World Health Organization

Working document QAS/10.378
July 2010
RESTRICTED

WHO GUIDELINES FOR DRAFTING A SITE MASTER FILE

DRAFT FOR COMMENTS

The Prequalification Programme currently uses a site master file (SMF). Your feedback would be very much appreciated as to whether this SMF needs to be revised in light of new developments, e.g. by the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

Please address any comments on this proposal, by 1 September 2010 to Dr A.J. van Zyl, Head of Inspections, Prequalification Programme, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or e-mail: vanzyla@who.int with a copy to gaspardm@who.int and to bonnyw@who.int.

During the past few years we have moved more towards an electronic system for sending out our working documents for comment, for convenience and in order to speed up the process. If you do not already receive our documents electronically, please let us have your e-mail address (to bonnyw@who.int) and we will add it to our electronic mailing list.

SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/10.378:
Guidelines for drafting a site master file

Need for possible revision identified by WHO Prequalification Programme	May 2010
Draft mailed out for comments	July-August 2010
Collation of comments received	September 2010
Presentation to the WHO Expert Committee on Specifications for Pharmaceutical Preparations	18-22 October 2010
Further action as necessary	…

GUIDELINES FOR DRAFTING A SITE MASTER FILE (SMF)

A site master file (SMF) for each manufacturing site of a finished pharmaceutical product (FPP) listed in a product dossier, should be submitted on a CD or DVD to the Inspection unit.

A SMF for each manufacturing site of active pharmaceutical ingredient (API) and contract research organization (CRO), listed in a product dossier, should be submitted on request from the Inspection unit.

A SMF should be succinct and, as far as possible, not exceed 25 A4 pages.

A SMF is a document prepared by the manufacturer containing specific and factual good manufacturing practice (GMP) information about the production and/or 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, the SMF need describe only those operations, e.g. analysis, packaging.

Layout of the SMF

Front page
Table of contents

Contents

1. General information

1.1 Brief information on the firm (including name and address), relation to other sites, and, in particular, any information relevant to understanding the manufacturing operations.

1.2 Pharmaceutical manufacturing activities as licensed by the national authority.

1.3 Any other manufacturing activities carried out on the site.

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

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

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

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

1.8 Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis.

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

2. Personnel

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

2.2 Qualifications, experience and responsibilities of key personnel.

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

2.4 Health requirements for personnel engaged in production.

2.5 Personnel hygiene requirements, including clothing.

3. Premises and equipment

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

3.2 Nature of construction and finishes.

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 the manufacture of sterile products should be mentioned.

3.4 Special areas for the handling of highly toxic, hazardous, and sensitizing materials.

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

3.6 Description of planned preventive maintenance programmes for premises and of the recording system. Equipment

3.7 Brief description of major equipment used in production and control laboratories (a list of equipment is not required).

3.8 Description of planned preventive maintenance programmes for equipment and of the recording system.

3.9 Qualification and calibration, including the recording system. Arrangements for computerized systems validation. Sanitation

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

4. Documentation

4.1 Arrangements for the preparation, revision, and distribution of necessary documentation for manufacture.

4.2 Any other documentation related to product quality that is not mentioned elsewhere (e.g. microbiological controls on air and water).

5. Production

5.1 Brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters.

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

5.3 Arrangements for the handling of rejected materials and products.

5.4 Brief description of general policy for process validation.

6. Quality control

6.1 Description of the quality control system and of the activities of the quality control department. Procedures for the release of finished products.

7. Contract manufacture and analysis

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

8. Distribution, complaints and product recall

8.1 Arrangements and recording system for distribution.

8.2 Arrangements for the handling of complaints and product recalls.

9. Self-inspection

9.1 Short description of the self-inspection system.

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