HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Good Manufacturing Practice of Cosmetic Products

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~~This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.~~

CONTENTS

1 SCOPE

The purpose of this document is to provide guidance to manufacturers regarding the good manufacturing practice (GMP) of cosmetic products, in addition to that outlined in the I.S. EN ISO 22716:2007 (hereafter known as 'the Standard').

GMP requirements clearly outlined in the Standard are not repeated within this guidance document as they are deemed to be self-explanatory and do not need additional clarification. This guide aims to explain in further detail the expectations of the Health Products Regulatory Authority (HPRA) with respect to the legal requirements of the Standard. Manufacturers should therefore ensure that they comply in full with all requirements of the Standard and the additional clarification of the requirements outlined in this HPRA guidance document.

2 INTRODUCTION

Regulation (EC) No. 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ('the Regulation') was transposed into national legislation as European Union (Cosmetic products) Regulation 2013 S.I. No. 440 of 2013 ('the S.I.'). The role of the HPRA, as the competent authority for cosmetic products, is to ensure that all cosmetic products on the Irish market meet the requirements of the cosmetic product legislation and in doing so, do not compromise the health and safety of consumers and any other person using or coming into contact with such products. Article 8 of the Regulation requires the manufacture of cosmetic products to comply with GMP.

The HPRA conducts regular inspections of manufacturers of cosmetic products based in Ireland to ensure compliance with GMP.

It should be noted that for the purposes of GMP inspections, authorised officers of the HPRA have the powers to enter and search any premises where manufacture of a cosmetic product may be taking place. Samples may be taken without payment for analysis and products or documentation may be detained.

3 DEFINITION OF A COSMETIC PRODUCT

A 'cosmetic product' means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, etc.) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours.

4 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, by the company's suppliers and by its 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 GMP and quality risk management (QRM) which are interdependent practices. GMPs 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 or any other person using or coming into contact with such products. This is done through the description of plant activities that are based on sound scientific judgement and risk assessments. QRM is the identification, assessment and prioritisation of risks to the quality of a cosmetic product followed by coordinated and economical application of resources to minimise, monitor, and control the probability and/or impact of compromised quality. The European Medicines Agency published their ICH guideline Q9 on Quality Risk Management which provides principles and examples of tools for quality risk management; it is suggested that this is used as reference material.

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, GMP and QRM is fundamental to the production and control of cosmetic products. GMP cannot be performed effectively without the application of QRM and a QMS in place.

4.1 Quality management system

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

(i) Product realisation is achieved by designing, planning, implementing, maintaining and continuously improving a system that allows 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 GMP.
(iii) Production and control operations are clearly specified and GMP adopted and implemented.

(iv) The facility is designed for easy cleaning, with validated cleaning procedures for removal of residues, implemented documented cleaning schedules, use of appropriate detergents and materials, and ongoing monitoring to prevent contamination.

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

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

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

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

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

~~(xi)~~(xii) 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~~,~~ (PIF), where required.

~~(xii)~~(xiii) After implementation of any change, an evaluation is undertaken to confirm that the quality objectives were achieved and there was no unintended deleterious impact on product quality.

~~(xiii)~~(xiv) 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)~~(xv) 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)~~(xvi) 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 organisation. Senior management's

leadership and active participation in the QMS is essential. This leadership should ensure the support and commitment to the quality system of staff at all levels and sites within the organisation ~~to 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.

4.1.1 Good ~~Manufacturing Practice~~manufacturing practice

Good manufacturing practice (GMP) is ~~that~~the 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:
- appropriately qualified and trained personnel
- adequate premises and space
- suitable equipment and services
- correct materials, containers and labels
- approved procedures and instructions, in accordance with the quality system
- 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~~CAPAs 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 minimises 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 taken in respect of the defective products and to prevent reoccurrence.

4.1.2 Quality control

Quality control is ~~that~~the part of GMP which is concerned with sampling, specifications and testing, and with the organisation, documentation and release procedures which ensure that the necessary and relevant tests are ~~actually~~ 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~~PIF, are of the purity required, and are enclosed within their proper containers and correctly labelled.
(vi) Records are made of the results of inspection and testing of materials, 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.
(vii) Sufficient reference samples of starting materials and products are retained to permit future examination of the product if necessary and the sample is retained in the final pack.

4.1.3 Quality risk management

Quality risk management (QRM) is a systematic process for the assessment, control, communication and review of risks to the quality of the cosmetic product. It can be applied both proactively and retrospectively. The principles of QRM are that:
(i) The evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the consumer.

(ii) The level of effort, formality and documentation of the QRM process is commensurate with the level of risk.

Examples of the processes and applications of quality risk management can be found in ICH Q9 on Quality Risk Management.

(Note: The guidance in this section is taken from Chapter 1 of the 'The Rules Governing Medicinal Products in the European Union, Volume 4, EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use' with appropriate amendments to reflect cosmetic products~~.~~.)

4.2 Personnel

Responsibilities of key personnel including representatives of the ~~Quality Unit~~quality unit should be documented in job descriptions~~.~~ and an organisational chart.

In addition to training on GMP, personnel should receive training in aspects of the company's QMS (e.g. policies, ~~standard operating procedures~~SOPs, etc.) relevant to their particular role and the duties assigned to them. Training should be refreshed regularly and training records should be ~~kept~~maintained.

With respect to personnel hygiene, the requirements should be documented in a procedure under the company's QMS and should include a specific requirement for hands to be washed prior to each entry to the production areas.

Garbing requirements for manufacturing operations including sampling of raw materials/intermediates should be appropriate to avoid contamination of cosmetic products.

4.3 Premises

Manufacturers should consider the design/lay-out and finish of manufacturing, filling and packaging areas with the view to ensuring protection of the product, efficient cleaning and maintenance and minimising the risk of mix up of products, raw materials and packaging materials.

Light fittings in manufacturing areas should be installed in such a manner to ensure containment of any debris from potential breakage.

Ventilation of the premises should be reviewed considering the nature of powder substances and volatile fragrances handled.

Manufacturers should assess and document the environmental conditions required for manufacture and storage of the different products. Monitoring of temperature and/or relative humidity should be conducted if considered important to the quality of the finished product.

A pest control system should be implemented and documented.

4.4 Equipment

Instructions for the operation, calibration, maintenance and cleaning of equipment should be documented in procedures and records under the company's QMS.

Consideration should be given to all equipment used during manufacture (e.g. weighing scales, temperature recorders, mixers, etc.) and requirements for calibration should be assessed and documented.

A risk assessment should be conducted to determine the requirement and frequency for certification of weights used to calibrate balances to national/international standards.

For sampling booths with HEPA filtration units installed, the period of time from switching on the unit to usage for sampling operations should be established and documented. Calibration certificates and records, maintenance records and cleaning records should be maintained.

A risk assessment should be performed with respect to the qualification/temperature monitoring requirements for storage areas, including cold stores, used to store raw materials, intermediates and products.

Cleaning procedures and records should include specific details of cleaning methods for utensils and surfaces including details of cleaning agents used.

4.5 Raw materials and packaging materials

With respect to the evaluation of new suppliers, it is recommended that comparative analysis be conducted on different supplier lots of raw materials using the principles of QRM.

The company should engage with suppliers of key raw materials with the view to obtaining a certificate of analysis for each batch of raw material supplied. These should be included in the ~~product information file~~PIF as described in the HPRA 'Guide to ~~Cosmetic Products~~cosmetic products for ~~Responsible Persons located at~~responsible persons', available on the HPRA website under ~~www.hpra.ie~~Regulatory guidance documents.

Specifications for raw materials (including water) and packaging materials should be documented including defined acceptance criteria relevant to the quality of finished products. Containers/bags of raw materials and packaging materials should be closed and sealed during storage to prevent contamination.

In circumstances where water is used in the manufacture of cosmetic products, consideration should be given to the water quality required and an assessment as to whether the raw town water should be tested on a periodic basis using the principles of QRM.

Appropriate arrangements should be implemented for tracking the usage of raw materials and packaging materials (e.g. stock cards).

Where physical labels are used to identify the status of containers of raw materials, packaging materials, intermediates and finished products, the previous status label on the container(s) should be defaced or alternatively the new status label may be placed over the previous label so that the superseded status is obliterated.

4.6 Production

Detailed instructions for cleaning, checking and approval of production areas should be documented in procedures and records under the company's QMS. Checks for cleanliness of rooms or equipment should be conducted by a second independent person and not by the person who conducted the cleaning operation(s).

Manufacturing operations should be carried out according to manufacturing documentation with detailed instructions regarding equipment to be used, the product formulation, addition of raw materials, temperatures, speeds, mixing times, etc. In process control checks should be documented. The weight requirements for the finished product (if applicable) should also be specified.

Records to confirm critical steps such as actual temperatures reached, heating times, speeds, mixing times, equipment cleaning operations, etc. should be maintained for each batch manufactured.

4.7 Finished products

Specifications for finished products should be documented including defined acceptance criteria relevant to the quality of finished products.

Consideration should be given to the type of outer packaging used with a view to maintaining the quality of the cosmetic product during its shelf life.

Appropriate arrangements should be implemented for tracking the distribution of finished product.

4.8 Quality control laboratory

Testing of materials and finished product should be conducted and documented as appropriate.

Acceptable quality levels (AQLs) for critical, major and minor defects for product inspections should be documented and records of the results of inspections conducted should be maintained.

Procedures and records should be documented and implemented for microbiological testing of cosmetic products (if applicable) including quality control requirements for the culture media used.

Stability testing should be performed on the products in their market packaging to support the release of products to the market with assigned ~~shelf-life/best before~~ period after opening/date~~(s).~~ of minimum durability. The results of this testing should be included in the ~~product information file~~PIF as described in the HPRA 'Guide to ~~Cosmetic Products~~cosmetic products for ~~Responsible Persons found at www.hpra.ie.~~responsible persons', available on the HPRA website under Regulatory guidance documents.

4.9 Treatment of product that is outside of specification

A procedure and records for the handling of product that is out of specification should be documented under the company's QMS and implemented.

4.10 Waste

Procedures and records for the segregation and handling of waste should be documented under the company's QMS and implemented, including the labelling requirements.

4.11 Subcontracting

Systems should be in place to ensure that a subcontractor is not used prior to their review and approval through the QMS.

Technical/quality agreements should be put in place with contract service providers outlining the roles, responsibilities and communication processes with respect to the service(s) provided.

Technical agreements should also be put in place with clients to whom the company provides a contract manufacturing service. These agreements should include the responsibilities of both parties with respect to the manufacturing, packaging, supply and distribution of cosmetic products~~.~~ and overall regulatory compliance roles. In such a scenario, it should be defined which party assumes the role of the responsible person for all cosmetic products for the European market and is therefore responsible for the documentation requirements of the ~~product information file~~PIF.

4.12 Deviations

A procedure and records for the handling of deviations should be documented under the company's QMS and implemented. The procedure should incorporate the principles of QRM and should provide for the identification and implementation of ~~corrective and preventive actions (CAPA),~~CAPAs, as appropriate.

4.13 Complaints and recalls

Procedures and records for complaints, returns and recalls should be documented ~~and implemented~~ under the company's QMS and implemented.

A list of all customers including contact details should be maintained so that, in the event a recall is required, there is full product traceability throughout the supply chain.

4.14 Change control

A procedure and records for change control should be documented under the company's QMS and should incorporate the principles of QRM. Arrangements should be in place for the prospective evaluation of planned changes and their approval, prior to implementation, taking into account updates to the ~~product information file~~PIF, where required. After the implementation of a major change, an evaluation should be undertaken to confirm the quality objectives were achieved and that there was no unintended deleterious impact on product quality.

4.15 Internal audit

A procedure and records for internal audit should be documented under the company's QMS and implemented.

4.16 Documentation

All documents implemented under the company's QMS should be approved, signed and dated by authorised persons before being used.

A procedure and records for QRM should be developed and implemented at the site.

5 FURTHER INFORMATION

For queries relating to cosmetic products, contact the HPRA ~~at the following address:~~via email to cosmetics@hpra.ie or use the 'contact us' form on the HPRA website.

~~Compliance Department~~
~~Health Products Regulatory Authority~~
~~Kevin O'Malley House,~~
~~Earlsfort Centre~~
~~Earlsfort Terrace~~
~~Dublin 2~~

~~Telephone: +353-1-6764971~~
~~Fax: +353-1-6764061~~
~~E-mail: cosmetics@hpra.ie~~