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Ershova Elena Vladimirovna[1]

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APPROACHES TO IMPLEMENTATION OF AN INTEGRATED MANAGEMENT SYSTEM IN THE PHARMACEUTICAL INDUSTRY.

GALENICAL PHARMACEUTICAL PRODUCTION

Abstract: *This article reviews the issues associated with development of an integrated quality management system and its implementation into a galenical pharmaceutical company. Recently, the Russian pharmaceutical industry has been developing extensively: pharmaceutical clusters are being formed, new and innovative technologies are being developed. For the enterprises producing galenical pharmaceutical products, which feature low prices and a high level of competition, development and implementation of management systems is a way to prove their competitiveness.*

The purpose of this article is to review the architecture and the key elements of integrated management systems for pharmaceutical enterprises, develop an integrated management system in terms of the upcoming revision of ISO 9001:2015, as well as to describe the benefits of implementation of such systems.

The presented approach is the result of an educational project implemented within the framework of the MBA programme in "Master of Business Administration (MBA)" in the Federal State Budgetary Educational Institution of Continuing Professional Education Pastukhov State Academy of Industrial Management.

Keywords: *pharmaceutical quality system, integrated management system, GMP (Good Manufacturing Practice), quality, drug safety*

1. Introduction

Drug effectiveness and safety depends on the quality of production processes, quality of the active substance, ingredients and quality of excipients. Currently, the priority areas of the national policy in the field of pharmaceutical drugs include universality, accessibility, quality, effectiveness and safety. The concept which defines the main development trends in pharmaceutical industry of the Russian Federation up to 2020 determines important problems of the industry and strategic solutions of the most important issues.

The main objective of the strategy is

[1] Corresponding author: Ershova Elena Vladimirovna
email: ershova.elena@mail.ru

transition to a new model of development of the Russian pharmaceutical industry, including:

- update of the Russian standards on drug development and production in line with the international requirements;
- raising profile of the domestic pharmaceutical industry in the international market, support of Russian drug export;
- restructuring and technological re-equipment of the Russian pharmaceutical companies;
- creation of a training base for specialists in the pharmaceutical industry, including development and use of new training programmes in accordance with the Russian and international standards.

For the last decade, we've gained enough experience with regard to implementation of different approaches and concepts for development of management systems and quality management in practical activities of the domestic pharmaceutical industry enterprises. Prospects of researches in the field of drug safety and quality control in the process of their production, sale and consumption remain topical. This trend is directly related to the toughening drug market conditions and constantly increasing consumer requirements with regard to special features, properties and characteristics of specific drugs.

To date, the domestic pharmaceutical enterprises have made substantial progress towards implementation and certification of quality management systems, environmental management systems, occupational health and safety management systems. At the same time, implementation and usage of such functionally separate systems at enterprises poses the problem of their coordination, harmonization, i.e. their integration. Various approaches to enterprise management used in the modern theory and practice (combined, integration, marketing, functional, dynamic, regulatory and administrative approaches) are applied for arrangement of individual management systems without regard to their relationships and interaction. Therefore, the issue of implementation of integrated management systems for improvement and harmonious development of organizational management in enterprises is especially acute.

In his book, *Management Challenges for the 21st Century*, Peter F. Drucker outlines: "Operating results of any organization exist outside such organization, in the external environment... While management is aimed at the results that the organization achieves in the external environment. The scope of attention and responsibility of management includes everything that in any way affects performance of the organization and efficiency of its operations: inside and outside the organization." (Drucker, 2000)

Analysis of successful development of pharmaceutical companies of the major economies has shown that to achieve the goals of management development, European quality management methods are used, quality systems in accordance with international standards ISO 9000, GMP, GLP, GCP, etc. are implemented and certified.

The purpose of this article is to analyze adoption of the integrated management system based on ISO 9001:2008, GMP, ISO 14001:2004, OHSAS 18001:2007, etc. by the domestic pharmaceutical enterprises.

The quality management system developed according to ISO 9001 differs from the other systems (ISO/IEC 14001, 2004; ISO/IEC 22000, 2005b; HACCP) primarily by approach targeted at meeting the needs of clients, where other systems also apply to other stakeholders such as government agencies, the public, community, consumer groups and conscious investors. That is why the premises of the implementation of integrated management systems can meet the requirements of many stakeholders (Figure 1). (Nowicki *et al*., 2013)

Diversity of management systems and standards applied for their development relates to various areas of activities: quality, environment, occupational health and safety, social responsibility, etc. In recent years, development of management systems is performed taking into account industry characteristics which affect such areas as safety of drugs, food, power supply, etc.

For the last several decades, Russian pharmaceutical companies and organizations have been extensively involved in implementation of quality management systems. The main motive of the introduction of these systems is improvement of enterprise management quality and ensuring more efficient development.

Quality management today is a hallmark of every pharmaceutical company which enters the market. It combines interrelated processes, human resources, process inputs and outcomes, programmes of continuous improvement. A characteristic feature of the modern approaches to quality management is the fact that the requirements are imposed not directly to product quality but to the management system, which, in turn, is designed to provide a predictable and stable level of product quality, production process and the company operations in general.

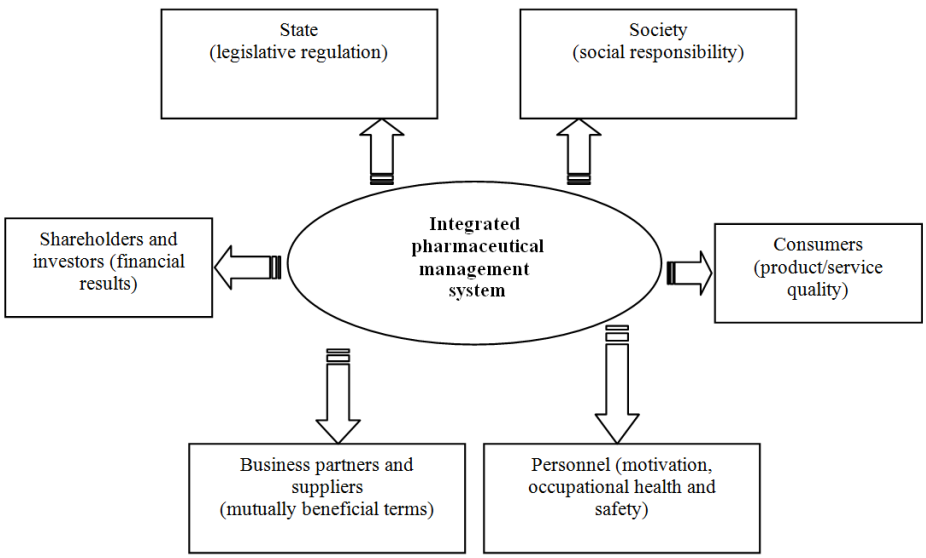

Figure 1. Interaction between the IPMS and stakeholders

A pharmaceutical quality system must ensure that:

- products are designed to meet all requirements and standards;
- all production and control operations are documented in accordance with the rules of the standard;
- responsibilities and authorities are clearly defined;
- activities for production, supply and use of appropriate raw and packaging materials are performed;
- intermediate products and processes, as well as validation, are being monitored;
- supervision and inspection of finished products is carried out in accordance with the standards and the applicable legislation;

- there is a procedure for self-inspection and/or quality audit which provides regular evaluation of efficiency and suitability of the quality assurance system.

2. Characteristics of Integrated Management Systems

A quality management system is a part of a single integrated pharmaceutical company's management system aimed at achieving results in line with the objectives with regard to quality to meet the needs, expectations and demands of customers and other stakeholders. Different parts of the quality management system can be integrated into a single management system which uses common elements. This can facilitate planning, resource allocation, definition of complementary objectives and evaluation of the overall performance of the organization. (Tatarnikov, 2011)

The objective of arranging an integrated management system of a pharmaceutical enterprise is creation of joint documented subsystems for quality management, risk management, product safety, environment safety, occupational health and safety, project management, etc., as well as their adjustment in terms of corporate management of the enterprise. To meet the legal and market requirements, pharmaceutical companies around the world are forced to implement several management systems simultaneously. Otherwise, it's difficult to find trading partners, chances to participate in tenders are quite low, etc.

The term "Integrated Management System" was adopted by the management practices of enterprises in the late 90s of the last century due to the development of systems meeting the requirements of several international standards (both official and those that became de facto) of management system - MSS (Management System Standard). The integration of management systems has become a natural stage of their operation, creating opportunities for sustainable development of organizations all over the globe. (Guseva, 2003)

An integrated management system shall be understood to mean a system that meets requirements of two or more international standards and functions as a single unit.

The study of theoretical material on the issues of disclosure of integrated management system helped formulate a number of definitions of IMS stated by domestic scientists and researchers (Table 1).

Table 1. Integrated Management System Definition

Author	Integrated Management System Definition
Inyats N (Inyats, 2012)	Integration means creating a single organizational structure, in which each sub-system maintains its purpose and integrity
Svitkin M.Z. (Svitkin, 2004)	Integrated Management System should be considered as a part of the general company management that meets two or more international management system standards and functions as a single unit.
Gafforova E.B. (Gafforova, 2010)	Integrative Management System (IMS) of a company is an integrated set of interrelated elements of management (objects, entities, functions), interacting within a unified structure and overall management mechanism to achieve enterprise objectives in meeting the balanced requirements of stakeholders and the ongoing development of the organization.
Gorbashko E.A. (Gorbashko, 2009)	Integrated Management System is considered as enterprise's management system operating in accordance with the requirements of two or more international management system standards.
Vasilevskaya S.V. (Vasilevskaya, 2010)	Integrated Management System is a big target system aimed at performing a specified function needed to achieve business objectives. An efficient IMS is a synthetic system that combines the best implemented approaches, practices and tools.

Table 1. (continued)

Author	Integrated Management System Definition
Katanayeva M.A. (Katanayeva and Bubko, 2005)	Integrated Management System is a part of the general company management that meets two or more international management system standards and functions as a single unit combining interactive and interrelated processes that constitute the essence of company and directs the work of its divisions to achieve the main business goals - making a profit by meeting customers' demands and expectations.
Serov G.P. (Serov, 2009)	Integrated Management System should be considered as a part of company administration, focused on providing high quality products (services) in obligatory and unconditional accordance with the requirements and standards of labor and environmental laws.
Malysheva E.U., Bobrovskiy S.M. (Malysheva and Bobrovskiy, 2012)	Integrated Management System should be considered as the integral part of company's management system functioning as a single unit and meeting the requirements of two or more international management system standards.
A.V. Aleksandrov, N.V. Lyulina, V.D. Barabanova (Aleksandrov *et al*., 2007)	Integrated Management System (IMS) should be considered as a part of company's general management, which meets the requirements of various international management system standards and functions as a single unit. It involves development and implementation of a unified system that provides local development of quality management (QMS), Environmental Management System (EMS), occupational health and safety management, etc.

Galenical pharmaceutical companies tend to establish integrated pharmaceutical management systems that meet requirements of ISO 9000 and the GMP rules.

An integrated management system of a galenical pharmaceutical company should be considered as a system which helps ensure high quality of products, processes and the structure. Therefore, galenical pharmaceutical enterprises need to implement integrated quality systems that meet requirements of the international standards which unite the global experience related to systematic management of quality, environment, personnel, OHS, information support, etc.

The concept of an integrated management system of a galenical pharmaceutical company is presented in Figure 2.

The number of pharmaceutical companies all over the globe that have certified their integrated management system has been growing steadily every year. (Table 2).

When referring to an integrated system, the term quality should be understood to mean the extent to which the actual operation of an enterprise corresponds to the plan (in terms of conformance with the appropriate technical processes, operational and strategic plans, etc.). Thus, any enterprise process, any activity is automatically subject to the management system, and the purpose of this system becomes apparent. It affects all aspects of enterprise management (financial, marketing, etc.), while the concepts of a quality management system and just a management system become interchangeable. Such system is represented graphically in Figure 3. (Ershova *et al*., 2012)

As a result of such integration, we obtain an integral, transparent and efficient management system which covers activities of the entire enterprise: manufacturing of quality and safe products in environmentally benign conditions that are harmless for personnel.

It's quite difficult to create an integrated management system at a galenical pharmaceutical enterprise as shown in Figure 3. Therefore, at the first stage, it is preferable to implement a simpler configuration of the integrated system.

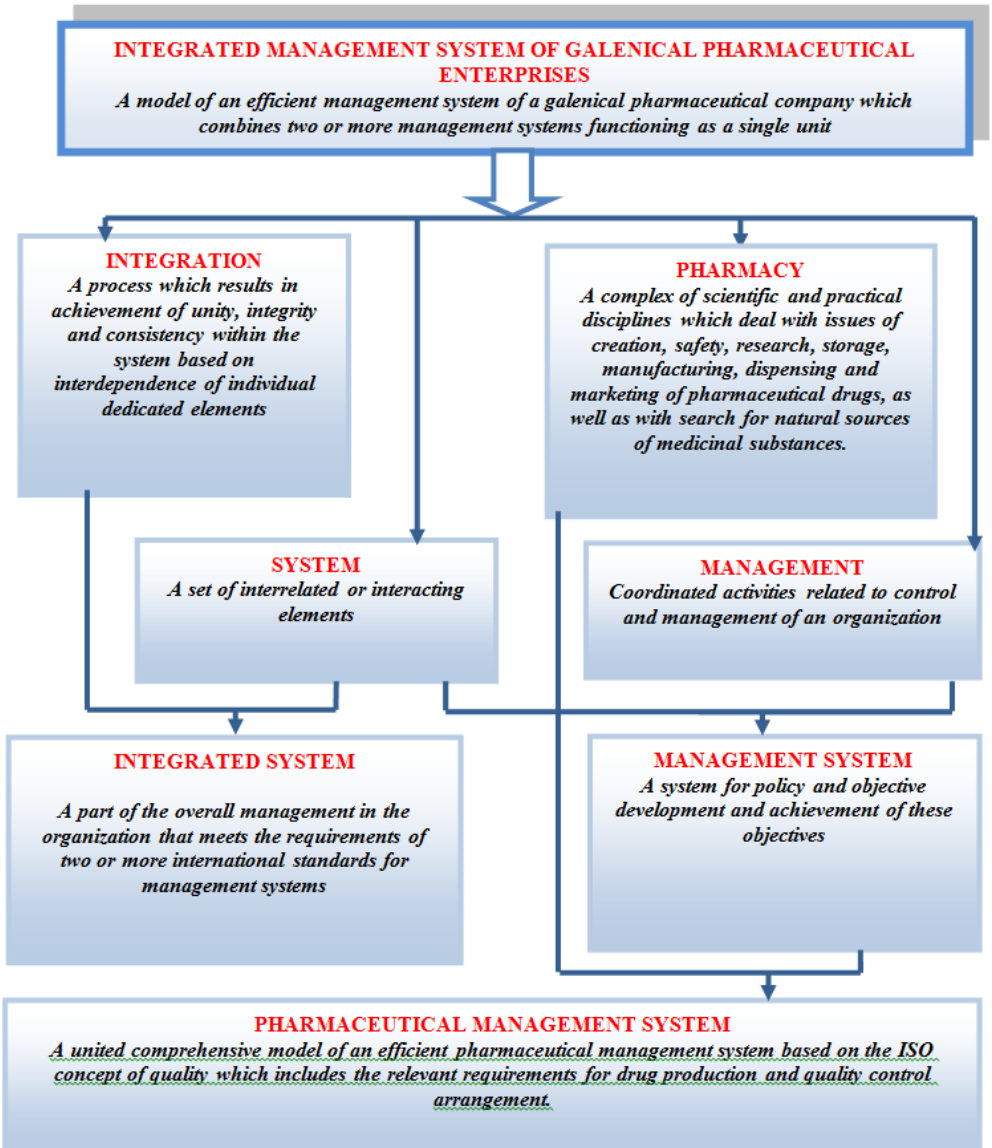

Figure 2. The concept of an integrated management system of a galenical pharmaceutical company

Table 2. The number of pharmaceutical companies over the globe that have certified their integrated management system

Country	Number of enterprises certified	Pharmaceutical enterprises	ISO 9001	ISO 14001	OHSAS 18001	HACCP ISO 22000	ISO 13485	Other
1	2	3	4	5	6	7	8	9
Austria	4022	11	5	-	-	-	4	2
Canada	283	10	4	2	1	-	2	1
China	33326	18	5	1	-	3	1	8

Table 2. (continued)

Country	Number of enterprises certified	Pharmaceutical enterprises	ISO 9001	ISO 14001	OHSAS 18001	HACCP ISO 22000	ISO 13485	Other
Czech Republic	2118	17	7	1	-	-	5	4
France	1068	9	1	1	-	2	3	2
Germany	26988	178	56	21	17	-	42	42
India	4033	25	14	4	4	2	-	1
Poland	1641	2	1	-	-	-	-	1
USA	4903	138	58	18	19	-	21	22
Russia	3521	30	22	5	-	-	-	3
Spain	18387	51	22	15	7	-	2	5

Data obtained from website http://www.iqnet-certification.com as of 01.01.2015

Other regulations: certificates used for certification of pharmaceutical enterprises in these countries

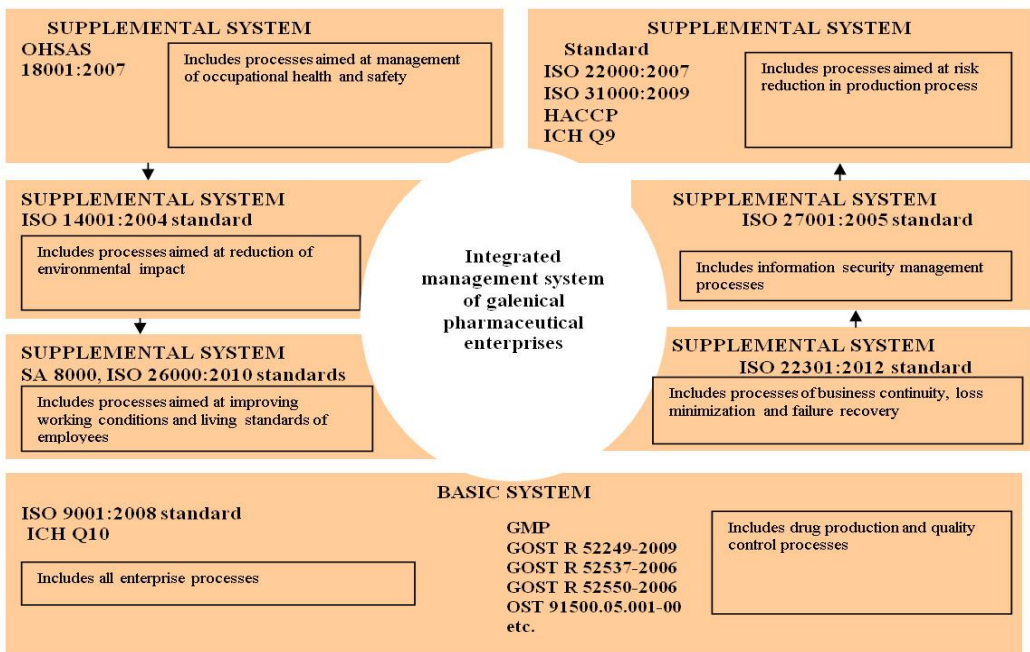

Figure 3. Scheme of the integrated management system of galenical pharmaceutical enterprises

Different parts of quality management systems can be integrated into a single management system which uses common elements. It facilitates planning, resource allocation, definition of complementary objectives and evaluation of the overall performance of the organization (Tatarnikov, 2011). Table 3 presents the main characteristics of integrated pharmaceutical management systems.

Efficiently integrated management system becomes the basis for improvement of performance of the enterprise, allows to work successfully in the future, unites all stakeholders with a common goal, and ultimately, the company operates effectively in a tough competitive environment.

The integrated management system of a galenical pharmaceutical company should be viewed as an integrated system based on the

following standards.

Basic standards:

- ISO 9000 which describes the organizational structure of quality management.
- GMP standards which contain requirements for production and quality control of pharmaceutical drugs for humans and animals. (ICH Q10, Rules for the Organization of Production and Quality Control of Pharmaceuticals (Ministry of Industry and Trade of Russia, 2013), GOST R 52249-2009, GOST R 52537-2006, GOST R 52550-2006, OST 91500.05.001-00, etc.).

Additional standards:

- Standards that establish requirements for the environmental management system (ISO/IEC 14001, 2004).
- Standards that establish requirements for the product safety management system (GOST R ISO 22000-2007, GOST R 51705.1-2001, Quality Risk Management ICH Q9, ISO/IEC 31000, 2009).
- Standards that establish requirements for information security (ISO/IEC 27001:2005).
- Standards that establish requirements for occupational health and safety (OHSAS 18001:2007).
- Standards that help the enterprise develop and implement an effective management system aimed at improvement of working conditions and living standards of employees (SA 8000, ISO/IEC 26000, 2010).

Table 3. Specifications of integrated management systems (Aleksandrov *et al*., 2007)

System type	System characteristic	Key application
1	2	3
Simple system	Arrangement of integrated pharmaceutical management systems in accordance with the requirements of GMP + ISO 9001:2008 + ISO 22000:2005 (HACCP).	Typical for companies producing drugs and dietary supplements.
Complex system Type 1	Arrangement of integrated pharmaceutical management systems in accordance with the requirements of GMP + ISO 9001:2008 + ISO 14001:2004.	Typical for the leading pharmaceutical companies and companies located in metropolitan areas.
Complex system Type 2	Arrangement of integrated pharmaceutical management systems in accordance with the requirements of GMP + ISO 9001:2008 + ISO 14001:2004 + OHSAS 18001:2007.	Typical for companies aimed at export of their products to the EU countries, as well as companies located in large cities (or cities without a buffer zone).
Complex system Type 3	Arrangement of integrated pharmaceutical management systems in accordance with the requirements of GMP + ISO 9001:2008 + ISO 22000:2005 (HACCP) + ISO 14001:2004 + OHSAS 18001:2007 + ISO 26000:2010.	Typical for the leading pharmaceutical companies striving for the highest level of business excellence.

A comparative analysis of standards that are used in development of management systems at galenical pharmaceutical enterprises most often is presented in Table 4.

This table demonstrates that these standards complement each other. They fit well in galenical pharmaceutical enterprises and include quality planning, quality management, quality assurance and quality improvement.

Table 4. Comparative analysis of the mentioned standards used in the development of quality systems of a galenical pharmaceutical enterprise

	ISO 9000 standards	**GOST R 52249-2009**	**ISO 22000:2005**	**GOST R 51705.1-2001**
Standard details	The latest revision of the document contains 4 volumes: 1) General provision and definitions; 2) Requirements 3) Recommendations for operation improvement 4) Guidelines for quality management system audit	One volume. This standard is identical to the EC Guide to Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use as of 31.01.2009, except Annex 20.	One volume. It includes development of HACCP plan, validation, verification and improvement of the food safety management system.	One volume. Background information for development of a HACCP system, critical control points, critical limits.
Principles	Set out in the General Provisions as 8 dogmas (quality management principles): customer focus; leadership of the head; involvement of workers; process approach; systematic approach; continuous improvement of quality; decision-making based on facts; mutually beneficial relationships with suppliers.	The quality assurance system is based on 10 main principles: • all manufacturing processes should be clearly regulated and reviewed; it should be demonstrated that they ensure drug production in accordance with specifications; • validation of production processes and their significant changes is required; • all means to meet the GMP requirements should be provided: trained personnel of relevant qualifications, suitable facilities, equipment and maintenance systems, the necessary starting and packaging materials, approved instructions and rules, appropriate storage and transport conditions; • all instructions and rules should be descriptive, clear and focused;	The food safety management system includes the following generally recognized key elements to ensure safety of food products throughout the food chain up to the stage of end use: • Interactive information sharing; • System management; • Preliminary mandatory measures programmes; • HACCP (Hazard Analysis and Critical Control Points) Principles	HACCP system should be developed taking into account seven basic principles: 1. Identification of potential risk or risks (hazards) associated with food production from receipt of raw materials (breeding or cultivation) to final consumption, including all stages of the product life cycle (handling, processing, storage and sale) in order to identify conditions of occurrence of potential risks. 2. Identification of critical control points in production to eliminate (minimize) the risk or its occurrences. 3. HACCP documents or process instructions should include the limit values of parameters which should be adhered to in order to confirm that the critical control point is under control; 4. Development of a monitoring system that allows for critical points control on the basis of planned measures or observations;

	ISO 9000 standards	GOST R 52249-2009	ISO 22000:2005	GOST R 51705.1-2001
		• operators should be trained in the correct instruction execution; • protocols ensure compliance with all steps of the procedure and the expected quality and quantity of products; deviations are recorded and investigated; • all production protocols, including documentation related to sale of products, allow to trace the history of each batch of products prepared in an accessible and easy-to-understandable form; • the order of sale of pharmaceutical drugs should minimize any risk to their quality; • there should be a system of recalling any batch of products from the market; • complaints related to products and causes of such deterioration should be thoroughly investigated, and measures to prevent their recurrence should be taken.		5. Development of corrective and preventive measures and their application in case of negative monitoring results; 6. Development of verification procedures that should be carried out regularly to ensure functioning efficiency the HACCP system; 7. Documentation of all procedures, forms and methods of data acquisition with regard to the HACCP system.

The mentioned documents evidence that the GMP and HACCP requirements are based on completely different principles than the requirements of ISO 9000, but these standards are complementary. They fit well in pharmaceutical enterprises and include quality planning, quality management, quality assurance and quality improvement.

Due to introduction of requirements of the administrative regulations on drug safety and monitoring of pharmaceutical drugs, the topicality of implementation of a risk management system into pharmaceutical companies becomes apparent. The standards complement each other in the process of development of risk analysis and drug safety.

3. Key elements of the integrated management system

And while quality systems based on GMP, HACCP standards imply analysis of all process operations to check how each one affects quality of the finished product, ISO system does not interfere with this process but performs arrangement of common activities. Therefore, to produce safe and high quality drugs, the enterprise has to comply with the GMP requirements; to ensure the most successful activities of the company in the market, it is necessary to implement ISO standards to manage quality risks; and to determine probability of occurrence of harm and its severity, Hazard Analysis and Critical Control Points system is required.

Figure 4 presents the key elements of the integrated quality system of a pharmaceutical enterprise. It is based on the primary model of a management system for a galenical pharmaceutical enterprise which ensures compliance with ISO 9001:2008, GMP. In addition, it uses some advanced requirements of other standards related to arrangement of an integrated quality system: ISO 22000:2005 (HACCP); GOST R ISO 51705.1-2011; ICH Q9. The management system of a pharmaceutical enterprise can also be easily integrated with ISO 14001, OHSAS 18001 and/or SA 8000 or ISO 27001, etc.

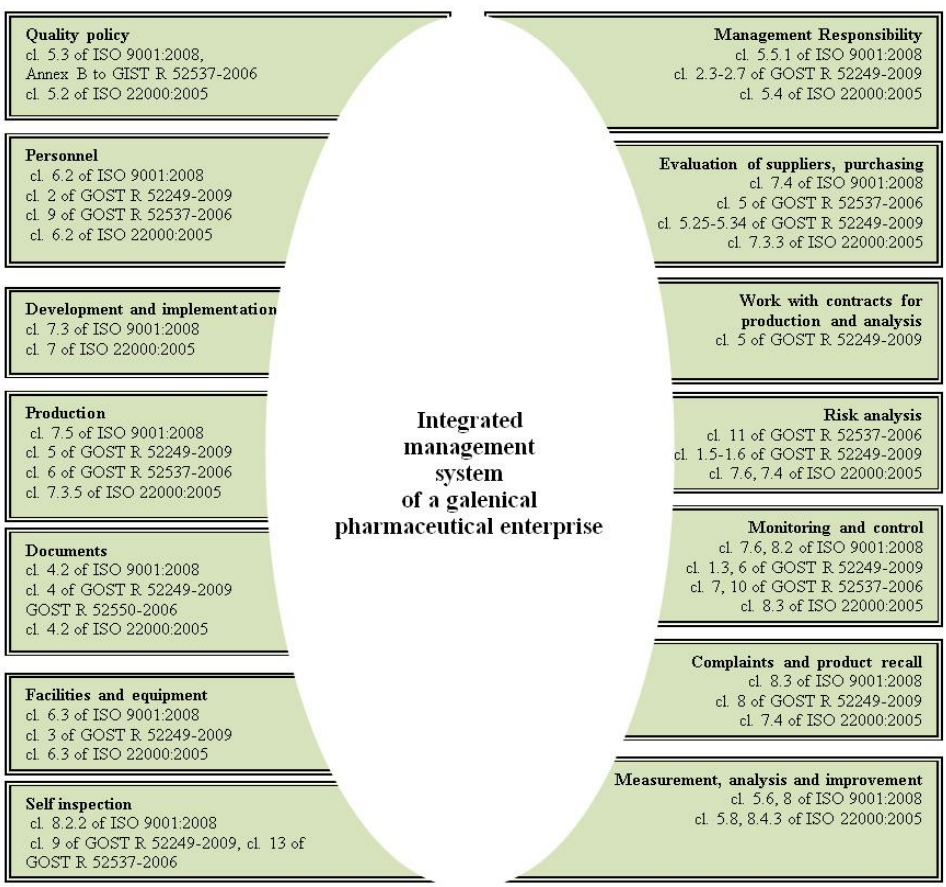

Figure 4. The key elements of the integrated management system of a galenic pharmaceutical enterprise

Figure 4 shows that all of the key elements of the integrated management system (IMS) of a galenic pharmaceutical enterprise are interconnected, and each element is supplemented by requirements of various standards. ISO 9001:2008 standard, GMP rules and HACCP system have the same ideology and complement each other, which is the basis for establishing the IMS.

ISO 9001, ISO 14001, OHSAS 18001 use a PDCA (Aleksandrov *et al.*, 2008) cycle, as well as the ideology of the process approach to enterprise management and uniform quality management principles: leadership of the management, customer focus, process and systematic approach, decision-making based on facts, involvement of personnel, mutually beneficial relationships with suppliers, continuous improvement. Continuous quality improvement is a continuous process of improvement of equipment, materials, tools, approaches to the use of human resources and production techniques. The consistent nature of continuous improvement process is shown by the PDCA cycle. The planning phase of the PDCA cycle is one of the most important.

This stage includes:

- selection of the topical field of activities of the company which needs improvement of quality;
- collection of the necessary information;
- assessment of the current situation;
- identification of priority problem areas;
- analysis of problem areas, including identification of critical cause-and-effect relationships;
- definition of specific targets that would eliminate the problem areas or significantly reduce their negative impact on product quality.

Table 5a, table 5.b, and Table5.c present a PDCA cycle in compliance with standards used in arrangement of an integrated quality system of a pharmaceutical enterprise.

Table 5.a A PDCA cycle in compliance with standards used for arrangement of an integrated quality system of a pharmaceutical enterprise

			GMP		ISO 9001:2008
			GOST R 52249-2009	GOST R 52537-2006	
PLAN **Planning of quality assurance system and its processes, including objectives and resources**	1	Management with the help of objectives and planning	-	4.8 Annex B	5.1, 5.2, 5.3, 5.4
	2	Management system and processes	4	4	4.1, 4.2, 7.1, 8.1
	3	Organizational structure and resources	3	4.5.2	5.5, 6.1, 6.3, 6.4, 7.6
	4	Human resource management	2	4.5.4, 4.5.5, 9	6.2
DO **Implementation of a quality assurance system**	5	Production processes	5	6 Annex E	7.5, 8.2.4, 8.3
	6	Communication with the customer	7	Attachment D	7.2
	7	Development, design and procurement		Para. 8 Annex C C.5, C6	7.3, 7.4

Table 5.a (continued)

			GMP		ISO 9001:2008
			GOST R 52249-2009	GOST R 52537-2006	
CHECK Measurement and assessment of efficiency of the management system and its processes	8	Measurement and analysis of results	1.4	Para. 7 cl. 11 Annex F	8.2.3, 8.4
	9	Result evaluation	-	Annex H	8.2.1, 8.2.2
ACT Continuous improvement of the quality management system and its processes	10	Corrective Actions	-	Annex H	8.5.2, 8.5.3
	11	Continuous improvement	-		8.5.1, 5.6

Table 5.b A PDCA cycle in compliance with standards used for arrangement of an integrated quality system of a pharmaceutical enterprise

			Food safety system		ISO 14001: 2004	OHSAS 18001:2007
			22000:2007	HACCP		
PLAN Planning of quality assurance system and its processes, including objectives and resources	1	Management with the help of objectives and planning	5.2, 5.3	-	4.2, 4.3.3	4.2, 4.3.1, 4.3.3
	2	Management system and processes	7.1	4.9	4.4.6, 4.5.4	4.4.4, 4.4.5, 4.4.6
	3	Organizational structure and resources	6.1, 6.3, 6.4	4.1.4.5	4.4.1	4.4.1
	4	Human resource management	6.2	4.1.4	4.4.2, 4.3, 4.4	4.4.2
DO Implementation of a quality assurance system	5	Production processes	7.1, 7.3.5	4.2.1, 4.2.2, 4.4	4.4.7	-
	6	Communication with the customer	5.6.1	-	4.4.3	4.4.3
	7	Development, design and procurement	7.5	-	4.3	4.3
CHECK Measurement and assessment of efficiency of the management system and its processes	8	Measurement and analysis of results	5.8	4.6, 4.4, 4.5	4.5.1, 4.6	4.5.1, 4.6
	9	Result evaluation	7.3.3, 7.3.4	4.8	4.5.5	4.5.2, 4.5.5
ACT Continuous improvement of the quality management system and its processes	10	Corrective Actions	7.10	4.7	4.5.2, 4.5.3	4.5.1, 4.5.3
	11	Continuous improvement	8.5	4.3.3	4.4.7	4.4.7

Table 5.c A PDCA cycle in compliance with standards used for arrangement of an integrated quality system of a pharmaceutical enterprise

			ISO 27001:2005	SA8000/ ISO 26000:2010	ISO 31000:2009	ICH Q10
PLAN Planning of quality assurance system and its processes, including objectives and resources	1	Management with the help of objectives and planning	5.1, 4.2.1	9.1, 9.5	4.2, 4.3.2, 5.3.4	2.1, 2.2, 2.3
	2	Management system and processes	4.2.1, 4.3.1	-	4.3.4, 5.7	1.8, 1.2, 3.1
	3	Organizational structure and resources	5.2	9.5	4.1, 4.2, 4.3.2, 4.3.5	2.5
	4	Human resource management	5.2	VI	4.3.3	2.4
DO Implementation of a quality assurance system	5	Production processes	4.2.4	-	4.3.4, 4.4.2, 5	1.2, 3.1
	6	Communication with the customer	-	9.7, 9.13	4.3.6, 4.3.7, 5.2	2.7
	7	Development, design and procurement	5.2.1	9.5	5.5.3	3.1.1
CHECK Measurement and assessment of efficiency of the management system and its processes	8	Measurement and analysis of results	4.2.3, 6, 7.1,7.2, 7.3	9.15	4.5, 5, 6	3.2.1
	9	Result evaluation	6	9.4	5.4	1.5.1, 3.2.4 a
ACT Continuous improvement of the quality management system and its processes	10	Corrective Actions	8.2, 8.3	9.11	-	3.2.2
	11	Continuous improvement	8.1	9.1	4.6	1.5.3, 2.6, 3.2.4, 4.1-4.3

An integrated quality management system is an important step in development of management quality control that ensures not only survival of a pharmaceutical company, but also, and more importantly, its success.

4. ISO 9001:2015. Actualization of the management system in the transition to the new standard

ISO 9001:2008 standard, which is one of the basic standards for arrangement of an

integrated management system of a galenical pharmaceutical enterprise, will undergo significant changes in 2015. In September 2015, a new revision of the standard is to be released. Its main advantage will be compatibility with other standards for quality management systems. This standard follows the "high level structure" (sequence of sections, general text, general terminology) developed by ISO to improve compatibility of its international management system standards. ISO 9001:2015 is not just a quality management system standard, it's a tool for promotion of a business to new heights.

This international standard does not include requirements specific to other management systems, such as environmental management, occupational health and safety management or financial management. However, this standard allows an organization to use a process approach together with the PDCA methodology and risk assessment to ensure compliance and integration of quality management systems with requirements of other management system standards in the relevant manner.

The new revision of the standard is aimed at high business performance and can be applied to any organization.

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This international standard does not include requirements specific to other management systems, such as environmental management, occupational health and safety management or financial management. However, this standard allows an organization to use a process approach together with the PDCA methodology and risk assessment to ensure compliance and integration of quality management systems with requirements of other management system standards in the relevant manner.

The new revision of the standard is aimed at high business performance and can be applied to any organization.

The document published in 2010 by Harvard Business School provides an empirical study which examined the benefits of 916 organizations which had implemented ISO 9001 standard versus 17,849 organizations which had not implemented it. (Levine and Toffel, 2010) Some business benefits noted by the organizations that had adopted this standard include higher levels of competitiveness, sales, workload growth and pay rise. In addition, these organizations also noted waste reduction, increase in labour productivity, improvement of the ability of workers to pay more attention to details, as well as improvement of occupational health and safety. Research proves that ISO 9001 offers not only quality benefits. The standard should be viewed as a business management tool which can be employed in the organization to add value, improve performance and reduce risks.

The revised ISO 9001:2015 standard is aimed at strengthening the principles of leadership, risk reduction and the use of the process approach. To comply with this standards, enterprises need to establish a risk reduction process. This standard is closer to the GMP requirements. Risk management process is the most important aspect of work of a galenical pharmaceutical enterprise. Risk management process is a mandatory input source. History knows a lot of examples when you could avoid dangerous situations had they been better managed.

Pharmaceutical practice is no exception. That's how GMP rules appeared.

Arrangement of efficient pharmaceutical manufacturing is a highly difficult task in today's business. In the absence of adequate control, product quality and patient safety may be at risk. Risk management should be aimed at improving the process by reducing the level of risk or by its complete elimination. It is necessary to establish a clear relationship between the principles of risk management, as described in the regulations, and methods used in practical production activities. (Mollah *et al*., 2014)

Risk management to ensure quality is an auxiliary process that accompanies the product throughout its life cycle. The life cycle of pharmaceutical products and examples of risks at each stage of the life cycle are shown in Figure 5.

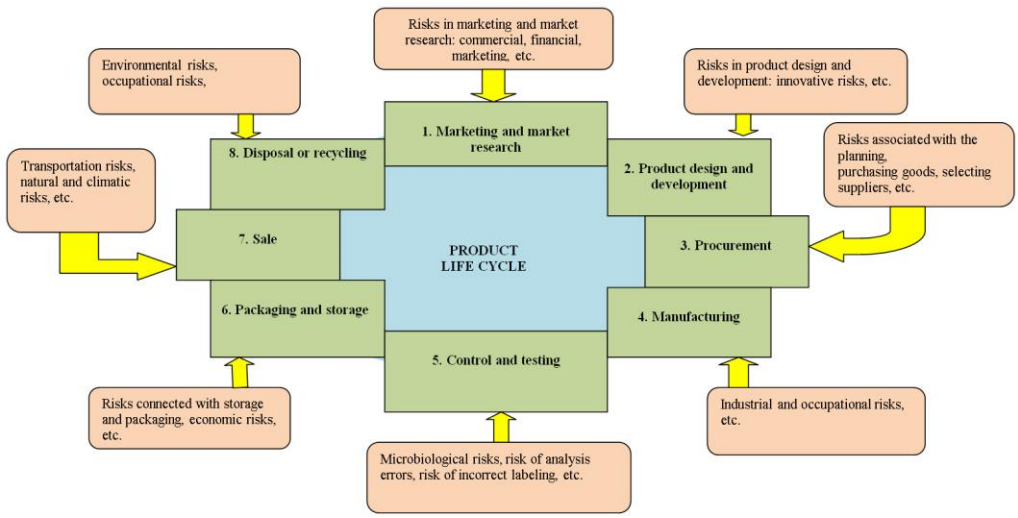

Figure 5. The life cycle of pharmaceutical products and examples of risks at each stage of the life cycle

This figure demonstrates that development of an integrated management system of a galenical pharmaceutical company implies integration of various management standards. Lifecycle processes include not only requirements of ISO 9001 but also requirements of the following regulations:

- environmental management system (ISO/IEC 14001, 2004);
- product safety management system (GOST R ISO 22000-2007, GOST R 51705.1-2001, Quality Rist Management ICH Q9, ISO/IEC 31000, 2009);
- information security (ISO/IEC 27001, 2005a);
- occupational health and safety (OHSAS 18001, 2007);
- regulations to improve working conditions and living standards of employees (SAI 8000, 2007; ISO 26000, 2010).

Implementation of ISO 9001:2015 standard will increase efficiency of the integrated pharmaceutical management system due to the "higher-level structure", which allows for reduction of the number of internal and external communications, unification of management practices, elimination of duplication of processes, documents, positions and department functions.

The main advantages of implementation of an integrated management system into a galenical pharmaceutical company are presented in Figure 6.

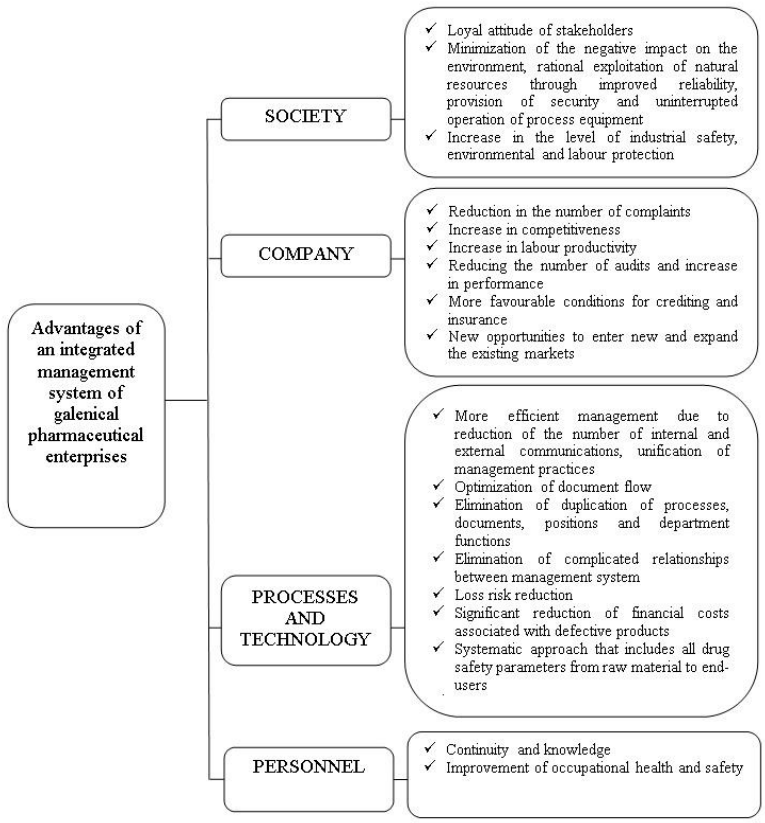

Figure 6. The main advantages of implementation of an integrated pharmaceutical management system

An integrated management system of a galenic pharmaceutical enterprise is an important step in improvement of management quality that helps ensure not only survival of a pharmaceutical company, but also its success.

5. Conclusions

In conclusion, we'd like to note:

1. Arrangement of an integrated management system of a galenic pharmaceutical enterprise is a labour-consuming innovative project aimed at improvement of performance and stability of the enterprise management.
2. Such integrated system requires initial arrangement of some basic QMS in terms of the requirements of ISO 9001:2008 which are complemented and supplemented by the industry requirements of GMP and vice versa, and if necessary, by ISO 22000:20005 (HACCP). After that, the system can be easily integrated with ISO 14001, OHSAS 18001 and/or SA 8000 or with ISO 27001.
3. A properly integrated pharmaceutical management system increases insignificantly the standard structure of the management system documentation, provides increased mobility and adaptability to changing conditions.

4. Incorporation of individual processes during integration (integrated management system control, management of documents, procurement, infrastructure, internal audits) is justified and appropriate.
5. Strong attraction for consumers, investors and other stakeholders.
6. Implementation of an integrated management system provides greater attractiveness of the company for consumers, investors and other stakeholders.
7. Usage of the proposed approaches helps reduce costs for development, operation and certification of the integrated management system

Integrated implementation of a management system provides the opportunity of substantial savings. The result of such work should be arrangement of a process-integrated system of effective management in the field of quality and safety assurance.

The key point is to remember that improvement of the management system cannot be completed. The management system is ready for new challenges and changing conditions and the result is stable and dynamic development of the company.

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Ershova Elena Vladimirovna
Yaroslavl Pharmaceutical Factory Closed Joint-Stock Company,
Rusia
ershova.elena@mail.ru