HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

DECEMBER 2022*

PREPARATION OF A SITE MASTER FILE FOR A MANUFACTURER OF COSMETIC PRODUCTS

HSA Health Sciences Authority

*The latest revision is related to the change in contact details and there is no change in technical requirements.

1 WHAT IS A SITE MASTER FILE

A Site Master File (SMF) is a document prepared by the manufacturer containing specific and factual Good Manufacturing Practice (GMP) information about the production and/or control of cosmetic products manufacturing operations carried out at the named site. If any part of a manufacturing operation is carried out on the site, a SMF need only describe those activities, eg packaging etc.

HOW SHOULD A SITE MASTER FILE BE SUBMITTED?

A Site Master File should be concisely written in English and, as far as possible, not exceed 25-30 A4 sheets.

The Site Master File should be a part of documentation belonging to the quality management system of the manufacturer. The Site Master File should have an edition number and an effective date, and preferably be submitted on loose individually numbered A4 sheets. It should be subjected to regular review to ensure that it is up to date and representative of current activities. The sheets should be ring-bound to ensure the integrity of the document. Wherever possible, simple plans, outline drawings or schematic layouts should be used instead of narrative. These plans etc., should fit on A4 sheets of paper. The Site Master File including the appendices should be readable when printed on A4 paper sheets. The format and heading of the site master file should be set out as follows:-

Chapter 1

C.1 GENERAL INFORMATION

REQUIREMENT

C.1.1 Brief information on the site (including name and address), relation to other sites and, particularly, any information relevant to understand the manufacturing operations.

GUIDANCE
(Not more than 250 words or one A4 sheet)

C.1.1 Outline the company's activities, other sites (if any), in addition to the site which is the subject of this report.

REQUIREMENT

C.1.2 Cosmetic product manufacturing activities as licensed by the Competent Authorities.

GUIDANCE

C.1.2.1 Indicate whether the site has been approved by any foreign Competent Authority (name the authority and state if approval granted is for the manufacture of medicinal products of the same or different description from that in the application).

C.1.2.2 Quote the relevant document (licence) as issued by the Competent Authority. State the period of validity of licence document (if the validity of the document is given in the country concerned). Any conditions and/or restrictions should be stated.

REQUIREMENT

C.1.3 Any other manufacturing activities carried out on the site.

GUIDANCE

C.1.3 This covers all other manufacturing activities besides manufacturing of cosmetic products.
NB: See Para. C.1.6

REQUIREMENT

C.1.4 Name and exact address of the site, including telephone, fax and 24-hour telephone numbers.

GUIDANCE

C.1.4.1 Name of Company, Site Address and Mailing Address (if different from site address).

C.1.4.2 Telephone and Fax Nos. of contact person.

C.1.4.3 24-hour contact Telephone No.

REQUIREMENT

C.1.5 Type of products manufactured on the site (see list at Appendix) and information about specifically toxic or hazardous substances handled, mentioning the way they are manufactured (in dedicated facilities or on a campaign basis).

GUIDANCE

C.1.5.1 Quote the type of products manufactured as described at Appendix. Are any toxic, hazardous, highly sensitising substances e.g. antibiotics, hormones, cytostatics manufactured? Are these produced in dedicated facility or on a campaign basis? Specify if the product is manufactured under a contractual agreement with a contract giver

REQUIREMENT

C.1.6 Short description of the site (size, location and immediate environment and other manufacturing activities on the site).

GUIDANCE
(Not more than 250 words or one A4 sheet).

C.1.6.1 Provide a map indicating the location of the manufacturing site and the surrounding area. Mark the site. Describe the surrounding area and use of properties near by.

C.1.6.2 The size of the site, types of buildings and their ages.

REQUIREMENT

C.1.7 Number of employees engaged in quality assurance, production, quality control, storage and distribution.

GUIDANCE
(Note: Include employees working only part-time on full-time equivalent basis. Indicate the academic and non-academic persons)

C.1.7.1 Quality Assurance

C.1.7.2 Production

C.1.7.3 Quality Control

C.1.7.4 Storage & Distribution

C.1.7.5 Technical & Engineering Support Services

C.1.7.6 Total of the above

REQUIREMENT

C.1.8 Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis (if so, see Chapter 7 for details).

GUIDANCE

For each outside contractor (including contract testing laboratories), give:

C.1.8.1 Name, address, telephone no. and fax. no. of contractor.

C.1.8.2 Brief outline of the activity being undertaken in not more than 100 words or half an A4 sheet.

REQUIREMENT

C.1.9 Short description of the quality management system of the company responsible for manufacture.

GUIDANCE
(Not more than 750 words or three A4 sheets).

C.1.9.1 State the company's Quality Policy.

C.1.9.2 Define the responsibility of the Quality Assurance function.

C.1.9.3 Describe the elements of the QA system e.g. organisational structure, responsibilities, procedures, processes.

C.1.9.4 Describe the audit programmes (self-inspection or audits by external organisations undertaken).

C.1.9.5 Describe how results are reviewed to demonstrate the adequacy of the quality system in relation to the objective i.e. quality, efficacy and safety of the product. (see also C.6.1.2)

C.1.9.6 Describe the release for sale procedure for finished products.

Chapter 2

C.2 PERSONNEL

REQUIREMENT

C.2.1 Organisation chart showing the arrangements for quality assurance, including production and quality control.

C.2.2 Qualifications, experience and responsibilities of key personnel.

C.2.3 Outline of arrangements for basic and in-service training and how records are maintained.

C.2.4 Health requirements for personnel engaged in production.

C.2.5 Personnel hygiene requirements, including clothing.

GUIDANCE

(Not more than 500 words of two A4 sheets)

C.2.1 Organogram for quality assurance including production and quality control. Record senior managers and supervisors only.

C.2.2 Brief details of academic qualifications, work-related qualifications and years of relevant experience since qualifying.

C.2.3 Give brief details of the training programme and include induction and continuous training, as follows:

C.2.3.1 Describe how training needs are identified and by whom.

C.2.3.2 Give details of training relative to GMP requirements.

C.2.3.3 State the form of training e.g. in-house, external, and how practical experience is gained and which staff are involved.

C.2.3.4 Explain how the efficacy of the training is assessed e.g. by questionaire.

C.2.3.5 Explain how retraining needs are identified.

C.2.3.6 Give brief details of training records kept.

C.2.4 Health requirements for personnel engaged in production

C.2.4.1 Who is responsible for checking health of employees?

C.2.4.2 Is there a pre-employment medical examination or routine medical examination depending on the nature of their work?

C.2.4.3 Is there a system for reporting sickness or contact with sick people before working in a critical area?

C.2.4.4 Is there a system of reporting back after illness?

C.2.5 *Personnel hygiene requirements including clothing*

C.2.5.1 Are there suitable washing, changing and rest areas?

C.2.5.2 Is the clothing suitable for the activity undertaken? Briefly describe the clothing.

C.2.5.3 Are there clear instructions on how protective clothing should be used and when it should be changed? Detailed procedures are not needed. Is in-house or external laundry used?

Chapter 3

C.3 PREMISES AND EQUIPMENT

REQUIREMENT

Premises

C.3.1 Simple layout plan and description of manufacturing areas with indication of scale (architectural or engineering drawings not required).

C.3.2 Nature of construction and finishes.

C.3.3 Brief description of ventilation systems. More details should be given for critical areas with potential risks of airborne contamination (schematic drawings of the systems are desirable).

C.3.4 Special areas for the handling of highly toxic, hazardous and sensitising materials, if any.

C.3.5 Brief description of water systems (schematic drawings of the systems are desirable) including sanitation.

C.3.6 Maintenance (description of planned preventive maintenance programmes and recording system).

Equipment

C.3.7 Brief description of major production and quality control laboratories equipment (a list of the equipment is NOT required).

C.3.8 Maintenance (description of planned preventive maintenance programmes and recording system).

C.3.9 Calibration, including the recording system.

Sanitation

C.3.10 Availability of written specifications and procedures for cleaning manufacturing areas and equipment.

GUIDANCE

C.3.1 Layout of premises

C.3.1.1 Provide a site layout plan highlighting all production areas, warehouses, laboratories and other functional areas.

C.3.1.2 Provide a simple plan of each production area with indication of scale. Label areas and annotate plan with names.

C.3.1.3 Plans should be legible and on A4 sheets. Plans could be on A3 sheets if considered necessary.

C.3.1.4 If a classified clean area is available, indicate room and area classification and pressure differentials between adjoining areas of different classifications.

C.3.2 Nature of construction and finishes
(500 words or two A4 sheets).

C.3.2.1 To reduce narrative for a large complex plant, the details should be limited to critical areas.

C.3.2.2 These areas must include all processing areas, packaging areas and critical storage areas.

C.3.2.3 A narrative format is preferred.

C.3.3 Brief description of ventilation systems etc.
(500 words or two A4 sheets).

Note: To reduce the narrative, schematic drawings should be used.
The following data should be given:

C.3.3.1 Design criteria e.g.
- *Specification of the air supply*
- *Temperature (if special environmental conditions are necessary)*
- *Humidity (if special environmental conditions are necessary)*
- *Pressure differentials and air change rate, if applicable*
- *Single pass or recirculation (%)*

C.3.3.2 Filter design and efficiency if applicable e.g.
- *Bag 99% efficiency*
- *HEPA 99.997% efficiency*
- *Details of any alarms on the ventilation system should be given.*

C.3.3.3 The limits for changing the filters should be given, if HEPA filters or other equivalents are used.

C.3.3.4 If DOP (dioctylphthalate) is introduced, the point must be shown.

C.3.4 Follow the same layout as C.3.1 above for description of special areas for the handling of highly toxic, hazardous and sensitizing materials.

C.3.5 Brief description of water system, including sanitation (500 words or two A4 sheets).
Note: Schematic drawings of the systems are preferred. The following information must appear:

C.3.5.1 The schematic drawing must go back to the city supply system.

C.3.5.2 The capacity of the system (maximum quantity produced per hour).

C.3.5.3 Construction materials of the vessels and pipework.

C.3.5.4 Specification of any filters in the system must be given.

C.3.5.5 If water is stored and circulated, the temperature at the point of return.

C.3.5.6 The specification of the water produced
a) chemical
b) conductivity
c) microbiological

C.3.5.7 The sampling points and frequency of testing.

C.3.5.8 The procedure and frequency of sanitation.

C.3.6 Maintenance (250 words or one A4 sheet).

Note : For the purpose of this guide "maintenance" is carried out by the manufacturer and "servicing" is by an outside contractor.

C.3.6.1 Describe the planned preventive maintenance programme.

C.3.6.2 Are there written procedures and suitable reporting forms for maintenance and servicing? Do the documents record type/frequency of services/checks, details of service, repairs and modifications?

C.3.6.3 Are the maintenance routines that could affect product quality clearly identified?

C.3.6.4 Are the reports made known to the users?

C.3.7 Brief description of major production and control laboratory equipment

(Not more than 250 words or one A4 sheet)

Note : Makes and model numbers of the equipment are not required. However the following points should be addressed.

C.3.7.1 *Is the machinery constructed of appropriate material (e.g. AISI grade 316 stainless steel for product contact equipment)?*

C.3.7.2 *Have other materials been suitably validated e.g. polypropylene, chrome-plated brass, PVC, non-reactive plastic materials?*

C.3.7.3 *Is the equipment designed with ease of cleaning in mind?*

C.3.7.4 *Only a general description is required. If the equipment has additional devices, these should be recorded e.g. automatic weighing machines with printer, a labeler incorporating a bar code reader for the label; a lot number and expiry date over-printer.*

C.3.7.5 *In the quality control laboratory only general descriptions such as pH meters, chromatographic equipment GLC, HPLC with computer systems, particle size analysers.*

C.3.8 *Maintenance (250 words or one A4 sheet).*

C.3.8.1 *Who is responsible for maintenance and servicing?*

C.3.8.2 *Are there written procedures and contractual details for external contractor?*

C.3.8.3 *Are maintenance routines which could affect product quality clearly identified?*

C.3.8.4 *Are records kept of:*
a) type and frequency of service/check
b) details of service repairs and modifications

C.3.8.5 *Are reports made known to the users?*

C.3.9 *Calibration*

C.3.9.1 *Describe equipment calibration policy and records kept. (See also Para. C.4.2.7)*

C.3.10 *Cleaning procedures for manufacturing areas and equipment (250 words or one A4 sheet).*

C.3.10.1 *Are there written specifications and procedures for cleaning, cleaning agents and their concentration for the method of cleaning and the frequency?*

C.3.10.2 What are the cleaning methods (and their frequency) for the water system, air handling system and dust extraction system (if any)?

Chapter 4

C.4 DOCUMENTATION

REQUIREMENT

C.4.1 Arrangements for the preparation, revision and distribution of necessary documentation for manufacture, including storage of master documents.

GUIDANCE
(500 words or two A4 sheets).

Note : This section refers to all documentation used in manufacture. Manufacture involves all activities relating to the production and control of cosmetic products.

C.4.1.1 Arrangement for the preparation, revision and distribution of documentation

C.4.1.1.1 A brief description of the documentation system.

C.4.1.1.2 Who is responsible for the preparation, revision and distribution of documents?

C.4.1.1.3 Where are the master documents stored?

C.4.1.1.4 Is there a standard format and instruction of how documents are to be prepared?
a) Product/Process Specifications
b) Raw Material Specifications
c) Packaging Component Specifications
d) Standard Process and Packaging Instructions i
e) Batch Manufacturing and Packaging Records
f) Analytical Methods
g) *QA Release Procedures*

C.4.1.1.5 How is the documentation controlled?

C.4.1.1.6 For how long are the documents kept after the release of the batch?

C.4.1.2 Other documentation related to product quality

C.4.2 Are the following documents available and in use?

C.4.2.1 Equipment Specifications

C.4.2.2 Specifications for disposables i.e. cleaning materials

C.4.2.3 Standard Operating Procedures

C.4.2.4 Quality Control Procedures

C.4.2.5 Training Procedures

C.4.2.6 Documentation Control of Process Deviations

C.4.2.7 Calibration and Test Documents (see Para. C.3.9.1)

C.4.2.8 Reconciliation of batches of raw materials and major packaging and printed materials.

C.4.2.9 List and briefly explain the use of any additional standard documentation used routinely.

Chapter 5

C.5 PRODUCTION

REQUIREMENT

C.5.1 Brief description of production operations using, wherever possible, flow sheets and charts specifying important process parameters (see at Appendix the list of products manufactured)

C.5.2 Arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage.

C.5.3 Arrangements for reprocessing or rework.

C.5.4 Arrangements for the handling of rejected materials and products.

GUIDANCE

C.5 Production

Note : This narrative should be kept to a minimum and generalized schematic layouts could be used where possible. The following points should be addressed.

C.5.1 *Describe the operations capable of being carried out at the site with the existing facilities and specify the types of cosmetic products. (See Para 1.5.1 and the Appendix for types of products manufactured).*

When only packaging is undertaken, give a brief description only, e.g. labelling, filling etc. and the nature of containers used e.g. sachets, tamper-proof glass containers.

Describe the production operations using flow charts if possible. Technical details are not required.

Describe how products are identified during production and how in-process storage is organised.

C.5.2 *Arrangements for handling starting materials, packing materials, bulk and finished products including sampling, quarantine, release and storage*

a) Identification of suppliers' lot number with the company's lot number.
b) Sampling plans.
c) Status labelling e.g. using labels or controlled via computer system/software.
d) Issue of materials to manufacture and package.
e) The control of weighing.
f) Checking methods.
g) How are materials being used for manufacture identified and released.

C.5.2.1 *Control of manufacturing:*

a) Checks on key process parameters during manufacture e.g. blend speed and times
b) Records of key process parameters.
c) In-process checks and records.

C.5.2.2 *Packing*

a) Release of bulk, semi-finished products, packing materials.
b) Confirmation of identity and line clearance checks.
c) In-process checks and records.

C.5.2.3 *Quarantine and release of finished products. (see also Para. C.1.9.6)*

C.5.2.4 *Explain the role of the Authorised Person(s).*

C.5.3 Arrangements for Reprocessing or Rework

C.5.3.1 What arrangements are in place for reprocessing or reworking batches of products?

C.5.4 Arrangements for Handling Rejected Materials and Products

C.5.4.1 Are rejected materials and products clearly labelled? Are they stored separately in restricted area?

C.5.4.2 Describe arrangements for sentencing the materials and their disposal. Is destruction recorded?

Chapter 6

C.6 QUALITY CONTROL

REQUIREMENT

C.6.1 Description of the Quality Control system and of the activities of the Quality Control Department. Procedures for the release of finished products.

GUIDANCE

C.6.1 Activities of the Quality Control Department

C.6.1.1 (a) Describe the elements of the QC system e.g. specifications, test methods, and other quality related data collection.

(b) Briefly describe the activities of analytical testing, packaging materials and component testing.

C.6.1.2 If the review of batch documentation and release of final documentation takes place in this department, give details (see Para. C.1.9.5).

C.6.1.3 Outline the involvement in the arrangements for the preparation, revision and distribution of documents in particular those for specification test methods and release criteria, if not mentioned elsewhere (see Chapter 4, Documentation).

Chapter 7

C.7 CONTRACT MANUFACTURE AND ANALYSIS

REQUIREMENT

C.7.1 Description of the way in which the GMP compliance of the contract acceptor is assessed.

GUIDANCE

C.7.1 Describe briefly the details of the technical contract between the contract giver and acceptor and the way in which the GMP compliance, or compliance with other appropriate standards, is assessed to ensure product specifications are complied. The type of products manufactured by the contract acceptor should be specified.

Chapter 8

C.8 DISTRIBUTION, COMPLAINTS AND PRODUCT RECALLS

REQUIREMENT

C.8.1 Arrangements and recording system for distribution.

C.8.2 Arrangements for the handling of complaints and product recalls.

GUIDANCE

C.8.1 A Description of Storage and Distribution Practices

a) Is the warehouse secure?
b) Is there refrigerated storage?
c) How are the materials stored e.g. pallet racking?
d) How is the status of the product controlled e.g. by computer, label?
e) What are the methods of distribution to customers?
f) Does the distribution ensure first in first out (FIFO) or first expire first out (FEFO) and identify the lot number?

C.8.2 Records of Distribution

Does the retained records permit full batch traceability from the factory to the customer in terms of the date of sale, customer details and quantity distributed?

C.8.2.1 Complaints

C.8.2.1.1 Is there a written procedure for product complaints?

C.8.2.1.2 Who is responsible for:
a) Logging;
b) Classifying;
c) Investigating complaints

C.8.2.1.3 Are records prepared and kept?

C.8.2.1.4 Who reviews these records?

C.8.2.1.5 For how long are complaint records kept?

C.8.2.2 Product Recalls.

C.8.2.2.1 Is there a written procedure which describes the sequence of actions to follow including:
(a) Retrieval of distribution data;
(b) Notification of customers;
(c) Receipt/segregation/inspection of returned products;
(d) Investigation/reporting of cause;
(e) Reporting corrective action.

C.8.2.2.2 Who is responsible for coordinating product recalls?

C.8.2.2.3 Who notifies the Competent Authority of complaints and recalls?

C.8.2.2.4 Is the Competent Authority informed of the complaints and the decision to recall?

C.8.2.2.5 Can recalls be effected below wholesale level?

Chapter 9

C.9 SELF INSPECTION

REQUIREMENT

C.9.1 Short description of the self-inspection system (see Para. C.1.9.4).

GUIDANCE

C.9.1.1 Describe how the self-inspection system verifies that those activities that have a bearing on product quality comply with the planned arrangement.

C.9.1.2 Are the quality systems effective?

C.9.1.3 *Are there documented procedures for the self-inspection and for follow-up actions?*

C.9.1.4 *Are the results of the self-inspection documented, brought to the attention of the personnel having responsibility for the area and activities inspected?*

C.9.1.5 *Does the system ensure that those responsible for the area or activity take timely corrective action on the deficiencies found?*

REFERENCE

1. PIC/S PE 008-4 : Explanatory Notes for Pharmaceutical Manufacturers on the Preparation of a Site Master File
2. GUIDE-MQA-016 : Guidance Notes on Good Manufacturing Practice Guidelines For Manufacturers of Cosmetic Products

END OF DOCUMENT

APPENDIX

TYPE OF PRODUCTS MANUFACTURED

(referred to in paragraph C.1.5)

A. Non-sterile products

A.1 Liquid dosage forms

A.2 Semi-solid dosage forms

A.3 Solid dosage forms

A.4 Other dosage forms

B. Packaging only

B.1 Liquid dosage forms

B.2 Semi-solid dosage forms

B.3 Solid dosage forms

B.4 Other dosage forms

C. Contract manufacturing (kind of products)

Company reported upon is:

C.1 Acceptor

C.2 Giver

D. Others
[e.g. veterinary products, pharmaceuticals (please give details of active pharmaceutical ingredients and dosage forms) health/dietary supplements and chemicals, etc)

HEALTH SCIENCES AUTHORITY

Health Products Regulation Group
Blood Services Group
Applied Sciences Group

www.hsa.gov.sg

Contact information

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