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RELEVANT PROBLEMS OF THE PHARMACEUTICAL INDUSTRY TRANSITION TO THE INNOVATIVE DEVELOPMENT MODEL

The innovative processes development trends in the global pharmaceutical market and the pharmaceutical market of Ukraine are investigated. It is proved that the pharmaceutical industry of foreign countries is characterized by forming a large diversified innovative manufacturing. The reasons that lead to the development of concentration processes in the area of research and development (R&D) in the pharmacy are analyzed. The main directions of improving innovative activities of the domestic pharmaceutical market entities are identified.

Key words: pharmaceutical industry, pharmaceutical market, innovative processes, research and development (R&D), drugs.

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АКТУАЛЬНІ ПРОБЛЕМИ ПЕРЕХОДУ ФАРМАЦЕВТИЧНОЇ ГАЛУЗІ ДО ІННОВАЦІЙНОЇ МОДЕЛІ РОЗВИТКУ

Досліджено тенденції розвитку інноваційних процесів на світовому фармацевтичному ринку й в Україні. Обґрунтовано, що для фармацевтичної промисловості зарубіжних країн характерне формування великого диверсифікованого інноваційного виробництва. Проаналізовано причини, які обумовлюють розвиток концентраційних процесів у сфері досліджень і розробок (R & D) в фармації. Визначені основні напрями підвищення інноваційної активності вітчизняних суб'єктів фармацевтичного ринку.

Ключові слова : фармацевтична галузь, фармацевтичний ринок, інноваційні процеси, сфера досліджень і розробок (R & D), лікарські засоби.

Problem statement

The need to reduce dependence on imported drugs and identifying key priorities of the pharmaceutical industry in Ukraine are caused by the real political and socio-economic processes: the integration of Ukraine into the global economic community; global structural processes in the economy; low socio-economic efficiency of resource use in pharmacy; the need to improve the efficiency of pharmacological support of the population in Ukraine.

The main goal of Ukraine state policy in the pharmaceutical industry for the period 2011 – 2020 years is the creation of conditions for the change-over to innovation-driven growth model, which have a beneficial effect on the level of pharmacological support of the population, health facilities by high quality and effective domestic drugs with an overall increase of the consumer level to the average European level as qualitative so quantitative indicators. In consequence of realization of the concept for development of the pharmaceutical sector of Health Care in Ukraine for 2011–2020 the share of domestic pharmaceutical products in the total volume of the internal market must be at least 50 % in value measurement.

Analysis of recent research and publications

Problem of innovation management of enterprises and organizations of the pharmaceutical industry is the subject of study of many domestic and foreign researchers. Thus, specific aspects of the organization and management of innovation processes in pharmacy were considered by T.A. Hroshovyi, Z.M. Mnushko, A.S. Nemchenko, M.S. Ponomarenko, O.V. Posylkina, E.P. Piven, M.M. Slobodyanyuk, V.M. Tolochko, V.M. Timanyuk, J.M. Derenskaya, G.V. Kostiuk et al. However, organizational-economic approaches to change-over of the pharmaceutical industry to innovation-driven growth model require rethinking and further testing.

According to expert opinion, in the pharmaceutical industry today, there is a steep fracture associated with a reinterpretation of the traditional business strategy. From the era when pharmaceutical companies received basic income from the sale of a limited number of drugs of mass demand they move into a new era with a new marketing strategy that is based on the production of a wide range of drugs intended for a narrow group of consumers, including drugs intended for people with a certain type of genetic code.

High scientific potential pharmaceutical production and consequently high knowledge content of modern pharmaceutical market determine its high saturation, which complicates implement of drugs and therefore intensifies competitive struggle. This in turn encourages manufacturers of drugs to further intensification of innovation, which is seen as the most important factor of competitiveness.

According to international experience, the key areas of realization of innovation development strategy of the national pharmacy can be:

1. Strategy “build-up”, which involves using its own scientific-technical potential and attraction of foreign experience. A rational combination of results of fundamental and applied science gradually increases the competitiveness of domestic drugs and develops the high technology of their production.

2. Strategy “borrowing” is that, use the scientific-technical capacity of national pharmacy, development of high-tech pharmaceutical production, which had previously been produced in developed countries. In future, with the formation of sufficient innovative capacity it can occur upgraded to increase production of innovative drugs on their own premises.

3. The strategy of “transfer”, which is the use of foreign scientific-technological capabilities by purchasing licenses of high technologies for the production of new generations of drugs that are in demand in foreign countries. Later on in the country sufficient innovative capacity has created and developed that is able to ensure the recovery of the entire cycle from fundamental research and development to manufacturing and sales of competitive pharmaceutical products in the domestic market and abroad.

But it should be noted that today pure form of these innovation-driven growth strategies in the domestic pharmacy may not be realized due to limited financial resources and the lack of material-technical base of pharmaceutical production. This requires study and selection of combinations of elements of different strategies, which initially focused on the current backlog of scientific-research results and capacity utilization of domestic pharmaceutical companies to accumulate investment resources which needed to further the change-over to innovation-driven growth model.

Objectives

The aim of the work is to analyze of trends in the innovative development of pharmaceutical sector in Ukraine and abroad, diagnosing the acutest and unresolved problems that limit the innovative activity of domestic subjects of pharmaceutical market, and grounding directions of building innovation-oriented model of the domestic pharmaceutical industry.

Materials

Today the pharmaceutical industry is one of the most profitable industries (the volume of world pharmaceutical market has reached 910 billion dollars in 2012 and according to the expert forecast of global research firm IMC Health, it will be 1.1 trillion dollars in 2015), but it is also one of the most “costly” and knowledge-intensive industries. According to experts, up to 2/3 of today’s global innovation market (for example, the volume of international market of nanotechnology pharmaceutical development has totaled $ 4.5 billion in 2012, an annual increase in this segment is 45%) is concentrated in the pharmacy. It has estimated “innovation” degree of the state by level of pharmaceutical industry development [1].

Development of R&D-segment of the world pharmaceutical market is very heterogeneous geographically. The United States has palm of victory in amount of pharmaceutical companies (FC)

working in R&D-segment in 2012. It contains half of all R&D-activities in the world of pharmacy. It is predicted that in the near future costs for development of new drugs in the U.S. amount to about 83 billion dollars. The share of European countries includes 26 % of pharmaceutical companies which working in R&D-segment.

Under conditions of increasing competition on the part of generic drug pharmaceutical industry is faced with the need to develop a new strategic direction of development – biotechnology, which gives companies the long-term perspective. According to the report "Biotech 2013-Life Sciences: Capturing Value", in recent 3 years, the companies of biotech sector are in advance of the pharmaceuticals companies in terms of investment in research and development [1].

In world practice, the lion's share of investments which focused on finance of developments in the biotechnology field is accumulated by developed company, e.g. the United States. Thus, biopharmaceutical companies in the U.S. have 907 drugs and vaccines to treat more than 100 diseases at the stage of the development. In this case, 465 R&D-products are designed to treat 10 major chronic diseases (such as diabetes, rheumatoid arthritis, Alzheimer's disease, chronic obstructive pulmonary disease, etc.) [6].

Government initiatives in the United States are aimed to support companies developing new biological drugs. For this reason, period of exclusive data for such drugs is 12 years and for synthetic drugs – 5 years in the U.S.

The results of analysis of the major therapeutic areas which attractive for R&D-segment of the pharmaceutical and biotech markets in 2012, give reason to believe that the absolute leader is the group of anticancer drugs. This is due to significant advances in molecular biology, which has opened opportunities for the development of new approaches to treat patients with cancer, which account for 13 % of deaths worldwide each year.

According to the analytical information of company "FactSet Research Systems Inc.", which have analyzed indicators of 98 biotechnology and pharmaceutical companies, whose shares are listed on stock exchanges in the U.S., the average cost of developing of the original drug is estimated at 4.2 billion dollars. In addition to the above the level of return of R&D-investments has decreased from 10.5 % in 2010 to 4.8 % in 2013. Thus investing in R&D-development of innovative drugs is one of the longest lasting and unreliable investments in high technology, which, however, in the best of circumstances, promise unprecedented financial success.

A list of the most promising, according to the analytical and investment companies, R&D-projects in pharmacy in 2013 are shown in table 1 [6].

Table 1

The most promising R & D-projects in pharmacy in 2013

Pharmaceutical company	Drug	Indications for use	Peak sales potential, billion dollars
Gilead Sciences Inc.	Sofosbuvir	Hepatitis C	7,4
Bristol-Myers Squibb	Nivolumab	Immunotherapy of melanoma	2,9
Pharmacyclics and Johnson&Johnson	Ibrutinib	Non-Hodgkin lymphoma	3*
Roche	MPDL3280A/RG7446	Immunotherapy of cancer	2,5-3
Vertex Pharmaceuticals	VX-809 и VX-661	Mucoviscidosis	4-6
Merck&Co.	MK-3475 (lambrolizumab)	Inoperable and metastasizing melanoma	3
Sanofi and Regeneron	Alirocumab (SAR236553/REGN727)	LDL cholesterol	3,7
AbbVie	ABT-450/r + ABT-267 + ABT-333	Hepatitis C	1
Roche and Biogen Idec	Obinutuzumab (GA101)	Chronic lymphocytic leukemia	2
Eli Lilly	Dulaglutide	Diabetes	1,7

* Drug will can be able to enter the top 20 orphan drugs in terms of global sales in 2018

As studies have shown, for the pharmaceutical industry of foreign countries is characterized by formation of a large diversified innovation manufacturing. The main driver of global innovation process in

pharmacy are large multinational companies (MNCs). That is to say TNCs with significant intellectual and financial resources could provide a breakthrough in technology. In the struggle for technological lead pharmaceutical MNCs actively use patents, know-how, trademarks, copyrights.

However, the undeniable fact is that the effectiveness of the innovation process in pharmacy can be ensured only under the optimal combination of small businesses and large companies. It can maintain high rates of scientific-technical progress.

However innovative technologies and products are used in the presence of the qualified experts, sufficient financial resources and efficient sales organization. These conditions are provided primarily by the concentration, cooperation and mergers of pharmaceutical companies (PC). Therefore, one of the major trends that define the structure of the global pharmaceutical market in the last 20 years is the consolidation of subjects of pharmaceutical industry. Today concentration processes are specific for the pharmaceutical industry, objectively are determined by such factors.

1. Leading FCs inject abnormal capital to conduct R&D to ensure its competitiveness.

2. Increase of sales effectiveness by reducing the costs associated with their organization. There is a clear correlation between the size of PC and the efficiency of its sales departments, which is defined sales volume attributable to one salesperson. PC with sales of less than 1 billion dollars on average is characterized by sales per salesperson in the range of 0.5 to 1 million dollars. While in companies with a turnover of around 10 billion dollars this figure could exceed $ 2 million dollars.

3. Significant costs of PC in alliance with biotech companies. Such costs are constantly increasing. Today PC are actively buying cost base technologies and expert evaluation of new areas such as genomics, proteomics and bioinformatics.

4. Size of PC influences the efficiency of scientific-research activities through synergy of merging of technologies, joint research and others. To be noticed is that large companies are able to fully amortize the cost of platform technology, and some platforms have a “high threshold payback”. In addition, a broader research portfolio reduces the risk of instability research-production chain and gives companies a greater chance of casual discovery.

5. Large sizes allow leading PC better use of their research and production chains for quicker product launch in the global market. The average time of the market launch of new drugs for the 6 largest companies is an average of 25 months, for companies which rated sales rank from 7th to 13th place – 39 months.

6. Significant potential licensing sales that have large PC. License sales are gaining overweigh for the pharmaceutical industry: today their volume is 30 % of the turnover of pharmaceutical companies.

Today in Ukraine more than 500 active foreign PC have launched, which brought to the domestic market highly effective strategy for its development, is proven in many countries. They set up their own infrastructure, using advanced marketing technology. All this has contributed to the intensive increase of drug import in Ukraine.

The world’s practice clearly shows that economic power of competing organizational and economic structures should be comparable. Therefore, the Ukrainian pharmaceutical industry will be able to withstand the attack of foreign corporations only on the condition that she restructures in powerful scientific and financial formation that has partnered with governmental authorities and uses benefits under the law. Thus, the creation of powerful pharmaceutical innovation clusters may be an important factor in competition with major foreign pharmaceutical corporations in the home market of Ukraine.

Such formations have greater opportunities in terms of solution of institutional and structural reforms based on the integration of financial and industrial capital, the development of relations as touching property management, new organizational-economic market structures, oriented on upgrade of scientific-technical and export potential of pharmaceutical industry and synergies businesses.

An innovation-driven growth model of domestic pharmaceutical industry is also possible on conditions that the state will assume the main burden of launching innovation cycle in the field, followed by increase of R&D refinancing at the expense of industry.

The key of successful implementation of this model is:

– resolve staffing issues;

– creating a market of innovative projects (layer of small innovative enterprises between science and industry);

– a massive increase in public and private investment in import substitution R&D;

– major technology modernization and development of pharmaceutical production according to international standards;

– increasing the level of innovation activity of pharmaceutical market subjects;

– the use of foreign scientific, technical, technological and production potential by attracting foreign direct investment in the production and development of innovative drugs.

Implementation of innovative scenario requires at the first stage active investment in upgrading science labs and strategic pharmaceutical companies. In the future, a mechanism of refinancing R&D funded by pharmaceutical manufacturers will be triggered.

In Ukraine, despite the presence of a number of innovative development programs, the share of innovative enterprises, expenditure on basic and applied research in the field of drugs, which are conducted at research institutions and universities in recent years have a strong tendency to decrease (table 2) [2].

Table 2

Financing of scientific and technical activities in pharmacy and related sciences, thousands hryvnia

	2005		2010		2011	
	Allo	Financed from the budget	All	Financed from the budget	All	Financed from the budget
All	5160399,8	1711174,5	8995893,9	3704338,6	9591349,5	3859679,0
Chemical	102363,2	63854,5	267666,3	199060,0	305994,4	212784,0
Biological	172957,4	133755,1	396769,8	296876,1	554832,4	314966,3
Medical	166610,6	97157,4	406646,0	264907,2	462883,0	293036,6
Pharmaceutical	27826,0	4057,4	17928,3	13779,4	23807,4	18240,3

This situation in a certain way determines that proportion of generic drugs versus innovative products in Ukraine is only 90 %, for comparison, in Russia – 80 % USA – 25 % Germany – 35 % UK – 55 %, Poland – 61 %, Japan – 22 %, France – 35 % [3].

Today creating of domestic innovative drugs in the main is financing at the cost of leading Ukraine PC (CJSC Farmak, CJSC "Pharmaceutical firm "Darnytsia", Arterium Corporation, PJSC SIC "Borshchahivskiy Chemical Pharmaceutical Plant", Pharmaceutical company "Zdorovie" Ltd et al.).

Analysis of strategies of PC functioning suggests that new approaches to enterprise development require shifting the focus of management actions to increase the share of innovative products such as the patenting of new substances, original and combination drugs.

Patenting of drugs allows domestic PC to take up positions in the domestic market of Ukraine, to effectively use existing intellectual capacity, to help lift the prestige of the national pharmacy. One should also note the following competitive advantages of domestic agents: affordability, quality and efficiency at which they are not inferior to foreign PC, optimal selection of excipients, in some cases, a decrease toxicity, side effects and improve efficiency. Finally, competitive domestic drugs are thousands of jobs for Ukrainian companies.

But even taking into account the contribution of domestic PC in create drugs, according to the State Enterprise "State Expert Center", the number of domestic registered drugs in Ukraine in comparison with foreign drugs is only 39 % (3716 vs. 9337 to 11.11.2013; table 3) [4].

Table 3

Registration status of domestic and foreign drugs in Ukraine

Group of drug	28.12.2010		29.11.2011		1.05.2012		11.11.2013		12.01.2014	
	Manufacturers of drugs									
	domestic	foreign	domestic	foreign	domestic	foreign	domestic	foreign	domestic	foreign
In bulk	137	942	156	930	162	1053	213	824	215	765
FPPs	3041	8447	3037	8020	2953	10585	3150	7140	3241	7004
substance	204	1020	220	1061	203	1269	238	1175	246	1187
pre-packing in bulk	296	108	299	113	296	409	15	377	14	381
All	3678	10517	3712	10124	3614	9702	3616	9516	3716	9337

FPPs – finished pharmaceutical products

These data indicate of a weak innovation activity of domestic PC. As a result, Ukraine is losing human resource who carry out research and development. In particular, these problems become apparent when comparing the performance of innovation activities in pharmacy in Ukraine with those of Europe, the USA and Japan.

There are various mechanisms by which in the developed countries the state is involved in creating a favorable climate for innovation in the pharmaceutical industry: state funding of projects and organizations, support links between the public and private sectors in research and innovation area, funding the creation of elements of industrial and technological infrastructure (technology parks, incubators, offices to promote the technology, etc.), tax incentives that encourage innovation and so on.

Well known international experience of implementing of joint projects are funded by various sources, resulting in a reduced risk for each individual investor. For example, the seven leading European pharmaceutical manufacturers (Bayer, AstraZeneca, Sanofi, Lundbeck, Merck, UCB, Janssen) announced February 7, 2013 the launch of a joint global project to develop a new generation of drugs under the Innovative Medicines Initiative. Budget Consortium European Leand Factory for the next five years is 196 million euros. About 80 million are provided by the European Commission, the rest – the consortium partners. The project will bring together around 30 partners, including 23 leading European universities, smaller pharmaceutical and research companies and various public, private and civil society organizations.

Traditionally abroad under the Ministry of Health, there are institutions that have significant budgets and the need to organize the financing of projects of R&D for new drugs: National Institute of Health USA (National institutes of health research), the Canadian Institute for Research on health, National Institute of studies in Health UK. In France, the main public institution of research in the health sector is the National Institute for Health and Medical Research, which reports to the Ministry of Health and the Ministry of Research, and coordinates the activities of 10 institutions in various therapeutic areas.

Despite the different approaches, these institutions have in common is that they play a key role in their countries in identifying priority areas of research in the development of new drugs. In their areas of expertise includes the creation and support infrastructure of research centers, forming a pool and competitive selection of researchers, allocation of finance for research and others. Researchers have access to appropriate information resources, advice on design research and allow for the exchange of ideas within the various working groups. The ultimate goal is to develop evidential base (preclinical and clinical) with regard to practice of decision-making at various levels of the health system.

It was established that in Ukraine incentives for intensification of scientific research in pharmacy is practically absent. Among the causes of this situation are:

– inadequate funding of research institutions and universities engaged in development of new drugs;
– lack of complex state programs for finding, developing and implementing innovative products involving scientists as research institutions, universities and enterprises;
– insufficient number of grants, scholarships and awards for young scientists in the field of pharmacy;
– lack of interest in large Ukraine PC with financial assets, but have no scientific schools to solve problems in the field of innovative products and advanced technologies for their production;
– lack of public funds to finance basic and applied research in pharmacy and others.

The way out of this situation is to adopt the draft amendments to the Law of Ukraine "On scientific and technical activities", which contains proposals on new articles 40-45, 48, who legally aimed at enhancing scientific and technical activities (table 4) [5].

Table 4

The provisions of the draft of Ukraine law "Amendments to Ukraine Law "On scientific and technical activities" which are oriented to activation of scientific research

Article of a law	Basic provisions
Article 40. Credits and tax levers of state regulation in the field of scientific and technical activities	State shall apply: tax incentives; financial and credit incentives to businesses and organizations providing preferential loans for research, science and technology (experimental) development
Article 42. supporting funds of scientific and technical activities	Financial support is provided by grants to research institutions, universities, research teams, other legal entities and individuals

Table 4 continued

Article of a law	Basic provisions
Article 44. State fund for applied research	The State Fund for Applied Research has created for grant support for projects of conduct applied research, scientific and technical (experimental) developments are aimed at the development of new competitive technologies and/or their components, to create new and modernization of existing production for the needs of enterprises
Article 45. Nongovernmental funds for grant support research and scientific and technological development	Non-government capital grant support of research and scientific and technological development – social-oriented fund has established by the entity (or entities) business to conduct systematic philanthropy grant support of specific research and scientific and technological development
Article 48. Creation of public research institutions, universities III - IV accreditation levels of business partnerships for the use of intellectual property rights	Public research institutions, state universities III – IV accreditation levels are entitled to be shareholders of joint stock companies and limited liability companies whose activity is the practical use of intellectual property rights, property rights are held by these institutions, universities III – IV accreditation levels

Conclusions

1. Change-over of the domestic pharmaceutical industry to innovation-driven growth model is aimed at organizing the production of high-tech pharmaceutical products, it will significantly enhance its competitiveness and contribute to compete with foreign pharmaceutical manufacturers, both at domestic and foreign markets. This will give new impetus to the development of domestic pharmaceutical science, and thus improve the efficiency of pharmacological support of the population in Ukraine.

2. Enough highly skilled staff who are able to carry out basic research using high-tech and high-performance equipment and advanced techniques of molecular biology, to have created skills commercialization of scientific results and their implementation in practice will be needed for succeed at goal.

3. The choice of strategy of change-over of the domestic pharmaceutical industry to innovation-driven growth model must take into account both existing material-technical resources and the capacity of pharmaceutical market to change-over to an innovative way of development. So, the best at this stage is the development of national pharmacy for investment scenario with subsequent change-over to innovation.

Prospects for further research

Adoption of the draft amendments to the Law of Ukraine "On scientific and technical activities" creates the necessary conditions for a revival of innovation processes, including the pharmaceutical industry.

1. Лукьянчук Е. Наиболее перспективные препараты, разработанные в 2013 г.: эра блокбастеров продолжается? / Е. Лукьянчук // Еженедельник "Аптека". – 2014. – № 2 (923). – С. 16–17. 2. Наукова та інноваційна діяльність в Україні: статист. Зб. / Державний комітет статистики України. – К.: Держкомстат, 2012. – 305 с. 3. Пашков, В.М. Інноваційна складова ринку лікарських засобів: проблеми господарсько-правового забезпечення / В.М. Пашков. – Аптека. – 2013. – № 19. – С. 10–12. 4. Посилкіна О.В. Патентознавство : навчальний посібник для студентів вищих фармацевтичних та медичних навчальних закладів / О.В. Посилкіна, О.В. Літвінова, Т.А. Грошовий. – Харків: НФаУ, 2013. – 272 с. 5. Семиноженко В.П. Пояснювальна записка до проекту Закону України "Про внесення змін до Закону України "Про наукову і науково-технічну діяльність" [Електронний ресурс] / В.П. Семиноженко. – Режим доступу: civic.kmu.gov.ua/.../attach-2471-382724662.d. – Заголовок з екрану. 6. Щеголь, С. Кто у штурвала? R&D-активность фармрынка в 2012 г. / С. Щеголь // Еженедельник "Аптека". – 2013. – № 22 (893). – С. 5–6.