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## GUIDELINES FOR PREPARATION OF SITE MASTER FILE

This document has been prepared as a guide to assist applicants to comply with the requirements for Site Master Files with regard to all sites for pharmaceutical business. SAHPRA is committed to ensure that all sites where medicines are manufactured, stored or tested are of good standard and that all premises where pharmaceutical business is conducted comply with statutory requirements. Applicants must ensure that all administrative requirements are adhered to.

### Document History

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## Glossary

Abbreviation/ Term	Meaning
SMF	Site Master File
GMP	Good Manufacturing Practice

## 1. INTRODUCTION

The Site Master File is prepared by the manufacturer and or wholesaler and contains specific information about the quality assurance, the production and/or quality control of pharmaceutical manufacturing operations and or wholesaling 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 a regulatory authority, the Site Master File provides information on the manufacturer's operations or the wholesaler's operations and procedures that can be useful in the efficient planning and undertaking of a GMP or GWP inspection.

These guidance notes have been set out in such a manner that each chapter and the paragraphs noted under "REQUIREMENT" is followed by "GUIDANCE" to provide details of how the requirements should be interpreted.

The Site Master File should have an edition number and an effective date. The Site Master file must be updated when a major constructional upgrade takes place or when key activities and or key personnel, changes. In addition, an updated Site Master File must be submitted to the office of the Chief Executive Officer (CEO) every five years.

### 1.1 Purpose

The purpose of this guideline is to guide the manufacturer or wholesaler of medicinal products in the preparation of a Site Master File that can be useful to the regulatory authority in planning and conducting GMP or GWP inspections.

### 1.2 Scope

The scope of this document applies to the preparation of the Site Master File. Refer to national regulatory requirements to establish whether it is mandatory for manufacturers or wholesalers of medicinal products to prepare a Site Master File.

## 2. LEGAL PROVISION

This guideline was prepared with reference to Medicines and Related Substances Act, 1965 (Act 101 of 1965).

## 3. PREPARATION OF SITE MASTER FILE

### C.1. GENERAL INFORMATION

#### REQUIREMENT

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

#### *C.1.1. GUIDANCE*

*C.1.1. In not more than 250 words (one A4 page) outline the firm's activities, other sites, in addition to the site which is the subject of this report*

#### REQUIREMENT

**C.1.2. Pharmaceutical manufacturing or wholesaling activities as licensed or approved by the Competent Authorities.***GUIDANCE*

*C.1.2. Quote the relevant document as issued by the Competent Authority. State 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 or wholesaling activities carried out on the site.***GUIDANCE*

*C.1.3. This covers both pharmaceutical and non-pharmaceutical activities. NB: See para-C.1.6*

**REQUIREMENT****C.1.4. Name and exact address of the site, including telephone, fax and 24 hrs telephone numbers.***GUIDANCE**C.1.4. Name and Address of Site*

*C.1.4.1. Name of Company (and trading style if different). Postal Address including. Code (street address if different).*

*C.1.4.2. Telephone No. of contact person.*

*C.1.4.3. Fax No. of contact person.*

*C.1.4.4. hour contact Telephone No.*

**REQUIREMENT**

**C.1.5. Type of actual products manufactured on the site (see list at Appendix A), or list of products wholesaled on site (as the case may be) and information about specifically toxic or hazardous substances handled, mentioning the way they are manufactured (in dedicated facilities or on a campaign basis) or in the case of a wholesaler (any special precautions taken for storage or distribution).**

*GUIDANCE*

*C.1.5. Type of Actual Products Manufactured or Wholesaled as the case may be*

*C.1.5.1. Quote the type of actual products as described at Appendix A, below.*

*C.1.5.2. Note any toxic or hazardous substances handled e.g., antibiotics, hormones, cytostatic. Note whether the products are manufactured in a dedicated facility or on a campaign basis or in the case of a wholesaler, any special precautions taken during the storage or distribution of the products...*

C.1.5.3. *In the case of a manufacturer, mention if human and veterinary products are both prepared on the site.*

#### **REQUIREMENT**

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

#### *GUIDANCE*

*C.1.6. A Short Description of the Site (not more than 250 words/one A4 page)*

*C.1.6.1. The location and immediate environment.*

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

*C.1.6.3. Other manufacturing activities on the site.*

#### **REQUIREMENT**

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

#### *GUIDANCE*

*C.1.7. (Note: Include employees working only part-time on full-time equivalent basis. Give the rate of 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 and 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; and in the case of a wholesaler any outside scientific, analytical, or other technical assistance relating to any wholesaling activities if applicable.**

#### *GUIDANCE*

*C.1.8. For each outside contractor give:*

*C.1.8.1. Name and address of the company. C.1.8... Telephone No.*

C.1.8.3. Fax No.

C.1.8.4. Brief outline of the activity being undertaken in not more than 100 words (half an A4 page).

## REQUIREMENT

**C.1.9. Short description of the quality management system of the firm responsible for manufacture or wholesaling.**

### GUIDANCE

C.1.9. (Not more than 750 words or three A4 pages)

C.1.9.1. State the firm'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 programs (self-inspection or audits by external organisations undertaken).

C.1.9.5. Describe how the 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 paragraph 6.1.2

C.1.9.6. Record if standards such as ISO 9001-9004 are used by the company to assess its suppliers.

C.1.9.7. When suppliers of critical starting materials and packing materials - actives, excipients, containers and closures and printed materials are assessed, give details of how this is done.

C.1.9.8. Describe the release for sale procedure for finished products.

## C.2. PERSONNEL

### REQUIREMENT

**C.2.1. Organisation chart showing the arrangements for quality assurance, including production and quality control in the case of a manufacturer. In the case of a wholesaler organisation chart showing the arrangements for quality assurance. (See also C.1.9.3)**

**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 or wholesaling.**

**C.2.5. Personnel hygiene requirements, including clothing.**

### GUIDANCE

C.2.1 PERSONNEL (500 words/two A4 pages)

### C.2.1.1. Organisation chart

*C.2.1.1.1 Organogram for quality assurance including production and quality control. In the case of a wholesaler, an organisation chart showing the arrangements for quality assurance. Record senior managers and supervisors only.*

### C.2.2. Qualifications, Experience and Responsibilities of Key Personnel.

*C.2.2.1. Brief details of academic qualifications and work-related qualifications and years relevant experience since qualifying.*

*C.2.3. Outline of Arrangements for Basic and In-service Training and how Records are maintained 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 or GWP 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 questionnaires.*

*C.2.3.5. Explain how retraining needs are identified.*

*C.2.3.6. Give brief details of records kept.*

*C.2.4. Health Requirements for Personnel Engaged in Production in the case of a manufacturer or picking and packaging in the case of a wholesaler*

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

*C.2.4.2. Is there a pre-employment medical examination?*

*C.2.4.3. Are employees routinely checked from time to time depending on nature of their work?*

*C.2.4.4. Is there a system for reporting sickness or contact with sick people before working in a critical area?*

*C.2.4.5. Is there a system of reporting back after illness?*

*C.2.4.6. Are those who work in clean areas (grade A-D) subject to additional monitoring?*

### 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 if required? Detailed procedures are not needed. Is in house or external laundry used?*

## **C.3. PREMISES AND EQUIPMENT**

### **REQUIREMENT**



- C.3.1. Simple plan or description of manufacturing or wholesaling areas with indication of scale (architectural or engineering drawings are 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). Classification of the rooms used for manufacture of sterile products should be mentioned.**
- C.3.4. Special areas for the handling of highly toxic, hazardous, and sensitising materials.**
- C.3.5. Brief description of water systems (schematic drawings of the systems are desirable) including sanitation if applicable.**
- C.3.6. Maintenance (description of planned preventive maintenance programmes and recording system).**
- C.3.7. Equipment**
- C.3.7. In the case of a manufacturer, a brief description of major production and control laboratories equipment (a list of equipment is not required).**
- C.3.8. In the case of a manufacturer and wholesaler details on maintenance (description of planned preventative maintenance programmes and recording system).**
- C.3.9. In the case of a manufacturer and wholesaler, details on qualification and calibration, including recording system. Arrangements for computerized systems validation.**
- C.3.10. Sanitation**
- C.3.11. Availability of written specifications and procedures for cleaning manufacturing or wholesaling areas and equipment.**

#### *GUIDANCE*

##### C.3.1. Premises

*C.3.1.1. Provide a site plan highlighting production or wholesaling areas.*

*C.3.1.2. Provide a simple plan of each production area or wholesaling area (as the case may be) with indication of scale. Label areas and annotate plan with names.*

*C.3. 1..3. Plans should be legible and on A4 sheets of paper. Plans could be on A3 sheets of paper if considered necessary.*

*C.3.1.4. In the case of manufacturing of sterile products, the sterile areas indicating the room and area classification and pressure differentials between adjoining areas of different classifications.*

##### C.3.2. Nature of Construction and Finishes (500 words/two A4 pages)

*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 and packaging and critical storage areas.*

*C.3.2.3. A narrative format is preferred.*

##### C.3.3. Brief Description of Ventilation Systems etc. (500 words/two A4 pages)

*Note 1: More details should be given for critical areas with potential risks of airborne contamination. This will include sterile product areas as well as areas for processing powders, granulation and tableting. For sterile product areas a summary of the results of the most recent qualification/requalification should be given.*

*For wholesaling activities, the ventilation system applicable to wholesaling activities should be described. Note 2: 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*

*Pressure differentials and air change rate*

*Simple pass or recirculation (%)*

*Temperature*

*Humidity*

*C.3.3.2. Filter design and efficiency e.g.*

*Bag 99% eff.*

*Hepa 99,997% eff.*

*Details of any alarms on the ventilation system should be given.*

*C.3.3.3. The limits for changing the filters should be given.*

*C.3.3.4. If DOP (dioctyl-phthalate) is introduced, the point must be shown.*

*C.3.3.5. Give the frequency of revalidation of the system.*

*C.3.4. Special Areas for the Handling of Highly Toxic Hazardous and Sensitising Materials*

*C.3.4.1. Follow the same layout as 3.1 above.*

*C.3.5. Brief Description of Water Systems, including sanitation (500 words / two A4 pages) Note: For wholesaling activities this section may be omitted.*

*Schematic drawings of the systems are preferred. The following information must appear:*

*C.3.5.1. The schematic 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, what is the temperature at the point of return.*

*C.3.5.6. The specification of the water produced;*

*chemical*

*conductivity*

*microbiological*

*The sampling points and frequency testing. The procedure and frequency for sanitation.*

C.3.6. Maintenance (250 words/one A4 page)

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

*C.3.6.1. Describe the planned preventative 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 Equipment (250 words/one A4 page)

*Brief Description of Major Production and Control Laboratory Equipment. Note: For wholesaling activities this section may be omitted.*

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

*C.3.7.1. Is the equipment designed with ease of cleaning in mind?*

*C.3.7.2. Only a general description is required e.g., a rotary tablet press etc. If the equipment has additional devices, these should be recorded e.g., automatic weighing machines with printer; a labeller incorporating a bar code reader for the label; a lot number and expiry date over printer; a freeze drier equipped with a steam sterilisation facility.*

*C.3.7.3. In the quality control laboratory only general descriptions such as pH meters, chromatographic equipment GLC (gas-liquid chromatography), HPLC (high performance liquid chromatography) with computer systems, particle size analysers.*

*C.3.7.4. Is the machinery constructed of appropriate material (e.g., AISI\* grade 316 stainless steel for product contact equipment?)*

*C.3.7.5. Have other materials been suitably validated e.g., polypropylene, chrome-plated brass, PVC (poly vinyl chloride), non-reactive plastic materials?*

*C.3.7.6. In microbiology use general descriptions such as incubators (temperature ranges) facilities for LAL (limulus amoebocyte lysate) testing, membrane filtration sterility testing, antibiotic assay, etc.*

*C.3.7.7. In particular give brief information on the use of computers, microprocessors etc. in the factory.*

C.3.8. Maintenance (250 words/one A4 page)

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

*C.3.8.2. Are there written procedures and contractual details for outside work?*

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

C.3.8.4. Are records kept of: type and frequency of service/check details of service repairs and modifications?

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

C.3.9. Qualification, validation, and Calibration (750 words/three A4 pages)

C.3.9.1. Briefly describe the Company's general policy and protocols for qualification and validation (prospective and retrospective).

C.3.9.2. Is there regular revalidation of critical equipment?

C.3.9.3. Describe equipment calibration policy and records kept.

C.3.9.4. An outline of process validation may be given here or cross-referenced to production para 5.4

C.3.9.5. What are the arrangements for computer validation, including software validation?

C.3.9.6. Describe the system for the release for sale or supply of development and validation batches.

C.3.10. Sanitation

*Cleaning procedures for manufacturing areas and equipment and cleaning procedures for wholesaling area in the case of a wholesaler (250 words/one A4 page)*

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. Are cleaning agents changed from time to time?

C.3.10.3. Have the cleaning procedures been validated and what was the method of evaluating the effectiveness of cleaning?

C.3.10.4. Are cleaning methods monitored routinely by chemical and/or microbiological methods?

C.3.10.5. What are the cleaning methods (and their frequency) for the water supply system, air handling system and dust extraction system?

**C.4. DOCUMENTATION**

**REQUIREMENT**

**C.4.1. Arrangements for the preparation, revision, and distribution of necessary documentation for manufacture or wholesale.**

**C.4.2. Any other documentation related to product quality which is not mentioned elsewhere (e.g., microbiological controls on air and water, etc.).**

**GUIDANCE**

**C.4.DOCUMENTATION (500 words/two A-4 pages)**

*Note: This section refers to all documentation used in manufacture or wholesale. Manufacture involves all activities relating to the production and control of pharmaceutical products with wholesale involving all activities relating to wholesaling and distribution.*

C.4.1. Arrangements for the Preparation, Revision and Distribution of Documentation

C.4.1.1. Is there a description of the documentation system?

C.4.1.2. Who is responsible for the preparation revision and distribution of documents?

C.4.1.3. Where are the master documents stored?

C.4.1.4. Is there a standard format and instruction of how documents are to be prepared? Are there documents for in the case of a manufacturer:

C.4.1.4.1. Product/process specification

C.4.1.4.2. Raw material specifications

C.4.1.4.3. Packaging component specifications

C.4.1.4.4. Standard process instructions including packaging

C.4.1.4.5. Batch records including packaging

C.4.1.4.6. Product/Process Specifications

C.4.1.4.7. Analytical methods

C.4.1.4.8. QA release procedures.

C.4.1.5. Are there documents for in the case of a wholesaler:

C.4.1.5.1. Receiving, dispatch and oversight of narcotic and psychotropic substances by the Pharmacist

C.4.1.5.2. Oversight of all wholesaling activities by the Responsible Pharmacist

C.4.1.5.3. Receiving, Picking, Packaging and Distribution of orders

C.4.1.5.4. Verification of the validity of clients in terms of the provisions of Section 22A of the Medicines and Related Substances Act, 1965

C.4.1.5.5. Quarantine of products following a notice of a recall from a Pharmaceutical company/applicant.

C.4.1.6. How is the documentation controlled?

C.4.1.7. For how long are documents kept after release of the batch?

C.4.1.8. Detail any arrangements for electronic or microfilmed records.

C.4.2. Other Documentation related to Product Quality Are the following documents available and in use?

C.4.2.1. Specifications for disposables i.e., cleaning materials.

C.4.2.2. Standard operating procedures.

C.4.2.3. Equipment specifications.

C.4.2.4. Quality Control Procedures.

C.4.2.5. Training procedures.

C.4.2.6. Computer program specifications.

C.4.2.7. *Documentation control of process deviations.*

C.4.2.8. *Calibration and test documents (see para 3.9.5)*

C.4.2.9. *Validation documents (see paras 3.9 and 5.4)*

C.4.2.10. *Reconciliation of batches of raw materials, major packing components i.e., product-contact, and printed materials.*

C.4.2.11. *List and briefly explain the use of any additional standard documentation used routinely.*

## **C.5. PRODUCTION OR WHOLESALING**

### **REQUIREMENT**

**C.5.1. Brief description of production operations or wholesaling activities using, wherever possible, flow sheets and charts specifying important parameters (see Appendix A for the list of products manufactured or wholesaled).**

**C.5.2. Arrangements for the handling of starting materials, packaging materials, bulk, and finished products, including sampling quarantine, release, and storage applicable to manufacturing or wholesaling.**

**C.5.3. Arrangements for reprocessing or rework.**

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

**C.5.5. In the case of a manufacturer a brief description of the general policy for process validation.**

### **GUIDANCE.**

*C.5. PRODUCTION OR WHOLESALING as the case may be*

*This narrative should be kept to a minimum and generalized schematic layouts 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 pharmaceutical products. (See para 1.5.1 and the Appendix A for types of products manufactured/wholesaled).*

*When only primary or secondary packaging, as in the case of a manufacturer, is undertaken, give a brief description e.g., labelling, filling etc., and the nature of containers used e.g., sachets, tamper evident glass containers.*

*If cytotoxic or radio-active substances are handled give details of the products.*

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

*In the case of manufacturing, describe how products are identified during production and how in-process storage is organized.*

*C.5.2. Arrangements for handling Starting Materials, Packing Materials, Bulk and Finished Products including Sampling Quarantine Release and Storage when applicable to manufacturing or wholesaling*

*Identification of suppliers' lot number with the company's lot number. Status labelling e.g., by using labels or by computer. Issue of materials to manufacture and package. The control of weighing, sampling plans, how are materials being used for manufacture identified and released? Information on checking methods?*

#### *C.5.2.1. Control of Bulk Manufacture*

*Checks on key parameters during manufacture e.g., blend times, filter integrity tests. Records of key parameters.*

*Records of in-process checks.*

*Compliance with the Marketing Authorisation. In-process checks.*

#### *C.5.2.2. Packing*

*Release of bulk, semi-finished products, packing materials; confirmation of identity and line clearance checks; in-process checks.*

*C.5.2.3. Quarantine and release of finished products; compliance with the Marketing Authorisation.*

*C.5.2.4. Explain the role of the Responsible pharmacist(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 Reject Materials and Products*

*C.5.4.1. Are reject materials and products clearly labelled? Are they stored separately in restricted areas?*

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

*C.5.5. Brief Description of the General Policy for Process Validation (note only applicable to Manufacturers)*

*An outline of process validation protocol only is required. (See para 3.9.3)*

### **C.6. QUALITY CONTROL (Note: Only applicable to Manufacturers)**

#### **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, component testing, biological and microbiological testing.*

*C.6.1.2. If the review of batch documentation and release of final documentation takes place in this department, give details. (See also para 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 also para 1.9 and Documentation)*

## **C.7. CONTRACT MANUFACTURE AND ANALYSIS (Note: Only applicable to Manufacturers)**

### **REQUIREMENT**

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

#### *GUIDANCE*

### **C.7. CONTRACT MANUFACTURE AND ANALYSIS**

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 is assessed to ensure product compliance with the Marketing Authorization*

## **C.8. DISTRIBUTION, COMPLAINTS AND PRODUCT RECALL**

### **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 DISTRIBUTION**

#### *C.8.1.1 A Description of Storage and Distribution Practices*

C.8.1.1.1 *Is the warehouse secure?*

C.8.1.1.2. *Is it environmentally controlled?*

C.8.1.1.3. *Is there refrigerated storage?*

C.8.1.1.4. *How are the materials stored e.g., pallet racking?*

C.8.1.1.5. *How is the status of products controlled e.g., by computer, by label?*

C.8.1.1.6. *What are the methods of distribution to customers?*

C.8.1.1.7. *Does the dispatch order ensure first in/first out and identify the lot number?*

#### *C.8.1.2. Records of Distribution*

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

### **C.8.2. Complaints**

C.8.2.1. *Is there a written complaints procedure?*

C.8.2.2 *Who is responsible for:*



*C.8.2.2.1 Logging**C.8.2.2.2 Classifying**C.8.2.3 Investigating complaints.**C.8.2.3.1. Are written reports prepared?**C.8.2.3.2 Who reviews these reports?**C.8.2.3.4 For how long are complaints records kept?**C.8.3 Product Recalls**C.8.3.1. Is there a written procedure which describes the sequence of actions to be followed including;**C.8.3.1.1. Retrieval of distribution data**C.8.3.1.2. Notification of customers**C.8.3.1.3. Receipt/segregation/inspection of returned product**C.8.3.1.4. Investigation/reporting of cause**C.8.3.1.5. Reporting corrective action.**C.8.3.2. Who is responsible for coordinating product recalls?**C.8.3.3. Who notifies the Competent Authority of complaints and recalls?**C.8.3.4. Is the Competent Authority involved in complaints and the decision to recall?**C.8.3.5. Can recalls be effected below wholesale level?***C.9. SELF INSPECTION****REQUIREMENT****C.9.1. Short description of the self-inspection system See also para 1.9.4.).***GUIDANCE**C.9.1.1. Describe how the self-inspection system verifies that those activities that have a bearing on 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 system and for the follow-up actions?**C.9.1.4. Are the results of the self-inspection system 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?*

## 4. REFERENCES

The following related documents are referenced:

- 4.1 Circular 34/93
- 4.2 PIC/S guide

## 5. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the guidelines for Preparation of Site Master File, old document number 4.08. It will be reviewed on this timeframe or as and when required.

## 6. APPENDICES

### 6.1 Appendix A: Type of Products Manufactured or Wholesaled (referred to in paragraph C.1.5)

#### A. Sterile products

##### A.1 Liquid dosage forms (large volume solutions, including LVP and rinsing solutions)

A.1.1 Aseptically prepared

A.1.2 Terminally sterilized A.2

##### A.2. Liquid dosage forms (small volume solutions, including SVP and eye drops)

A.2.1 Aseptically prepared

A.2.2 Terminally sterilized

##### A.3 Semi-solid dosage forms A4 Solid dosage form

A.4.1 Solid fill

A.4.2 Freeze-dried

#### B. Non-sterile products

##### B.1 Liquid dosage forms

##### B.2. Semi-solid dosage forms

##### B.3. Solid dosage forms

##### B.4. Unit dose form (tablet, capsules, suppositories, pessaries)

##### B.5 Multi dose form (powder, granules) C. Biological products

##### C.1. Vaccines C.

##### C.2 Sera C.

##### C.3 Blood products

##### C.4 Others (describe)

#### D. Specifically, toxic, and hazardous substances

##### D.1 Penicillin's

D.2 Cephalosporins

D.3. Hormones

D.4. Cytostatic

D.5. Others (describe)

E. Primary and or Secondary Packaging only

E.1 Liquid dosage forms

E.2 Semi-solid dosage forms

E.2 Solid dosage forms

F. Contract manufacturing (kind of products)

F.1. Firm reported upon is:

F.2. Contract Acceptor.

F.3. Contract Giver G. Contract analysis

Firm reported upon is:

F.1. Contract Acceptor

F.2. Contract Giver

H. Drugs for clinical trials

I. Others

(e.g., veterinary products, cosmetics, etc.)