Site Master File – Guidelines for structure, contents and extent

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Regulatory requirements

The Site Master File as a document describing the GMP related activities of the manufacturer is mentioned in chapter 4 of the EU GMP Guideline in the section *Required GMP documentation*. The obligation for a company to answer questions and provide information to regulatory authorities is fixed in national legislation, as for example in § 66 of the *German Act on Medicinal Products* (AMG).

As for the EMA the *Guideline on the Compilation of community procedures on inspections and exchange of information* (February 2011) makes a number of references to the necessity of consulting a Site Master File. It is a document aimed at standardizing inspections by regulatory authorities within the EU.

Guidelines for structure, contents and extent

The document structure of PIC/S PE 008-4 is similar to the previous versions:

1. Document history
2. Introduction
3. Purpose
4. Scope
5. Content of Site Master File
6. Revision history

Annex

In the following the different sections will be presented and commented. For visual differentiation the original text will be highlighted with a blue background.

"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 needs only describe those operations, e.g. analysis, packaging, etc."

The pharmaceutical manufacturer is responsible for the **preparation** of the Site Master File. In practice it is left to the respective company to decide who actually prepares the document. The contents of the Site Master File should reflect actual processes and procedures and must not conflict with the corresponding documentation. Therefore it makes sense to entrust an interdisciplinary team of all divisions concerned under a coordinator`s leadership with the preparation of the Site Master File. In many cases the coordination will be assured by Quality Assurance.

„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."

PIC/S PE 008-4 guidelines are primarily intended for submission to the regulatory authority. If the document is used for other purposes the manufacturer shall decide whether the document is shortened or shall include further contents or information.

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„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 ..."

An inspector does not expect narrative but rather short texts with references to appendices, simple plans, drawings and schematic layouts in DIN A4 format instead of detailed text. If necessary, he will ask questions. However, the complete Site Master File including lists, appendices and references may - depending on the size of the site and particularities of the mode of operation - reach a considerable **extent**.

„... The Site Master File, including appendices, should be readable when printed on A4 paper sheets."

The Site Master File must not necessarily be available in printed form. A transmission in electronic form is also possible. However, the Site Master File should be readable when printed on A4 paper sheets, which has in particular to be considered for plans, schematic layouts or comprehensive tables.

„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."

The Site Master File should be prepared and administered according to GMP requirements. This would include **updating** at defined intervals. An interval of two years has proved useful. Establishing a change history is helpful to ensure transparency of changes and amendments made.

Conclusion

Considerable effort is associated with the preparation and maintenance of a Site Master File. However, the importance of the Site Master File for the authorities and other external interested parties justifies the effort. On the other hand the Site Master File - used as a checklist - offers the manufacturer the possibility to reconsider all operations and procedures. Gaps may thus be closed and the quality management system be optimized.

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