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DEVELOPMENT OF AN ALGORITHM FOR COMPILING A STANDARD OPERATING PROCEDURE (SOP) IN THE CONDITIONS OF COMPOUNDING PHARMACIES

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The article presents the algorithm for creating a standard operating procedure (SOP) for pharmacy organizations that carry out quality control of prepared medicines. The relevance of developing the SOPs is determined by the implementation of international industry standards in pharmaceutical field. In order to ensure the uniformity of the documentation system of the pharmacy organization, we suggested the general structure of the standard operating procedure for the quality control of dosage forms prepared at the pharmacy. The main stages of the development of the SOP are specified, recommendations are given on the execution of the document, its updating, making amendments. The development of templates for standard operating procedures will allow pharmacies to create their own SOPs that take into account the features of a particular organization.

Keywords: standard operating procedure, quality control, pharmaceutical organization

One of the priorities of the national healthcare system is to improve the quality and accessibility of medical care, which also includes the availability of medicines. The current trend of reducing the number of compounding pharmacy organizations does not contribute to this task solution.

Compounding pharmacies are a necessary part of the medicine supply system, since they allow to meet the needs of healthcare in dosage forms that do not have commercial analogues, to provide individual dosage of medicinal substances, as well as to manufacture dosage forms without preservatives and other non-indifferent additives [1,4].

Pharmacies engaged in the manufacture of medicines have a number of unresolved problems. Primarily, they are organizational and legal (legislative) issues. The current Federal law No. 61-FZ "On circulation of medicines" and the Guidelines of GMP GOST R 52249–2009 set high requirements for personnel, premises and equipment of compounding

pharmacies, manufacturing of medicines and the system of quality control as wellas for documentation maintained in the pharmacy organization. Another document regulating the activities of pharmacy organizations is the Order of the Ministry of Health of the Russian Federation No. 647n dated 31.08.2016 "On approval of the Guidelines of Good Pharmacy Practice of medicines for medical use". This document defines the transition of pharmacy organizations to GPP (Good Pharmacy Practice) standards [2]. In accordance with this concept, all the activities of pharmacy organizations are considered as a set of processes that should be described in detail in internal controlled documents specifying the sequence of actions when performing any work, in the so-called SOPs – standard operating procedures.

Thus, compounding pharmacies, usually with small staff, must fulfill not only their main responsibilities for the production and quality control of dosage forms, but also develop a number of documents of the quality management system.

In this regard, it is relevant to develop templates of SOPs, which will allow employees of compounding pharmacies to use them as a sample when developing their own documents.

Currently, quite a large number of SOPs have been developed that describe the activities of pharmacies when ordering and accepting inventory, when working with customers, selling goods, and on labor protection. The section of activity of pharmacy organizations on quality control of prepared dosage forms is not sufficiently covered. Quality control of manufactured dosage forms and dosage forms prepared in the pharmacy are significantly different. For manufactured dosage forms pharmacopoeial monographs have been developed, which are actually legally approved methods for quality control of the dosage form or substances. The development of SOPs describing the procedure for quality control of dosage forms prepared in a pharmacy is associated with a number of difficulties. In a pharmacy, the pharmacist-analyst must independently develop methods for analyzing dosage forms, guided by the current State Pharmacopoeia and other legal acts. At the same time, it is necessary to take into account the material and technical equipment of the pharmacy, which, as a rule, significantly limits the possibility of using a number of pharmacopoeial methods of analysis.

Thus, standard operating procedures developed for compounding pharmacies will also be documents containing step-by-step instructions for performing analysis of the prepared dosage form. SOPs should make the process of medicine quality control in the pharmacy to be consistent, coordinated, predictable and reproducible. It is necessary the SOPs to be compiled according to a standard scheme, unambiguously, clearly, so that pharmacy employees, including newly recruited ones, could easily orientate themself and perform the analysis without the help of colleagues.

In connection with the above, the **purpose** of the work is to develop an algorithm for compiling a standard operating procedure (SOP) in the conditions of compounding pharmacies.

MATERIALS AND METHODS

The algorithm for compiling SOP for quality control of dosage forms prepared in compounding pharmacies was developed in accordance with the current regulatory documentation regulating the activities of pharmacy organizations [2,3].

RESULTS AND DISCUSSION

The first stage in the development of SOP for any type of activity is to determine its structure, form, procedure for approval, approval, making amendments, updating, cancellation. When

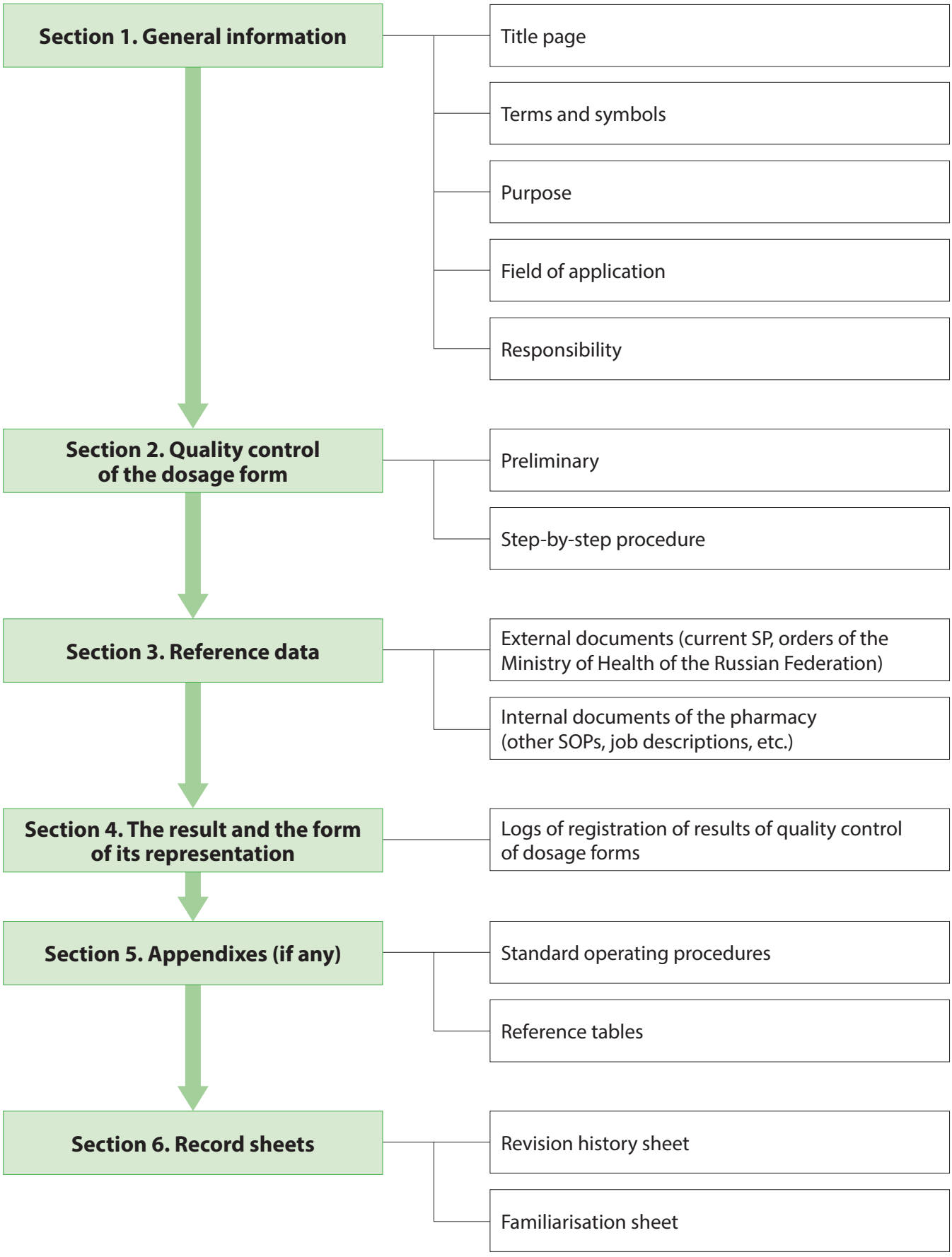

FIG. 1. *Content of sections of the SOP on quality control of dosage forms prepared in compounding pharmacies*

the SOP is first implemented, the SOP version number is assigned as 1, and the version number increases with subsequent revisions.

When making a SOP, it is necessary to develop the document structure, which can be presented in the following form (Fig. 1):

Section 1. General information

Execution of the "Title page" subsection

The title page of the document may contain the columns shown in Table 1.

A unique code is assigned to each SOP:

СОП-XX.YY,

where

СОП (SOP) – a letter combination that defines the document type (short for "Standard operating procedure");

XX – a combination of digits that defines the scope of the document (for example,

01 – SOP, describing the analysis of purified water and/or water for injections;

02 – SOP, describing the analysis of eyedrops;

03 – SOP, describing the analysis of liquid dosage forms;

04 – SOP, describing the analysis of concentrated solutions);

YY – sequential number of the document in the classification group.

The developed SOP should be updated. The SOP is usually updated every three years [5]. After updating, a mark is made on the title page (date, signature of the person who updated) of the original and copies of the document.

Execution of subdivision "Purpose"

Specify the main purpose of using the procedure. For example: standardization of the procedure for monitoring the quality of purified water.

Execution of subdivision "Responsibility"

Specify the positions of employees responsible for the implementation of the developed SOP. If necessary, specify the required level of competence of the executors, conditions for preliminary training. Specify the person responsible for monitoring the procedure. If necessary, specify the official responsible for timely revision and updating of the SOP text.

Execution of subdivision "Terms and Symbols"

Specify all the terms that are necessary for the SOP executor to correctly interpret the SOP text. Pay special attention to special terms and give them clear and concise definitions. Decode specific acronyms and/or abbreviations. Check the consistency of terms and definitions in the

Table 1

TITLE PAGE OF SOP

<table>
<tr><td colspan="4">Name of SOP: _____</td></tr>
<tr><td colspan="4">Name of the pharmacy organization _____</td></tr>
<tr><td colspan="4">Code (number) of document: СОП-XX.YY
Version №</td></tr>
<tr><td colspan="2">Compiled:
Pharmaceutist-analyst

_____ _____
full name signature</td><td colspan="2">Approved:
Head

_____ _____
full name signature</td></tr>
<tr><td colspan="2">The document put into effect:
“____” _____ 20____</td><td colspan="2">Document updated:
“____” _____ 20____</td></tr>
</table>

developed SOP with other documents of the pharmacy quality system.

Execution of subdivision "Field of application"

This section can contain information about the place where the procedure is performed and description of the situations in which it is performed. In addition, this section should specify the types of dosage forms the quality control of which is described in this procedure.

Section 2. Quality control of the dosage form

Execution of subdivision "Preliminary measures"

List the laboratory utensils and auxiliary materials required to perform quality control of a single dosage form. Specify all the necessary reagents and their quantity for performing a single analysis. If necessary, specify the procedure for preparing devices and equipment, specify their operating conditions. Describe the procedure for sampling the dosage form for quality control.

Execution of subdivision "Step-by-step procedure"

Step by step, in a clear sequence, exhaustively and realistically describe the actions that must be performed in the quality control of the dosage form specified in the name of the SOP.

The description of actions should be divided into several main parts:

- In accordance with current legislation, describe in detail all types of control that should be subjected to the dosage form specified in the name of the SOP.
- In cases where chemical control is mandatory, perform preliminary calculations of the required amount of the dosage form that will be used for the analysis. At the same time, it is necessary to take into account the sensitivity of the reactions carried out, the norms of permissible deviations, and to provide for the need for further release of this dosage form to the pharmacy customer. It is also necessary to make preliminary calculations of the volume of the titrated solution, which will be spent on titrating the sample weight of the studied dosage form. In this section, it is possible to draw up chemical equations that underlie the reactions, calculate equivalence factors, and titrate titrants for the substances to be determined.
- Describe in detail and step-by-step the implementation of the main operations for quality control of the dosage form: determining the authenticity of the incoming ingredients and their quantitative content.
- Final operations (evaluation of the quality of the dosage form).

When describing all stages of quality control of dosage forms, the safety requirements of the work performed must be specified or references to the relevant internal documentation.

Section 3. Reference data

Provide references to external documents used in the development of SOP (laws and regulations, state standards, reference books, etc.).

Specify the internal documents of the pharmacy organization that should be taken into account when performing the developed SOP.

The developed SOPs must not contradict the requirements of the legislation regulating pharmaceutical activities in the territory of the Russian Federation.

Section 4. The result and the form of its representation

Specify what is the result of performing the SOP and how it is registered, which logs are filled in. Keep in mind that any analysis, control, or verification can have at least two results – positive and negative. It is required to describe the sequence of actions when receiving each of the results, and specify the persons responsible for making decisions.

Section 5. Appendixes (if any)

Appendices may contain an operating instruction that briefly describes the tests being performed. The operating instruction can be

Table 2

REVISION HISTORY SHEET

Revisions of SOP-XX.YY	Basis for revisons in СОП-XX.YY	Executor (full name)	Signature	Date
1	2	3	4	5

Table 3

FAMILIARIZATION SHEET

Number of version of SOP-XX.YY	Full name of an employer	Signature	Date
1	2	3	4

presented as a visualized card or table and placed directly on the workplace of the pharmacist-analyst.

Appendices may also contain reference tables (refractometric, standards of acceptable deviations, etc.) that can (or should) be used by the executor when performing the SOP.

Section 6. Record sheets

Amendments to the SOP may be made in connection with changes in the regulatory framework or in the activities of a pharmacy organization. The developer makes amendments to the SOP and registers them in the Revision history sheet. The head of the pharmacy or the responsible person must inform on the amendments made the employees who participate in this procedure. After reviewing the employee puts his signature in the Revision history sheet. When a large number of amendments are made, a new version of the SOP is published.

The Revision history sheet and the Familiarization sheet can be presented in the form of tables (table 2 and 3).

The required number of copies of a particular SOP in a pharmacy is determined based on the number of employees who use this SOP in their activities, but there must be at least two copies. All first copies of SOP are marked as "Control copy", these samples are stored by the Head of Pharmacy. The remaining copies of SOPs are stored at the workplaces of pharmacists who perform quality control of dosage forms.

CONCLUSION

The proposed structure and algorithm for creating SOPs can be used as a template for developing own standards in compounding pharmacies. The implementation of SOPs into the activities of pharmacies will ensure a logical sequence of actions in the process of quality control of medicines, clearly distribute tasks by competence, and increase the responsibility of employees for performing certain operations. All this will eventually ensure that the availability and quality of medicines will increase.

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