STANDARD OPERATING PROCEDURES IN PHARMACEUTICAL QUALITY SYSTEMS

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Abstract

Objective To develop explanatory texts for a pharmacy curriculum and reference textbook and to develop model standard operating procedures (SOPs) on key quality and operational pharmaceutical activities.

Method Explanatory texts were written and model SOPs were developed. Emphasis on clarity, conciseness and user-friendliness was made when selecting the writing style and format of the documents.

Key Findings Three explanatory texts entitled 'Master Standard Operating Procedure', 'Preparing a Standard Operating Procedure' and 'Good Manufacturing Practice' were compiled and sixteen model SOPs were developed.

Conclusion Effective SOPs are required to achieve compliance with regulatory requirements and good practice guidelines. Explanatory texts and model SOPs are provided to assist in the development of a pharmaceutical quality management system. The texts developed are an effective training tool on the development of good quality SOPs and the model SOPs are an example of the good quality procedures being recommended.

Keywords Quality Management System, Standard Operating Procedure, Explanatory texts.

Introduction

In the pharmaceutical industry, the quality of medicinal products must be assured throughout the production process of each batch. Quality standards in both design and operation are required to ensure that the production of medicinal products is consistent and controlled to ascertain that the medicinal products are appropriate for their intended use. Good Manufacturing Practice (GMP) is the area of quality assurance which ensures that this requirement is met.[1]

One of the requirements of GMP is for a manufacturer or an importer of medicinal products to have a quality management system (QMS) implemented.[2] Standard Operating Procedures (SOPs) forming part of this QMS transpose the principles and guidelines of GMP into the operations of the organisation and assign responsibilities. Distribution of medicinal products must maintain the standard of quality attained in manufacture and/or importation. This is achieved by following Good Distribution Practice (GDP) guidelines. A distributor of medicinal products should also have a QMS implemented.[3] SOPs forming part of this QMS transpose the requirements of GDP into the actual operations of the wholesale distributing organisation and assign responsibilities.

The design of the QMS will depend on the organisational environment, needs, objectives, products it provides, processes employed and the size and complexity of the organisation itself.[4] The SOPs need to be effective in reaching their objective and need to be relevant for the organisation. For GMP/GDP purposes, SOPs should be available for all activities that can have an impact on product quality. One must establish the steps to be included in a written procedure as it would directly affect the product quality and what may be dealt with otherwise.[5] A simple but effective process of SOP development should be followed and the SOPs must be written, reviewed and approved by the appropriate authorised personnel.

Method

Explanatory texts about the Master SOP, the procedure followed when developing SOPs and the GMP process were compiled. The recommendations in these texts were followed to develop model SOPs covering core quality activities and key operational procedures. The SOPs were developed following a review of the requirements of GMP and also through personal experience of the researcher. The first step in the process was to identify the scope and objective of the SOP. A flowchart was designed where appropriate to simplify the procedure. The procedural steps were written followed by an assignment of responsibilities and appendices. Self-explanatory forms were developed where necessary and included as appendices. The first draft of the model procedures were validated through discussion with peers and amended accordingly producing the final draft. The model SOPs were formatted in a way so as to ensure user-friendliness. An electronic template for these SOPs was made available for adaptation to any particular pharmaceutical organisation.

Results

Three explanatory texts entitled 'Master Standard Operating Procedure', 'Preparing a Standard Operating Procedure' and 'Good Manufacturing Practice' were compiled. The explanatory text of the 'Master SOP' describes the process of SOP management. It defines the procedure for assigning an author, one or more reviewers and an approver and describes the procedure to follow for the effective distribution and updating of the SOPs. The procedure to follow when an SOP is superseded is also described.

The text entitled 'Preparing a Standard Operating Procedure' deals with the process involved in developing the SOP and proposes a practical and effective style for writing the procedure. It discusses the need to plan ahead when developing a pharmaceutical quality system, the procedure of planning, writing, checking and approving the SOP. This text also discusses the need for SOPs within a pharmaceutical organisation.

The third text on 'Good Manufacturing Practice' describes how to apply the principles and guidelines of GMP to a manufacturing organisation through its SOPs. It lists common activities for which SOPs should be implemented and describes them concisely.

Sixteen model SOPs were developed (Table 1).

Discussion

SOPs are a tool for efficiency and regulatory compliance within the pharmaceutical sector when used correctly. They are not written just for the sake of doing so or to satisfy customers and regulators.

The SOP development process starts off by identifying the SOPs to be written, their authors, reviewers and approver. Processes which impact on product quality should all be described by written procedures. Authors should be experienced in the procedure. The person responsible for the execution of procedure should check the SOP. The manager responsible for the QMS should approve it after verifying its conformance with good practice and regulatory requirements and its convergence with the rest of the QMS.

The author begins the SOP development process by planning the SOP, preferably using a tool such as a process flow chart. Visual aids such as flow charts, diagrams, photographs and tables are incorporated to facilitate comprehension of the procedure. SOPs are written for users to follow and should therefore be clear, concise and avoid complex linguistics which users may find difficult to understand. Ambiguity should also be avoided. A logical stepwise procedure is easier to follow correctly and easy-to-follow SOPs are more likely to be correctly interpreted and are less prone to deviations due to human error.

SOP Management	Training
Change Control	Good Documentation Practice
Deviation Management	Self-Inspection
Supplier Approval	Recalls
Equipment Identification	Entry and Gowning
Visitors	Batch Manufacturing Record
Packaging Record	Cleaning of Production Area
Cleaning of Production Equipment	Receipt of Goods

Table 1: Model SOPs developed

Responsibilities should be clearly defined in SOPs. Procedures have a starting point and an endpoint and should never overlap. Trivial instructions should not be included. SOPs should ideally be validated prior to implementation. They must be regularly reviewed and any changes made to the procedure should be controlled and tracked. They should be directed at the user and preferably written in the present or affirmative tense. Changes in the procedure should be effected after the relevant SOP is changed and training has been given to the personnel responsible for its execution.

The first SOP to include in a QMS is the Master SOP. This defines the structure of the QMS and the format of the written procedures. SOP distribution and training to be imparted are defined. The documents to be used in the QMS are defined and formalised. A system for documenting, investigating, correcting, preventing and trending deviations should be defined. The quantity of deviations, their severity and the number of open investigations are key performance indicators for the organisation and should be actively tracked.

SOPs are an effective training tool. They can ensure that a process is performed in the same way irrespective of who is performing the steps and of when the tasks are performed providing harmonisation within the organisation.

SOP writing is a complex task. It is one that requires skill to fulfil its goals. Training may be needed in writing effective SOPs. The reviewers must fulfil their task carefully. This time-consuming activity is an investment that will save on resources at a later stage when senior staff would otherwise be engaged in investigating and managing deviations.

The texts developed are an effective training tool on the development of good quality SOPs and the model SOPs are an example of the good quality procedures being recommended.

Good quality SOPs are the key to an effective QMS and to compliance in operations. They clearly define responsibilities, harmonise activities, facilitate training and enable effective and efficient quality assurance.

Conclusion

It is envisaged that the texts will be of interest to students who intend to take up a career in pharmaceutical manufacture and distribution, as well as to anyone entrusted with developing or maintaining a pharmaceutical QMS. The model SOPs can be used as a template for the key procedures considered. They can also be used to develop further SOPs for the organisation as may be required in the future. The guidance provided in the explanatory texts will be useful in providing direction, for SOPs should be effective in attaining the objectives of the QMS. The benefits to be gained from the effort and manpower used in writing SOPs will be maximised if the guidance and model SOPs are followed.

Good quality SOPs translate into better compliance, less deviations and therefore fewer investigations and corrective actions, no ambiguity regarding responsibilities and less rejection of costly pharmaceutical actives, intermediates and product. These texts and model SOPs serve as a tool to develop better quality procedures.

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