PRACA ORYGINALNA
ORIGINAL ARTICLE

PROCESS MODEL OF THE PHARMACEUTICAL INTEGRATED MANAGEMENT SYSTEM

MODELOWANIE PROCESÓW FARMACEUTYCZNEGO ZINTEGROWANEGO SYSTEMU ZARZĄDZANIA

Serhii H. Ubohov, Viktor V. Trokhymchuk, Violetta I. Todorova, Volodymyr A. Zahoriy
SHUPYK NATIONAL MEDICAL ACADEMY OF POSTGRADUATE EDUCATION, KYIV, UKRAINE

ABSTRACT

Introduction: One of the innovative trends in the modern development of the pharmaceutical sector is the introduction of integrated management systems (IMS) at the enterprises for the production and distribution of medicines.

The aim: to substantiate and develop a process model and approaches to the regulation and documentation, performance evaluation and improvement of the IMS within the pharmaceutical institution (PI) and hospital pharmaceutical service (HPS).

Materials and methods: research materials used: international standards, regulations and guidelines of the Ministry of Health of Ukraine, scientific publications, information of PI and hospitals, placed on official websites and collected in the process of direct observation. Research methods are: systemic-review, generalization, observation, documentary, structural-logical and graphic modeling.

Results: Based on the requirements of good practices and international standards in the field of management of quality, ecology, occupational health and safety, social responsibility, a typical process model of the IMS of PI and HPS (pharmaceutical integrated management system – PIMS) has been substantiated and developed. The content of each process of a typical PIMS model is described and structured. The expected results (outputs) of the PIMS processes are determined. The approaches to the regulation and documentation of the PIMS processes in the conditions of functioning of the four-level documented information system are substantiated. A matrix of responsibility and authority of the staff of PI and hospitals within the PIMS is developed. The structurally hierarchical model of the performance evaluation and improvement of the PIMS has been designed and described.

Conclusions: The results are the basis for the establishing, regulating and documenting of the PIMS and the development of a system for its performance evaluation and continual improvement.

KEY WORDS: medicines, pharmaceutical institution, hospital pharmaceutical services, integrated management system, process model

Wiad Lek 2019, 72, 2, 201-208

INTRODUCTION

One of the innovative trends in the modern development of the pharmaceutical sector is the introduction of integrated management systems (IMS) at the enterprises for the production and distribution of medicines. Over the past ten years, a number of studies have been carried out by scientists to substantiate the benefits and principles of the implementation IMS of pharmaceutical companies based on good practices (GxP) and international standards in the field of management of quality, ecology, occupational health and safety, as well as social responsibility [1, 2]. As part of this research direction, the staff of the Shupyk National Medical Academy of Postgraduate Education was substantiated the scientific and practical approaches to the formation of the IMS in pharmaceutical institutions (PI), which carry out wholesale, retail sales and extemporal manufacturing of medicines [3]. The next stage is the development of IMS process models for their implementation in different types of PI, as well as in hospital pharmaceutical services (HPS), which determined the relevance and aim of this work.

THE AIM

The research aim is to substantiate and develop a process model and approaches to the regulation and documentation, performance evaluation and improvement of the IMS within the pharmaceutical institution and hospital pharmaceutical service.

MATERIALS AND METHODS

Research materials used: international standards, regulations and guidelines of the Ministry of Health of Ukraine, scientific publications, information on PI and hospitals (Ternopil, Zaporizhya, Dnipro, Chernihiv regions), posted on official websites and collected in the process of direct observation. Research methods are: systemic-review, generalization, observation, documentary, structural-logical and graphic modeling.

RESULTS AND DISCUSSION

In the previous work, we developed a structural and logical model for the implementation of the IMS in PI, as well as

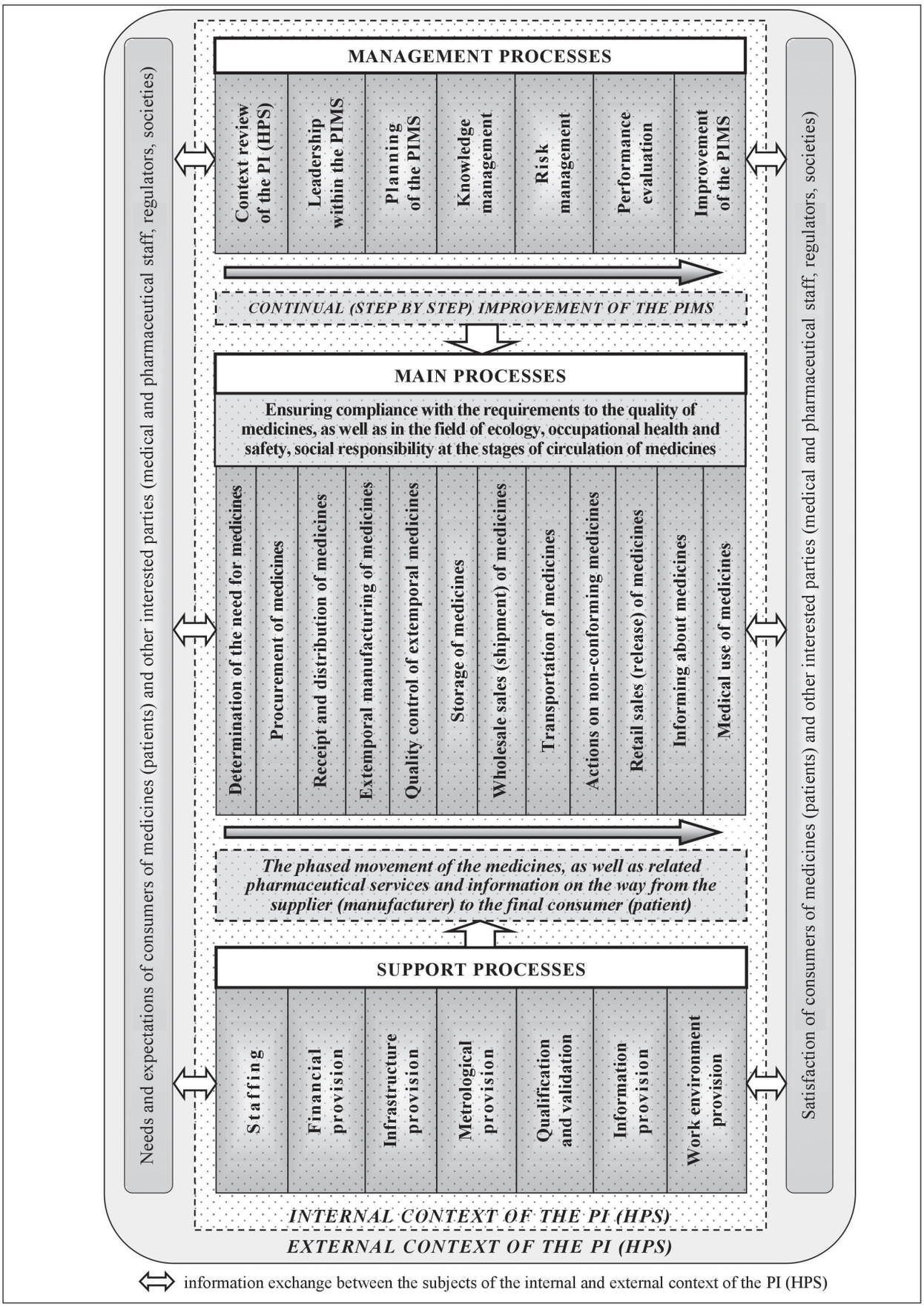

Fig. 1. Typical process model of the pharmaceutical integrated management system.

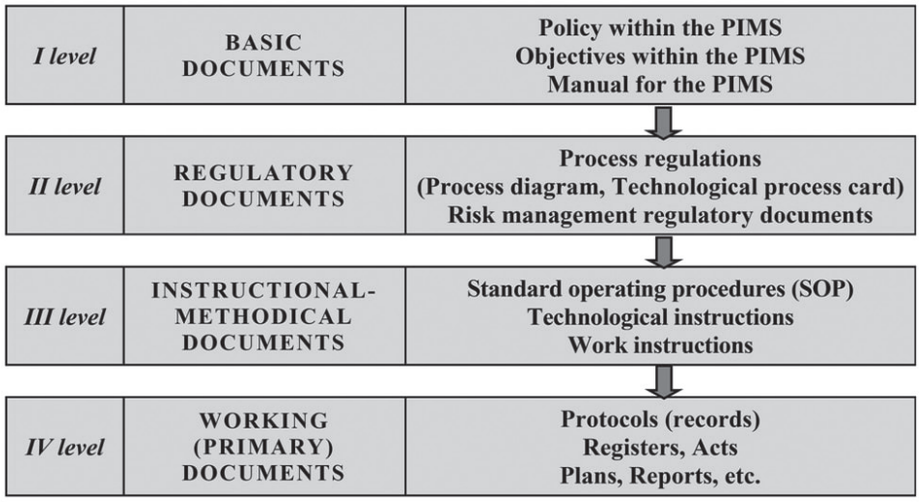

Fig. 2. Documented information system of the pharmaceutical integrated management system.

the integration and identification of potential spheres of synergy of structural elements and requirements of the GxP (GDP/GSP/GPP/GVP) and international standards (ISO 9001, ISO 14001, OHSAS 18001, SA 8000), based on which the IMS is built [3]. The results of these studies became the basis for the development of a typical process model of the IMS of PI (pharmaceutical integrated management system – PIMS) (Fig. 1). This model was developed as a unified one and therefore it can be used for the formation of the PIMS in different types of PI (pharmaceutical warehouses, retail and production pharmacies), as well as in pharmaceutical services of hospitals (secondary and tertiary levels of medical care), which includes pharmaceutical subdivisions (pharmacy, warehouse of medicines, department of clinical pharmacists, etc.). The importance of formation the PIMS in HPS confirms our analysis of the information of those domestic hospitals, with a Quality Management System (QMS) already in place, which showed that the QMS is short of covering the processes of circulation of medicines in hospitals. Therefore, the integration of the PIMS into the general QMS or IMS of hospital will contribute to the improvement of the pharmaceutical component of the hospital activity.

The objective of the PIMS model developed is to satisfy the interests of consumers of medicines (patients) and other interested parties (medical and pharmaceutical staff, regulators, society). The realization of this objective is achieved through the implementation of three categories of processes: management processes, main processes and support processes. The management processes of the PIMS include: context review of the PI (HPS), leadership within the PIMS, planning of the PIMS, knowledge management, risk management, performance evaluation and improvement of the PIMS. The support processes of the PIMS include: staffing, provision of financial resources and infrastructure, metrological provision, equipment qualification and processes validation, information provision, work environment provision (physical, social, psychological, etc.). The group of main processes of the PIMS includes activities to ensure compliance with the requirements of legislation, GxP, normative documents (Pharmacopoeia, Quality Control Methods, Protocols of the pharmacist, etc.) on the quality of medicines and related pharmaceutical services, as well as international standards in the field of management of quality, ecology, occupational health and safety, social responsibility at the following stages of circulation of medicines: determination of the need for medicines, procurement of medicines, receipt and internal distribution of medicines, extemporal manufacturing of medicines in pharmacies, quality control of extemporal medicines, storage of medicines, wholesale sales (shipment) of medicines, transportation of medicines, actions on non-conforming medicines (low-quality, falsified, unregistered, forbidden for circulation, expired), retail sales (release) of medicines to patients and medical staff, informing patients and medical staff about medicines, medical use of medicines (in outpatient or inpatient settings). It is important to note here that the main processes of a typical model of the PIMS, which are uncharacteristic for a PI of the corresponding type or HPS, are not included in the process structure of the PIMS implemented in a particular institution. For example, the PIMS of pharmaceutical warehouse does not include the processes of manufacturing and retail sales of medicines, to the PIMS of pharmacy – the processes of wholesale sales of medicines, etc. In the event that it is necessary to add a new process (for example, an outsourcing process) to the group of main processes of the PIMS, then this typical model is open for extension. Another important point is that, in the presented model of the PIMS, the management of the aspects of ecology, occupational health and safety, social responsibility is not highlighted in separate processes. This is due to the interprocess character of these aspects in the context of the peculiarities of pharmaceutical activity, in particular regarding the management of the movement of medicines on the way from the supplier (manufacturer) to the final consumer (patient). Therefore, these aspects "permeate" both the main processes and the processes of management and support of the PIMS.

An important requirement of GxP and international

Table I. Matrix of responsibility and authority of the staff of pharmaceutical institutions and hospitals within the pharmaceutical integrated management system

Names of the PIMS processes	Expected results (outputs) of the PIMS processes	The posts and levels of responsibility and authority of the staff of pharmaceutical institutions and hospitals*												
		Head of the PI (hospital)	Responsible person of the PI (hospital)	Chief human resources officer	Senior pharmacist, chief of the HPS	Pharmaceutical department managers	Pharmacists, clinical pharmacists	Assistant pharmacists, pharmacy technician	Medical department managers	Senior nurses of the medical department	Physicians, nurses	Accountant, legal advisor, maintenance/supply manager	Engineers, technicians	Auxiliary staff of the PI (HPS)**
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
MANAGEMENT PROCESSES														
Context review of the PI (HPS)	Understanding of the context (environment) of PI (HPS)	M	R	I	P	P	I	I	I	I	I	I	I	I
Leadership within the PIMS	Effective and efficient implementation of vision, policy and obligation within the PIMS	M	R	P	P	P	I	I	P	P	I	I	I	I
Planning of the PIMS	Established objectives of the PIMS, planned actions and performance indicators for their achievement	M	R	P	P	P	I	I	I	I	I	I	I	I
Knowledge management	Effective and efficient knowledge management within the PIMS	M	R	P	P	P	I	I	P	P	I	I	I	I
Risk management	Effective and efficient elimination (reduction) of potential risks in the PI (HPS)	M	R	I	P	P	I	I	P	P	I	I	I	I
Performance evaluation of the PIMS	Effective and efficient monitoring, review (analysis) and performance evaluation of the PIMS	M	R	I	P	P	I	I	I	I	I	I	I	I
Improvement of the PIMS	Effective and efficient corrective and preventive actions to eliminate non-conformities, continual (step-by-step) improvement of the PIMS	M	R	I	P	P	I	I	P	P	I	I	I	I
MAIN PROCESSES														
Determination of the need for medicines	List and planned volume of procurement of medicines are determined according to the established requirements***	M	У	I	P	R	P	I	P	P	P	I	I	I
Procurement of medicines	Good quality medicines purchased in accordance with the established requirements	M	R	I	P	I	I	I	I	I	I	P	I	I
Receipt and internal distribution of medicines	Good quality medicines accepted and distributed in accordance with the established requirements	M	R	I	P	P	P	I	P	P	I	I	I	P
Extemporal manufacturing of medicines in pharmacies	Good quality medicines manufactured (made) in pharmacies in accordance with the established requirements	M	P	I	P	R	P	P	I	I	I	I	I	P

Quality control of extemporal medicines	Extemporal medicines that have passed quality control in accordance with the established requirements	M	R	I	P	P	I	I	I	I	I	I	I	I
Storage of medicines	Good quality medicines stored in the PI (hospitals) in accordance with the established requirements	M	P	I	P	R	P	I	P	P	P	I	I	I
Wholesale sales (shipment) of medicines	Good quality medicines sold (shipped) to recipients (pharmacies, hospitals) in accordance with established requirements	M	P	I	P	R	P	P	I	I	I	I	I	P
Transportation of medicines	Good quality medicines transported in accordance with established requirements	M	P	I	P	R	P	P	I	I	I	I	P	P
Actions on non-conforming medicines	Non-conformity quality medicines withdrawn from circulation and transferred for utilization or disposal in accordance with established requirements	M	R	I	P	P	I	I	P	P	I	I	I	I
Retail sales (release) of medicines to patients and medical staff	Good quality medicines sold (released) to consumers (patients, medical staff) in accordance with established requirements	M	P	I	P	R	P	P	I	I	I	I	I	I
Informing patients and medical staff about medicines	Good information about the medicines provided to patients and medical staff in accordance with established requirements	M	P	I	P	R	P	P	P	I	P	I	I	I
Medical use of medicines (in outpatient or inpatient settings)	Good quality medicines used for medical purposes in accordance with established requirements	M	R	I	P	P	P	I	P	P	P	I	I	I
SUPPORT PROCESSES														
Staffing	Good staffing and training to provide of the PIMS functioning	M	P	R	P	P	I	I	P	I	I	I	I	I
Financial provision	Good financial provision of the PIMS functioning	M	P	I	P	P	I	I	P	P	I	R	I	I
Infrastructure provision	Good infrastructure provision (premises, equipment, vehicles, communication technologies, etc.) for the functioning of the PIMS	M	P	I	P	P	I	I	P	P	I	R	P	I
Metrological provision	Provision with suitable monitoring and measurement tools necessary for the functioning of the PIMS	M	P	I	P	P	I	I	P	P	I	R	P	I
Qualification and validation	Effective and efficient procedures for the equipment qualification and validation of the PIMS processes	M	R	I	P	P	I	I	I	I	I	P	P	I
Information provision	Good documentary and information provision of the PIMS functioning	M	R	I	P	P	I	I	P	P	I	P	P	I
Work environment provision	Good working conditions (physical, social, psychological) for the efficient functioning of the PIMS	M	P	P	P	R	I	I	P	P	I	P	I	I

Notes:
*Levels of responsibility and authority: M – process manager; R – responsible for the functioning of the process; P – process participant; I – person informed about the process.
**The auxiliary personnel include: packers, sanitary cleaners, cleaners, loaders, driver forwarders, etc.
***The requirements of legislation, good practices and normative documents (Pharmacopoeia, Quality Control Methods, Protocols of the pharmacist, etc.) on the quality of medicines and related pharmaceutical services, as well as international standards in the field of quality, ecology, occupational health and safety, social responsibility.

standards is the good documentation of the corresponding management system. Therefore, at the second stage of research, we have substantiated approaches to the regulation and documentation of the PIMS processes. Based on the study of the requirements of the aforementioned normative documents, the analysis of scientific literary sources and own observations, we propose to introduce, within the PIMS, a four-level documented information system, which includes: basic, regulatory, instructional-methodical and working (primary) documents (Fig. 2) [4, 5].

All of the basic documents of the PIMS (documented information of the first level) shown in Figure 2 can be merged into a single document, namely the Manual for the PIMS, the main sections of which should be: policy and objectives of the PI (hospital) within the PIMS; scope of the PIMS; description of structure of the PI (HPS); list and description of the PIMS processes, indicating the interconnections and interactions of these processes and the personnel responsible for their execution (using graphic charts and tables) [5]. In the context of the above-mentioned we described and structured the content of each process of a typical model of the PIMS, where the structural elements of the processes can be considered as separate subprocesses (procedures). After the development of the basic documents, the regulation and documentation of each individual process (subprocess) of the PIMS should be carried out. This is done by developing regulatory and instructional-methodical documents (documented information of the second and third levels), namely: process regulations and specific instructions describing the algorithms for performing certain types of work (operations) within the PIMS processes (standard operating procedures, work and technological instructions, etc.) [4, 5]. Obligatory components of the process regulations should be a process diagram and technological process card (TPC). Process diagram is a graphical model that shows the sequence of operations and interconnections between different participants in the process. One of the most convenient and effective modern tools for constructing process diagrams is the methodology of modeling IDEF0 and IDEF3 [6, 7]. TPC is a document that contains brief information on the consistent description of operations, terms and conditions for their execution, the responsible executors and other process participants, the names and format of the input and output documentation, the results of operations and facilities to ensure their execution. Each concrete institution (PI, hospital) approves the form of the TPC, which is most consistent with the content and specificity of its activities. The regulatory documents should also include such risk management documents as risk classifier, risk profile passport and risk register [8]. The PIMS working documentation (documented information of the fourth level) includes a wide range of primary documents (protocols, records, registers, acts, plans, reports, etc.), which include information on planned and executed operations (actions), monitoring and measurement results, detected non-conformities (defects), etc. The system of primary documentation of each type of institution (PI, hospital) has its own peculiarities. At the same time, the unification of the types and forms of primary documentation and the transition to electronic document circulation (internal and external) will contribute to improving the efficiency of the PIMS.

Taking into account the leading role of personnel in the implementation and maintaining of the PIMS, at the next stage of our research we have developed a matrix of responsibility and authority of the staff of PI and hospitals within the PIMS and identified the expected results (outputs) of the PIMS processes (table I). Within the PIMS, a four-level system of responsibility and authority is offered: process manager (first level); responsible for the functioning of the process (second level); process participant (third level); person informed about the process (fourth level). This system covers all main groups of posts that are in the PI and hospitals, namely: top management staff (head of the PI (hospital), Responsible person, chief human resources officer, chief of the HPS, legal advisor); pharmaceutical staff (senior pharmacist, pharmaceutical department managers, pharmacists, clinical pharmacists, assistant pharmacists, pharmacy technician); medical staff (medical department managers, physicians, senior nurses, nurses); economic and technical staff (accountant, maintenance and supply manager, engineers, technicians, etc.); auxiliary staff (packers, sanitary cleaners, cleaners, loaders, driver forwarders, etc.). The management of the PI (hospital) should provide a clear definition, inclusion in job descriptions and informing all employee of their functions, responsibilities and authority within the PIMS. This approach is fully in line with one of the basic principles of quality management enshrined in the ISO 9001 standard, which implies "the engagement of all personnel" [9].

At the last stage of this work, we designed the structurally hierarchical model of the performance evaluation and improvement of the PIMS, which is an important part of the general management process within the PIMS (Fig. 3). The model, depicted in the form of a "pyramid", contains a hierarchical list of concrete actions to performance evaluation and improvement of the PIMS, with a clear periodicity of these actions. At the bottom of the "pyramid" there is a constant monitoring and measurement of the functional characteristics of main processes of the PIMS and the quality of medicines and pharmaceutical services. This is done daily in the current mode. Here it is recommended to adhere to the following principle: one person performed an operation (work) – another (who has the appropriate authority and is independent in administrative terms from the first one) has checked the correctness (quality) of its execution [10]. The next step in the "pyramid" is the periodic monitoring of the functional characteristics of the management and maintenance processes of the PIMS, which is recommended to be conducted on a monthly basis. The results of monitoring and measurement, as well as the results of their analysis and evaluation, are documented in the protocols (records) of the established form. The following in the hierarchy of actions on performance evaluation of the PIMS include

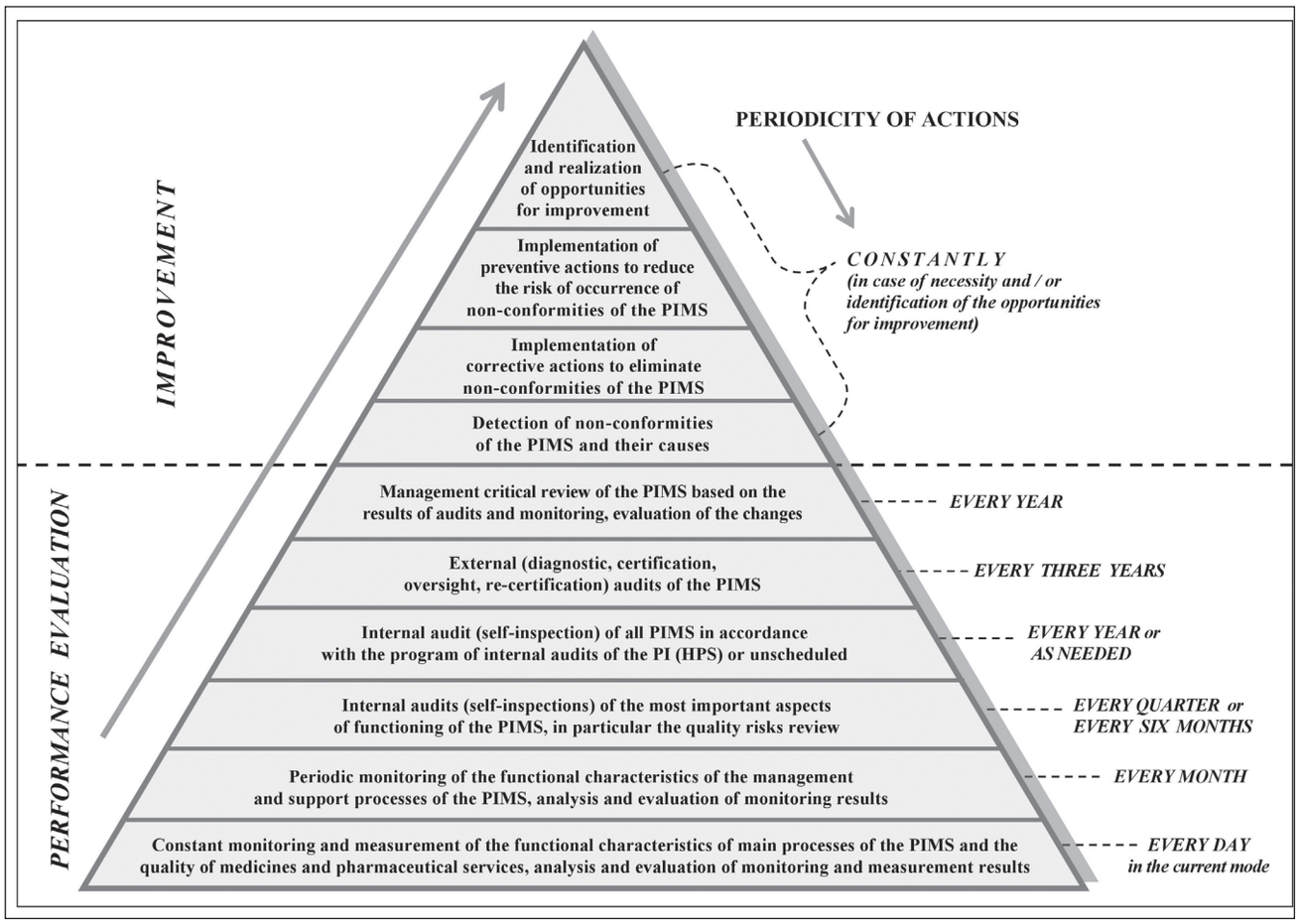

Fig. 3. Structural hierarchical model of performance evaluation and improvement of the pharmaceutical integrated management system.

the planned internal audits (self-inspections) conducted in PI (HPS) in accordance with the approved program (schedule) of internal audits. The most important aspects of the functioning of the PIMS, in particular the quality risks review, are recommended to be audited quarterly or every six months, and audit of all PIMS – at least once a year. If necessary (in case of receipt of complaints, claims, detection of non-conformities, etc.) unscheduled audits may be conducted. It is advisable to involve external experts in conducting diagnostic audits of the PIMS at least once every three years. In this case, the requirements of GxP for outsourcing should be respected [10]. External audits also include certification (primary), oversight and recertification audits carried out by certifying organizations. Based on the results of audits and monitoring, the management of the PI (hospital) conducts a critical reviews of the performance of the PIMS every year, as well as an evaluation of the changes (proposed, implemented). And only after that, there is a transition to the peak of the "pyramid", where there are actions to improve the PIMS, namely: detection of non-conformities and their causes, implementation of corrective and preventive actions (CAPA), identification and realization of opportunities for improvement. These actions are performed continuously whenever necessary and/or as the opportunities for improving the PIMS are identified. The arrow shown in Figure 3 is directed to the top of the "pyramid". This symbolizes the desire of the PIMS to continual improvement. The structurally hierarchical model of the performance evaluation and improvement of the PIMS, together with its description, as well as the general process model of the PIMS and the matrix of responsibilities and authority, should be included in one of the sections or annexes of the Manual for the PIMS.

CONCLUSIONS

Based on the requirements of GxP and international standards in the field of management of quality, ecology, occupational health and safety, social responsibility, a typical process model of the PIMS has been substantiated and developed. The content of each process of a typical PIMS model is described and structured. The expected results (outputs) of the PIMS processes are determined.

The approaches to the regulation and documentation of the PIMS processes in the conditions of functioning of the four-level documented information system are substantiated. A matrix of responsibility and authority of the staff of PI and hospitals within the PIMS is developed. The structurally hierarchical model of the performance evaluation and improvement of the PIMS has been designed and described.

Thus, the above results are the basis for the establishing, regulating and documenting of the PIMS and the development of a system for its performance evaluation and continual improvement. A promising direction for further research is the development of models for concrete processes of the PIMS, as well as the identification of indicators, criteria and methods for the evaluation of their performance.

REFERENCES

1. Kaidalova A.V., Kovalenko S.M., Pidpruzhnykov Yu.V., Chystiakov O.H. Vyznachennia etapiv rozrobky ta vprovadzhennia system yakosti na farmatsevtychnomu pidpryiemstvi vidpovidno do vymoh ISO ta GMP [Determine the phases of development and implementation of quality systems in the pharmaceutical enterprise in accordance with ISO and GMP requirement]. Visnyk farmatsii. 2008; 4:65–67.
2. Svitlychna K.S., Posylkina O.V. Pobudova intehrovanoi systemy menedzhmentu na farmatsevtychnykh pidpryiemstvakh [Construction of an integrated management system at pharmaceutical enterprises]. Farmakom. 2010; 3:88–96.
3. Trokhymchuk V.V., Ubohov S.H. Naukovo-praktychni pidkhody do formuvannia intehrovanykh system upravlinnia na optovykh ta rozdribnykh farmatsevtychnykh pidpryiemstvakh [Scientific and practical approaches to the formation of integrated management systems at the wholesale and retail pharmaceutical enterprises]. Liky Ukrainy Plius. 2018; 2(35):29–33.
4. Suchasna kontseptsiia zabezpechennia yakosti likarskykh zasobiv: kolektyvna monohrafiia [Contemporary concept of quality assurance of medicines: collective monograph]. Vinnytsia: Nilan-LTD; 2018.
5. Kotvitska A.A., Lebedynets V.O. Rehlamentatsiia I dokumentuvannia systemy upravlinnia yakistiu pidpryiemstva z vyrobnytstva likarskykh zasobiv: metod. rek. [Regulation and documentation of the quality management system of the enterprise for the production of medicines: method. rec.]. Kharkiv: NTMT; 2015.
6. Vetiutneva N.O., Ubohov S.H., Zahorii H.V., Pylypenko H.H., Fedorova L.O. Funktsionalna model provedennia vkhidnoho kontroliu yakosti likarskykh zasobiv v aptechnykh zakladakh. Chastyna I [Functional model of incoming quality control of medicines in pharmaceutical institutions. Part I]. Zbirnyk naukovykh prats spivrobitnykiv NMAPO imeni P. L. Shupyka. 2015; 5(24):276–288.
7. Kotvitska A.A., Lebedynets V.O. Modeliuvannia systemy upravlinnia yakistiu ta reformuvannia orhanizatsiinoi struktury pidpryiemstva z vyrobnytstva likarskykh zasobiv: metod. rek. [Modeling the quality management system and reforming the organizational structure of the enterprise for the production of medicines: method. rec.]. Kharkiv: NTMT; 2015.
8. Trokhymchuk V.V., Hudz N.Ia., Ubohov S.H., Zahorii V.A. Upravlinnia ryzykamy dlia yakosti v aptechnykh zakladakh: metod. rek. [Quality risks management of in pharmaceutical institutions: method. rec.]. Kyiv: Ratibor; 2018.
9. Quality management systems. Requirements: ISO 9001:2015 [download: 01.08.2018]; https://www.iso.org/obp/ui/#iso:std:iso:9001:ed-5:v1:en.
10. Podpruzhnykov Yu.V., Nemchenko A.S., Andriukova L.N., Humeniuk N.Y. Systemi kachestva y nadlezhashchye praktyky v farmatsyy: uchebnoe posobye [Quality Systems and Good Practices in Pharmacy: tutorial]. Kyiv: SIC GROUP UKRAINE; 2017.

Authors' contributions:
According to the order of the Authorship.

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Serhii H. Ubohov
Department of quality control and standardization of medicines
of the Shupyk National Medical Academy of Postgraduate Education
9 Dorohozhytska Str., 04112 Kyiv, Ukraine
tel: +380672317656
e-mail: ubogov@ukr.net ; kaf-kontryak@ukr.net

Received: 20.11.2018
Accepted: 30.01.2019