الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Guidance for the Preparation of a Site Master File (SMF)

Version 3.1

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Saudi Food & Drug Authority

Drug Sector

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Saudi Food and Drug Authority

Vision and Mission

Vision

To be a leading international science-based regulator to protect and promote public health

Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed

Document Control

Version	Author	Date	Comments
1.0	Inspection department	23/12/2009	Initial draft for internal consultation
2.0	Inspection department	06/01/2010	Published for comments
2.1	Inspection department	31/08/2010	Final
3.0	Inspection department	3/10/2016	This update includes new reference: The reference changed from MHRA to PIC/S
3.1	Executive Directorate of Regulatory Affairs	09 November 2022	Update (This version doesn't include any scientific update)

Contents

1. Introduction

This document gives guidance to product license holders regarding factual information on the site at which their products are manufactured and which are inspected by the Saudi Food and Drug Authority. The Site Master File is prepared by the pharmaceutical manufacturer and should contain specific information about the quality management policies and activities of the site, the production and/or quality control of pharmaceutical manufacturing operations carried out at the named site and any closely integrated operations at adjacent and nearby buildings. If only part of a pharmaceutical operation is carried out on the site, a Site Master File need only describe those operations, e.g. analysis, packaging, etc.

When submitted to the Authority, the Site Master File should provide clear information on the manufacturer's GMP related activities that can be useful in general supervision and in the efficient planning and undertaking of GMP inspections.

A Site Master File should contain adequate information but, as far as possible, not exceed 25-30 pages plus appendices. Simple plans, outline drawings or schematic layouts are preferred instead of narratives. The Site Master File, including appendices, should be readable when printed on A4 paper sheets.

The Site Master File should be a part of documentation belonging to the quality management system of the manufacturer and kept updated accordingly. The Site Master File should have an edition number, the date it becomes effective and the date by which it has to be reviewed. It should be subject to regular review to ensure that it is up-to-date and representative of current activities. Each Appendix can have an individual effective date, allowing for independent updating.

2. Purpose

The aim of these Explanatory Notes is to guide the manufacturer of medicinal products in the preparation of a Site Master File that is useful to the Authority in planning and conducting GMP inspections.

3. Scope

These Explanatory Notes apply to the preparation and content of the Site Master File.

These Explanatory Notes apply for all kind of manufacturing operations such as production, packaging and labelling, testing, relabeling and repackaging of all types of medicinal products.

The outlines of this guide could also be used in the preparation of a Site Master File or corresponding document by Blood and Tissue Establishments and manufacturers of Active Pharmaceutical Ingredients.

4. Content of Site Master File

Refer to Annex for the format to be used.

5. Annex

1. General Information on the Manufacturer:

1.1 Contact information on the manufacturer:

- Name and official address of the manufacturer (For local manufacturers, national address "WASEL" should be provided)
- Names and street addresses of the site, buildings and production units located on the site;
- Contact information of the manufacturer including 24 hrs telephone number of the contact personnel in the case of product defects or recalls;
- Identification number of the site as e.g. GPS details, or any other geographic location system.

1.2 Authorized pharmaceutical manufacturing activities of the site

- Copy of the valid manufacturing authorization issued by the relevant Competent Authority in Appendix 1. If the Competent Authority does not issue manufacturing authorizations, this should be stated;
- Brief description of manufacture, import, export, distribution and other activities as authorized by the relevant Competent Authorities including foreign authorities with authorized dosage forms/activities, respectively; where not covered by the manufacturing authorization;
- Type of products currently manufactured on-site (list in Appendix 2) where not covered by Appendix 1.
- List of GMP inspections of the site within the last 5 years; including dates and name/country of the Competent Authority having performed the inspection. A copy of current GMP certificate (Appendix 3).

1.3 Any other manufacturing activities carried out on the site

- Description of non-pharmaceutical activities on-site, if any.

2. Quality Management System of the Manufacturer

2.1 The quality management system of the manufacturer

- Brief description of the quality management systems run by the company and reference to the standards used;
- Responsibilities related to the maintaining of quality system including senior management;
- Information of activities for which the site is accredited and certified, including dates and contents of accreditations, names of accrediting bodies.

2.2. Release procedure of finished products

- Detailed description of qualification requirements (education and work experience) of the Authorized Person(s) / Responsible Person / Qualified Person(s) responsible for batch certification and releasing procedures;
- General description of batch certification and releasing procedure;
- Role of Authorized Person / Responsible Person / Qualified Person in quarantine and release of finished products and in assessment of compliance with the Marketing Authorization;
- The arrangements between Authorized Persons / Responsible Person / Qualified Persons when several Authorized Persons / Responsible Persons / Qualified Persons are involved;
- Statement on whether the control strategy employs Process Analytical Technology (PAT) and/or Real Time Release or Parametric Release.

2.3 Management of suppliers and contractors

- A brief summary of the establishment/knowledge of supply chain and the external audit program;
- Brief description of the qualification system of contractors, manufacturers of active pharmaceutical ingredients (API) and other critical materials suppliers;

- Measures taken to ensure that products manufactured are compliant with TSE (Transmitting animal spongiform encephalopathy) guidelines.
- Measures adopted where counterfeit/falsified products, bulk products (i.e. unpacked tablets), active pharmaceutical ingredients or excipients are suspected or identified;
- Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;
- List of contract manufacturers and laboratories including the addresses and contact information and flow charts of supply-chains for outsourced manufacturing and Quality Control activities; e.g. sterilization of primary packaging material for aseptic processes, testing of starting raw- materials etc, should be presented in Appendix 4;
- Brief overview of the responsibility sharing between the contract giver and acceptor with respect to compliance with the Marketing Authorization (where not included under 2.2).

2.4 Quality Risk Management (QRM)

- Brief description of QRM methodologies used by the manufacturer;
- Scope and focus of QRM including brief description of any activities which are performed at corporate level, and those which are performed locally. Any application of the QRM system to assess continuity of supply should be mentioned.

2.5 Product Quality Reviews

- Brief description of methodologies used

3. Personnel

- Organization chart showing the arrangements for quality management, production and quality control positions/titles in Appendix 5, including senior management and Authorized Person(s) / Responsible Person(s) / Qualified Person(s);

- Number of employees engaged in the quality management, production, quality control, storage and distribution respectively.
- For local manufacturers, detailed description of qualifications and responsibilities of the Technical Manager.

4. Premises and Equipment

4.1 Premises

- Short description of plant; size of the site and list of buildings. If the production for different markets, i.e. for local, Saudi Arabia, GCC Countries, etc. takes place in different buildings on the site, the buildings should be listed with destined markets identified (if not identified under 1.1);
- Simple plan or description of manufacturing areas with indication of scale (architectural or engineering drawings are not required);
- Lay outs and flow charts of the production areas (in Appendix 6) showing the room classification and pressure differentials between adjoining areas and indicating the production activities (i.e. compounding, filling, storage, packaging, etc.) in the rooms;
- Lay-outs of warehouses and storage areas, with special areas for the storage and handling of highly toxic, hazardous and sensitizing materials indicated, if applicable;
- Brief description of specific storage conditions if applicable, but not indicated on the lay-outs.

4.1.1 Brief description of heating, ventilation and air conditioning (HVAC) systems

- Principles for defining the air supply, temperature, humidity, pressure differentials and air change rates, policy of air recirculation (%)

4.1.2 Brief description of water systems

- Quality references of water produced;
- Schematic drawings of the systems in Appendix 7.

4.1.3. Brief description of other relevant utilities, such as steam, compressed air, nitrogen, etc.

4.2 Equipment

4.2.1 Listing of major production and control laboratory equipment with critical pieces of equipment identified should be provided in Appendix 8.

4.2.2 Cleaning and sanitation

- Brief description of cleaning and sanitation methods of product contact surfaces (i.e. manual cleaning, automatic Clean-in-Place, etc).

4.2.3 GMP critical computerized systems

- Description of GMP critical computerized systems (excluding equipment specific Programmable Logic Controllers (PLCs)).

5. Documentation

- Description of documentation system (i.e. electronic, manual);
- When documents and records are stored or archived off-site (including pharmacovigilance data, when applicable): List of types of documents/records; Name and address of storage site and an estimate of time required retrieving documents from the off-site archive.

6. Production

6.1. Type of products

(References to Appendix 1 or 2 can be made):

- Type of products manufactured including
  - list of dosage forms of both human and veterinary products which are manufactured on the site
  - list of dosage forms of investigational medicinal products (IMP) manufactured for any clinical trials on the site, and when different

from the commercial manufacturing, information of production areas and personnel

- Toxic or hazardous substances handled (e.g. with high pharmacological activity and/or with sensitizing properties);
- Product types manufactured in a dedicated facility or on a campaign basis, if applicable;
- Process Analytical Technology (PAT) applications, if applicable: general statement of the relevant technology, and associated computerized systems.

6.2 Process validation

- Brief description of general policy for process validation;
- Policy for reprocessing or reworking.

6.3 Material management and warehousing

- Arrangements for the handling of starting materials, packaging materials, bulk and finished products including sampling, quarantine, release and storage;
- Arrangements for the handling of rejected materials and products.

7. Quality Control (QC)

- Description of the Quality Control activities carried out on the site in terms of physical, chemical, and microbiological and biological testing.

8. Distribution, Complaints, Product Defects and Recalls

8.1 Distribution (to the part under the responsibility of the manufacturer)

- Types (wholesale license holders, manufacturing license holders, etc) and locations (Saudi Arabia, GCC Countries, etc.) of the companies to which the products are shipped from the site;
- Description of the system used to verify that each customer / recipient is legally entitled to receive medicinal products from the manufacturer;

- Brief description of the system to ensure appropriate environmental conditions during transit, e.g. temperature monitoring/ control;
- Arrangements for product distribution and methods by which product traceability is maintained;
- Measures taken to prevent manufacturers' products to fall in the illegal supply chain.

8.2 Complaints, product defects and recalls

- Brief description of the system for handling complains, product defects and recalls.

9. Self-Inspections

- Short description of the self- inspection system with focus on criteria used for selection of the areas to be covered during planned inspections, practical arrangements and follow-up activities.

Appendix 1	Copy of valid manufacturing authorization
Appendix 2	List of dosage forms manufactured including the INN-names or common name (as available) of active pharmaceutical ingredients (API) used
Appendix 3	Copy of valid GMP Certificate
Appendix 4	List of contract manufacturers and laboratories including the Addresses and contact information, and flow-charts of the supply-chains for these outsourced activities
Appendix 5	Organizational charts
Appendix 6	Lay outs of production areas including material and personnel flows, general flow charts of manufacturing processes of each product type (dosage form)
Appendix 7	Schematic drawings of water systems
Appendix 8	List of major production and laboratory equipment

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6. Reference

- Explanatory Notes For Pharmaceutical Manufacturers on The Preparation of A Site Master File, Pharmaceutical Inspection Convention Pharmaceutical Inspection Co-Operation Schem (PIC/S), 2011.