152011 PIC-S 工厂主文件指南

制药工厂现场主文件编写说明

PIC/S January 2011

TABLE OF CONTENTS 目录

MANUFACTURERS ON THE

1 DOCUMENT HISTORY 文件历史

2 INTRODUCTION 简介

2.1 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.

现场主文件是由制药厂家编写，并包含以下信息：质量管理方针及现

场活动、在对在指定现场进行生产或/和对在指定现场的制药生产操作进行的质量控制以及在临近及附近建筑内进行的一体化操作。如果仅有一部份制药操作在该现场进行，那么 SMF 仅需描叙该类操作即可，如：分析、包装、等。 2.2 When submitted to a regulatory 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. 提交至监管机构时，SMF 需提供明确信息，说明厂家进行的有助于一般监管和 GMP 审查有效计划和应对的相关 GMP 活动

2.3 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.

SMF 应包含足够的信息，但是加上附件不得超过 25-30 页。相较于详述，简单性计划、简略的原理图布局图为首选。SMF，包括附件，用 A4 纸打印出来应当可读。

2.4 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.

SMF 厂家质量管理系统文件的一部分，应进行相应更新。SMF 应当有一个版本号、生效日期以及需进行审核的日期。应对 SMF 进行定期审核以保证其为最新版本并体现最新行动。每个附件可有单独的生效日期，允许单独对附件进行更新。

3 PURPOSE 目的

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 regulatory authority in planning and conducting GMP inspections.

本说明的目的是指导医药生产厂家进行 SMF 的编写。SMF 在监管机构进行 GMP 审查计划和执行 GMP 审查中是有用的。

4 SCOPE 适用范围

These Explanatory Notes apply to the preparation and content of the Site Master File. Manufacturers should refer to regional / national regulatory requirements to establish whether it is mandatory for manufacturers of medicinal products to prepare a Site Master File.

本说明使用与 SMF 的编写及内容。厂家应参考地区 / 国家法规要求以确定是否强制要求医药用品厂家编写 SMF。

These Explanatory Notes apply for all kind of manufacturing operations such as production, packaging and labelling, testing, relabelling 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.

本说明适用于下述此类生产操作：所有类型医药产品的生产、包装和贴标、检验、再贴标和再包装。本指南的大纲也可以用于编写 SMF 或 API 血液和组织制造机构以及生产厂家相关文件的编写。

5 CONTENT OF SITE MASTER FILE ＳＭＦ内容

Refer to Annex for the format to be used.

SMF 格式见附件。

6 REVISION HISTORY 修订历史

Annex to PE 0084

CONTENT OF SITE MASTER FILE 现场主文件内容

1 GENERAL INFORMATION ON THE MANUFACTURER 工厂一般信息

1.1 Contact information on the manufacturer 生产商联系信息

— Name and official address of the manufacturer;

— 生产商名称和办公地址；

— Names and street addresses of the site, buildings and production units located on the site;

— 厂址名称和街道地址、厂内建筑和生产单元的名称；

— Contact information of the manufacturer including 24 hrs telephone number of the contact personnel in the case of product defects or recalls;

— 生产商联系信息，包括产品缺陷或召回时联系人的 24 小时电话号码；

— Identification number of the site as e.g. GPS details, DUNS (Data Universal Numbering System) Number (a unique identification number provided by Dun & Bradstreet) of the site or any other geographic location system.

— 工厂识别信息，如全球定位信息（GPS 信息）或其他的地理定位系统，以及邓氏编号。

1.2 Authorised pharmaceutical manufacturing activities of the site. 授权的药物生产活动

— Copy of the valid manufacturing authorisation issued by the relevant Competent - Authority in Appendix 1; or when applicable,

reference to the EudraGMP database. If the Competent Authority does not issue manufacturing authorisations, this should be stated; — 在附件 1 中，附上相关主管当局颁发的有效生产许可证的复件；或者可能的话，引用欧洲 GMP 数据库；如果主管当局不颁发生产许可证，这应该加以说明。

— Brief description of manufacture, import, export, distribution and other activities as authorised by the relevant Competent Authorities including foreign authorities with authorised dosage forms/activities, respectively; where not covered by the manufacturing authorisation; — 药政机构许可的生产、进口、出口、分销和其他活动的简要描述，包括生产许可证上没有的国外当局许可的剂型/活动；

— Type of products currently manufactured onsite (list in Appendix 2) where not covered by Appendix 1 or the EudraGMP database;

— 目前在厂生产的产品类型（在附件 2 中列出），如果未被包含在附件 1 中或欧洲 GMP 准入中

— 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) or reference to the EudraGMP database should be included, if available.

— 列出过去 5 年的现场 GMP 检查清单，包括日期和进行检验的药政机构的名称/国家。如果有，应当提供现行的 GMP 证书（附件 3）或引用欧洲 GMP 数据库中的副本。

1.3 Any other manufacturing activities carried out on the site 厂区内进行的任何其他生产活动

— Description of nonpharmaceutical activities onsite, if any.

— 如果有的话，描述厂区内的非制药活动。

2 QUALITY MANAGEMENT SYSTEM OF THE MANUFACTURER 公司的质量管理体系

2.1 The quality management system of the manufacturer 公司质量管理体系

— Brief description of the quality management systems run by the company and reference to the standards used;

— 公司质量管理运行系统的简要说明和所参考的标准;

— Responsibilities related to the maintaining of quality system including senior management;

— 包括高级管理层在内的质量体系维护职责;

— Information of activities for which the site is accredited and certified, including datas and content of accreditations, name of accrediting bodies.

— 公司认证的活动信息，包括日期和认证内容，认证机构名称。

2.2 Release procedure of finished products 最终产品放行程序

— Detailed description of qualification requirements (education and work experience) of the Authorised Person(s) / Qualified Person(s) responsible for batch certification and releasing procedures;

— 负责批量证明和放行程序的授权人/有资质人（简称：QP）的资格要求（教育/工作经验）的详细说明;

— General description of batch certification and releasing procedure;

— 批合格和放行过程的一般描述;

— Role of Authorised Person / Qualified Person in quarantine

and release of finished products and in assessment of compliance with the Marketing Authorisation;

— 授权人/有资质人（简称：QP）在待验、放行最终产品、上市授权符合性评估中的角色。 — The arrangements between Authorised Persons / Qualified Persons when several Authorised Persons / Qualified Persons are involved;

— 涉及到多个授权人/有资质人时，他们之间的安排

— Statement on whether the control strategy employs Process Analytical Technology (PAT) and/or Real Time Release or Parametric Release.

— 采用 PAT（过程分析技术）控制策略和/或实时放行或参数放行的描述

2.3 Management of suppliers and contractors 承包商和供应商的管理

— A brief summary of the establishment/knowledge of supply chain and the external audit program;

— 供应链和外部审计程序建立和信息的一个简要介绍;

— Brief description of the qualification system of contractors, manufacturers of active pharmaceutical ingredients (API) and other critical materials suppliers;

— 简要说明承包商、活性药物成分（API 供应商）和其他关键材料供应商的资格审查系统； — Measures taken to ensure that products manufactured are compliant with TSE (Transmitting animal spongiform encephalopathy) guidelines.

— 采取的措施，以确保生产出的产品符合 TSE（动物海绵状脑病传染）指南

— Measures adopted where counterfeit/falsified products, bulk

products (i.e. unpacked tablets), active pharmaceutical ingredients or excipients are suspected or identified;

— 假冒/伪造产品，散装产品（即拆开的片剂），药物活性成分或辅料的怀疑或确定方法 — Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;

— 外部研究、分析或其他有关生产的技术支援;

— List of contract manufacturers and laboratories including the addresses and contact information and flow charts of supplychains for outsourced manufacturing and Quality Control activities; e.g. sterilisation of primary packaging material for aseptic processes, testing of starting rawmaterials etc, should be presented in Appendix 4;

— 合同生产商和实验室的名单，包括地址和联系方式，以及外包生产和质量控制活动的供应链流程图。如无菌工艺的内包装材料灭菌，起始物料的检测，应显示附件 4

— Brief overview of the responsibility sharing between the contract giver and acceptor with respect to compliance with the Marketing Authorisation (where not included under 2.2).

— 上市授权符合性中，合同双方责任划分（如果未在 2.2 项下描述）的简要概述。

2.4 Quality Risk Management (QRM) 生产商质量风险管理（QRM）

— Brief description of QRM methodologies used by the manufacturer;

— 生产商 QRM 方针的简要描述

— 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.

— QRM 的范围和关注点的详细描述，包括全体公司层所有活动和仅在局部执行活动的简要描述。任何采用 QRM 体系对供应连续性进行的评估，都应当被讨论。

2.5 Product Quality Reviews 产品质量回顾

— Brief description of methodologies used

— 方法的简要描述

3 PERSONNEL 人员

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

— 显示质量管理、生产和质量控制安排以及职位/职称的图表附于附件 5，包括高级管理人员和 QP 的安排;

— - Number of employees engaged in the quality management, production, quality control, storage and distribution respectively.

— 参与质量管理、生产、质量控制、储存和发放的各自员工数目;

4 PREMISES AND EQUIPMENT 厂房和设施

4.1 Premises 厂房

— Short description of plant; size of the site and list of buildings. If the production for different markets, i.e. for local, EU, USA, etc. takes place in different buildings on the site, the buildings should be listed with destined markets identified (if not identified under 1.1);

— 厂房的简单描述：场地大小和建筑清单。如果不同市场的产品，如本地、欧盟、美国等地，在不同的建筑中生产，清单中应在建筑上列出目标市场（如果未在 1.1 中描述）；

— Simple plan or description of manufacturing areas with indication of scale (architectural or engineering drawings are not required);

— 示意图或生产区的简单描述，要指出生产规模（不要求建筑或工程图纸）；

— 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;

— 应在附件 6 提供生产区域的布局图和流程图。图上应当显示房间级别，相邻区域之间的压差，并指出房间内进行的生产活动即混合、填料、储存、包装等。

— Layouts of warehouses and storage areas, with special areas for the storage and handling of highly toxic, hazardous and sensitising materials indicated, if applicable;

— 仓库和储存区域的示意图和高毒高危害高敏感物料储存和处理区域的描述，如果适用。 — Brief description of specific storage conditions if applicable, but not indicated on the layouts.

— 特定储存条件（如果适用）的简要描述，不需要在示意图中指出。

4.1.1 Brief description of heating, ventilation and air conditioning (HVAC) systems 供暖，通风和空调（HVAC）系统的简要描述

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

— 系统设计标准，例如，空气供应、温度、湿度、压差和换气次数、空气循环方法（%）；

4.1.2 Brief description of water systems 水系统的简要描述

— - Quality references of water produced;

— 产水的质量标准

— - Schematic drawings of the systems in Appendix 7.

— 水系统的示意图附于附件 7

4.1.3 Brief description of other relevant utilities, such as steam, compressed air, N2, etc. 其他相关单元的简要描述，如蒸汽，压缩空气，氮气等。

4.2 Equipment 设备

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

在附件 8 中列出生产和实验室控制设备中已确定的关键设备

4.2.2 Cleaning and sanitation 清洁和卫生

— Brief description of cleaning and sanitation methods of product contact surfaces (i.e. manual cleaning, automatic CleaninPlace, etc).

— 产品接触表面的清洁和卫生方法的简要描述（即人工清洗，自动清洁等）。

4.2.3 GMP critical computerised systems GMP 的关键电脑系统

— Description of GMP critical computerised systems (excluding equipment specific Programmable Logic Controllers (PLCs)). GMP 关键电脑系统的描述（不包括特定设备的可编程逻辑控制器 PLC）

5 DOCUMENTATION 文件

— Description of documentation system (i.e. electronic, manual);

— 公司文件体系的描述

— When documents and records are stored or archived offsite (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 offsite archive.

— 文件和记录在厂外存储或归档（包括药物警戒的数据，如果适用）：文件/记录的类型列表，存储地点的名称和地址以及异地存档时检索取回文件所需时间的评估。

6 PRODUCTION 生产

6.1 Type of products 产品类型

(references to Appendix 1 or 2 can be made 可参考附件 1 或 2):

— Type of products manufactured including

— 生产的产品类型包括

n list of dosage forms of both human and veterinary products which are manufactured on the site;

n 工厂生产的人用和兽用产品的剂型的列表

n 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;

n 临床试验用的研究性新药（IMP）的剂型列表，如果不同于商业生

产工艺，要给出生产区域和人员信息

— Toxic or hazardous substances handled (e.g. with high pharmacological activity and/or with sensitising properties);

— 有毒有害物质处理（如，高药物活性或致敏物质）

— Product types manufactured in a dedicated facility or on a campaign basis, if applicable;

— 在专用车间生产的产品剂型，如果适用

— Process Analytical Technology (PAT) applications, if applicable: general statement of the relevant technology, and associated computerised systems.

— 过程分析技术（简称：PAT）的应用，如果适用：相关计算机系统和相关技术的简要描述。

6.2 Process validation 工艺验证

— Brief description of general policy for process validation;

— 工艺验证方法的简要描述。如适用，连续的验证方法；

— Policy for reprocessing or reworking.

— 返工或再加工的方法

6.3 Material management and warehousing 物料管理和仓储

— Arrangements for the handling of starting materials, packaging materials, bulk and f inished products including sampling, quarantine, release and storage;

— 起始物料、包装材料、原料药和成品的处置管理，包括取样、待验、放行和储存。

SMF 应包含足够的信息，但是加上附件不得超过 25-30 页。相较于详

述，简单性计划、简略的原理图布局图为首选。SMF，包括附件，用 A4 纸打印出来应当可读。

2.4 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.

SMF 厂家质量管理系统文件的一部分，应进行相应更新。SMF 应当有一个版本号、生效日期以及需进行审核的日期。应对 SMF 进行定期审核以保证其为最新版本并体现最新行动。每个附件可有单独的生效日期，允许单独对附件进行更新。

3 PURPOSE 目的

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 regulatory authority in planning and conducting GMP inspections.

本说明的目的是指导医药生产厂家进行 SMF 的编写。SMF 在监管机构进行 GMP 审查计划和执行 GMP 审查中是有用的。

4 SCOPE 适用范围

These Explanatory Notes apply to the preparation and content of the Site Master File. Manufacturers should refer to regional / national regulatory requirements to establish whether it is mandatory for manufacturers of medicinal products to prepare a Site Master File.

本说明使用与 SMF 的编写及内容。厂家应参考地区 / 国家法规要求以确定是否强制要求医药用品厂家编写 SMF。

These Explanatory Notes apply for all kind of manufacturing operations such as production, packaging and labelling, testing, relabelling 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.

本说明适用于下述此类生产操作：所有类型医药产品的生产、包装和贴标、检验、再贴标和再包装。本指南的大纲也可以用于编写 SMF 或 API 血液和组织制造机构以及生产厂家相关文件的编写。

5 CONTENT OF SITE MASTER FILE ＳＭＦ内容

Refer to Annex for the format to be used.

SMF 格式见附件。

6 REVISION HISTORY 修订历史

Annex to PE 0084

CONTENT OF SITE MASTER FILE

现场主文件内容

1 GENERAL INFORMATION ON THE MANUFACTURER 工厂一般信息

1.1 Contact information on the manufacturer 生产商联系信息

— Name and official address of the manufacturer;

— 生产商名称和办公地址；

— Names and street addresses of the site, buildings and production units located on the site;

— 厂址名称和街道地址、厂内建筑和生产单元的名称；

— Contact information of the manufacturer including 24 hrs telephone number of the contact personnel in the case of product defects or recalls;

— 生产商联系信息，包括产品缺陷或召回时联系人的 24 小时电话号码；

— Identification number of the site as e.g. GPS details, DUNS (Data Universal Numbering System) Number (a unique identification number provided by Dun & Bradstreet) of the site or any other geographic location system.

— 工厂识别信息，如全球定位信息（GPS 信息）或其他的地理定位系统，以及邓氏编号。

1.2 Authorised pharmaceutical manufacturing activities of the site. 授权的药物生产活动

— Copy of the valid manufacturing authorisation issued by the relevant Competent - Authority in Appendix 1; or when applicable, reference to the EudraGMP database. If the Competent Authority does not issue manufacturing authorisations, this should be stated;

— 在附件 1 中，附上相关主管当局颁发的有效生产许可证的复件；或者可能的话，引用欧洲 GMP 数据库；如果主管当局不颁发生产许可证，这应该加以说明。

— Brief description of manufacture, import, export, distribution and other activities as authorised by the relevant Competent Authorities including foreign authorities with authorised dosage forms/activities, respectively; where not covered by the manufacturing authorisation;

— 药政机构许可的生产、进口、出口、分销和其他活动的简要描述，包括生产许可证上没有的国外当局许可的剂型/活动；

— Type of products currently manufactured onsite (list in

Appendix 2) where not covered by Appendix 1 or the EudraGMP database;

— 目前在厂生产的产品类型（在附件 2 中列出），如果未被包含在附件 1 中或欧洲 GMP 准入中

— 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) or reference to the EudraGMP database should be included, if available.

— 列出过去 5 年的现场 GMP 检查清单，包括日期和进行检验的药政机构的名称/国家。如果有，应当提供现行的 GMP 证书（附件 3）或引用欧洲 GMP 数据库中的副本。

1.3 Any other manufacturing activities carried out on the site 厂区内进行的任何其他生产活动

— Description of nonpharmaceutical activities onsite, if any.

— 如果有的话，描述厂区内的非制药活动。

2 QUALITY MANAGEMENT SYSTEM OF THE MANUFACTURER 公司的质量管理体系

2.1 The quality management system of the manufacturer 公司质量管理体系

— Brief description of the quality management systems run by the company and reference to the standards used;

— 公司质量管理运行系统的简要说明和所参考的标准;

— Responsibilities related to the maintaining of quality system including senior management;

— 包括高级管理层在内的质量体系维护职责;

— Information of activities for which the site is accredited and certified, including datas and content of accreditations, name of accrediting bodies.

— 公司认证的活动信息，包括日期和认证内容，认证机构名称。

2.2 Release procedure of finished products 最终产品放行程序

— Detailed description of qualification requirements (education and work experience) of the Authorised Person(s) / Qualified Person(s) responsible for batch certification and releasing procedures;

— 负责批量证明和放行程序的授权人/有资质人（简称：QP）的资格要求（教育/工作经验）的详细说明；

— General description of batch certification and releasing procedure;

— 批合格和放行过程的一般描述；

— Role of Authorised Person / Qualified Person in quarantine and release of finished products and in assessment of compliance with the Marketing Authorisation;

— 授权人/有资质人（简称：QP）在待验、放行最终产品、上市授权符合性评估中的角色。 — The arrangements between Authorised Persons / Qualified Persons when several Authorised Persons / Qualified Persons are involved;

— 涉及到多个授权人/有资质人时，他们之间的安排

— Statement on whether the control strategy employs Process Analytical Technology (PAT) and/or Real Time Release or Parametric Release.

— 采用 PAT（过程分析技术）控制策略和/或实时放行或参数放行的描述

2.3 Management of suppliers and contractors 承包商和供应商的管理

— A brief summary of the establishment/knowledge of supply chain and the external audit program;

— 供应链和外部审计程序建立和信息的一个简要介绍;

— Brief description of the qualification system of contractors, manufacturers of active pharmaceutical ingredients (API) and other critical materials suppliers;

— 简要说明承包商、活性药物成分（API 供应商）和其他关键材料供应商的资格审查系统； — Measures taken to ensure that products manufactured are compliant with TSE (Transmitting animal spongiform encephalopathy) guidelines.

— 采取的措施，以确保生产出的产品符合 TSE(动物海绵状脑病传染）指南

— Measures adopted where counterfeit/falsified products, bulk products (i.e. unpacked tablets), active pharmaceutical ingredients or excipients are suspected or identified;

— 假冒/伪造产品，散装产品（即拆开的片剂），药物活性成分或辅料的怀疑或确定方法 — Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;

— 外部研究、分析或其他有关生产的技术支援;

— List of contract manufacturers and laboratories including the addresses and contact information and flow charts of supplychains for outsourced manufacturing and Quality Control activities; e.g. sterilisation of primary packaging material for aseptic processes, testing of starting rawmaterials etc, should be presented in Appendix 4;

— 合同生产商和实验室的名单，包括地址和联系方式，以及外包生产和质量控制活动的供应链流程图。如无菌工艺的内包装材料灭菌，起始物料的检测，应显示附件 4

— Brief overview of the responsibility sharing between the contract giver and acceptor with respect to compliance with the Marketing Authorisation (where not included under 2.2).

— 上市授权符合性中，合同双方责任划分（如果未在 2.2 项下描述）的简要概述。

2.4 Quality Risk Management (QRM) 生产商质量风险管理（QRM）

— Brief description of QRM methodologies used by the manufacturer;

— 生产商 QRM 方针的简要描述

— 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.

— QRM 的范围和关注点的详细描述，包括全体公司层所有活动和仅在局部执行活动的简要描述。任何采用 QRM 体系对供应连续性进行的评估，都应当被讨论。

2.5 Product Quality Reviews 产品质量回顾

— Brief description of methodologies used