented.

14. Out-of-specification (OOS) results: OOS results should be reviewed by authorized personal and properly investigated. There should be sufficient justification for any re-testing to be performed. After the investigation, a decision by authorized personal should be made, notably in terms of deviation, rejection or pending.

15. Finished product release: Prior to being placed on the market, all finished products should be controlled in accordance with established test methods and should comply with acceptance criteria. Finished product releases should be carried out by authorized personal responsible for quality.

16. Internal audit is a tool designed to monitor the implementation and the status of these cosmetic Good Manufacturing Practices and propose corrective actions (if necessary).

17. Documentation: Each company should establish, design, install and maintain its own system of documentation. Documentation is an integral part of Good Manufacturing Practices.

18. Regulatory Affairs (RA): Regulatory Affairs have responsibility for (1) ensuring that their companies comply with all of the regulations and laws pertaining to their business;(2) working with federal, state, and local regulatory agencies and personnel on specific issues affecting their business, i.e., working with such agencies as FDA and European agencies; (3) advising their companies on the regulatory aspects and climate that would affect proposed activities.