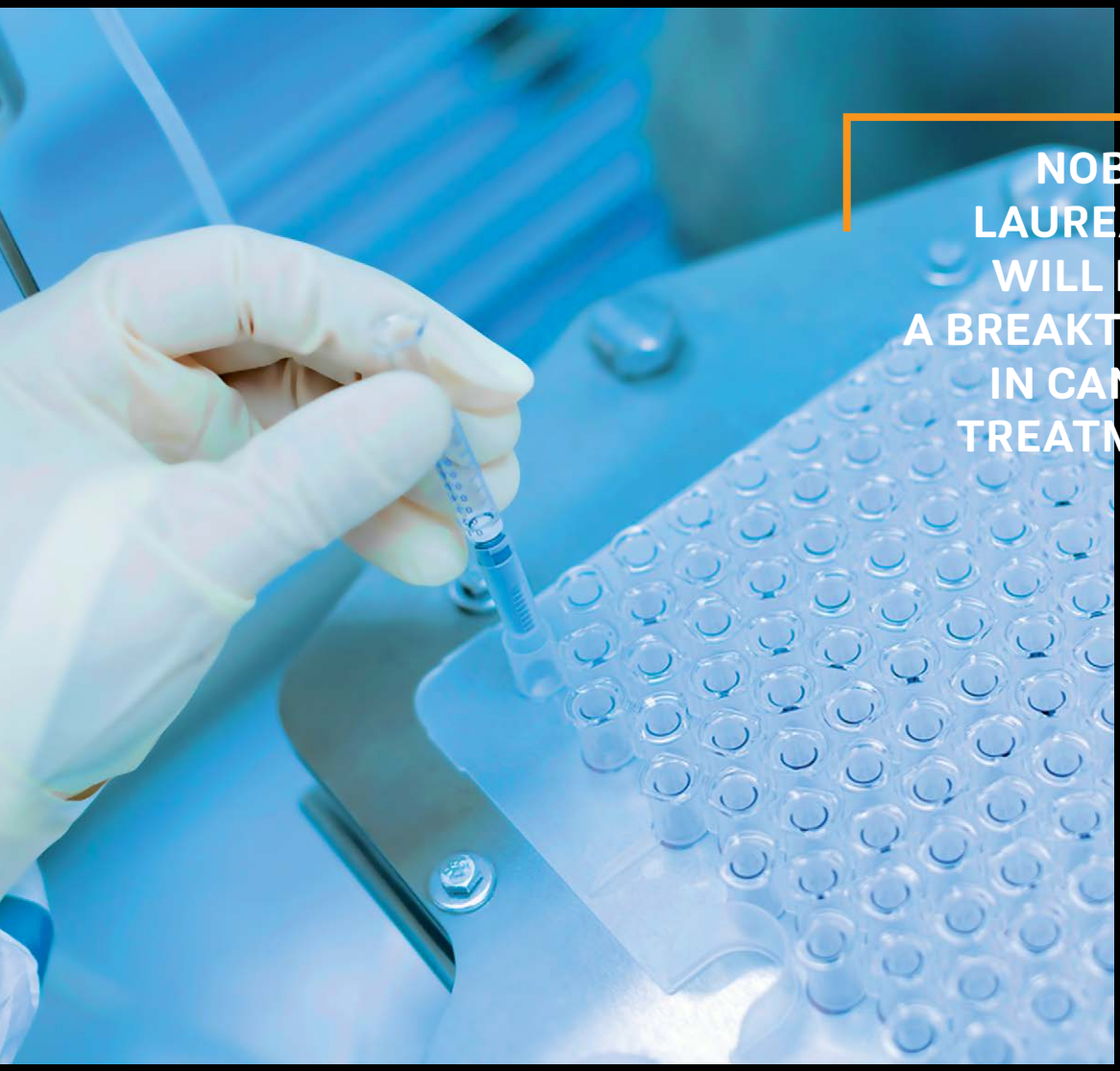

NOBEL LAUREATES: WILL IT BE A BREAKTHROUGH IN CANCER TREATMENT?

Clear imaging: achievable for CT and MRI due to contrast media

Biohacking: how to live 120 years

Farmak

04 / 19

SCIENCE INSIDE

EDEM — Enjoy Life Without Allergies!

Short instruction for the medical use of the medicinal products Edem, Edem Rino:

1. EDEM. Dosage form: tablets, syrup. **Active substance:** desloratadine. Each tablet contains 5 mg of desloratadine, 1 ml of syrup contains 0.5 mg of desloratadine; **ATC code** R06A X27. **Indications.** Relief of symptoms associated with allergic rhinitis, urticaria. **Method of administration.** The medicinal product is prescribed for adults and children aged over 12 years at a dose of 5 mg (1 tablet) once daily with or without food. Children aged 6 to 11 months: 2 ml of syrup once daily; children aged from 6 to 11 years: 5 ml of syrup once daily. **Contraindications.** Hypersensitivity to active substance or to any of the components of the medicinal product or loratadine. **Side effects.** Gastrointestinal disorders: Dry mouth, diarrhoea, abdominal pain, nausea, vomiting, dyspepsia.

2. EDEM RINO. Active substances: 1 ml of the medicinal product contains 2.5 mg of phenylephrine, 0.25 mg of dimetindene maleate; **ATC code** R01A B01. **Indications.** Symptomatic treatment of colds, nasal congestion, acute and chronic rhinitis, seasonal (hay fever) and non-seasonal allergic rhinitis, acute and chronic sinusitis, vasomotor rhinitis. **Posology and method of administration.** For adults and children aged over 6 years, one spray in each nostril 3-4 times daily. The treatment duration should not exceed 7 days and depends on the course of the disease. **Contraindications.** Hypersensitivity to any component of the medicinal product. Due to phenylephrine content, this medicinal product, like other vasoconstrictor agents, is contraindicated in atrophic rhinitis, as well as in patients taking monoamine oxidase inhibitors (MAO) or have been taking them over the previous 14 years. **Side effects.** Mild temporary local nasal mucosa reactions (burning sensation or dryness) are possible. **MA No. UA/8360/01/01 dated 02.04.2015; MA No. UA/T46/01/01 dated 21.10.2013; MA No. UA/14054/01/01 dated 01.12.2014**

Adults and children aged over 12 years:[1]

1 tablet/day

Adults and children aged over 6 years:[2]

1 spray in each nostril 3-4 times daily

Children:[1]

6-11 months — 2 ml once daily
1-5 years — 2.5 ml once daily
6-11 years — 5 ml once daily
Children aged 12 years and older:
10 ml once daily

SELF-TREATMENT MAY BE HARMFUL FOR YOUR HEALTH

Drug advertisement. Be sure to read the instructions and consult your physician prior to use it.
Manufacturer Farmak JSC 63 Frunze Str., Kyiv, 04080, Ukraine. Tel.: + 38 (044) 496-87-87, HYPERLINK "mailto:info@farmak.ua" info@farmak.ua UKR/PROMO/10/2018/EDE/DM/004

Dear friends,

if you hold this journal in your hands, it means that Farmak has opened its doors to you and can confidently consider you to be its friend. For us, this word has many aspects, and its meaning is unchanged, because our mission is to make people healthy, and we have been a faithful friend of the society for almost 100 years.

Farmak has undoubtedly transformed into a successful, modern, transnational company during this time. As a leader in the Ukrainian market, we export medicinal products to over 20 countries and strive to increase our presence in the international markets.

Due to our professionalism, responsibility and understanding, we are attractive to partnership and cooperation. We have been cooperating with international financial institutions, globally known manufacturers, suppliers, contractors, partners for many years. It may take a lot of time to list our friends around the world. Our spotless reputation opens different doors to us, and it is a matter of honour and dignity for us to justify your confidence. Therefore, we allow no compromises and we always fulfil our obligations.

We do our business honestly and transparently. This is our contribution to the development of Ukraine. And the fact that Kyiv remains the centre of our production proves our belief in the bright future of our country.

Farmak has always been and remains an intellectual pride of the country, a driver of the pharmaceutical industry and an opportunity for Ukrainians to obtain affordable, high-quality and efficient modern medicinal products. This is our path, our social mission and part of our sustainable development.

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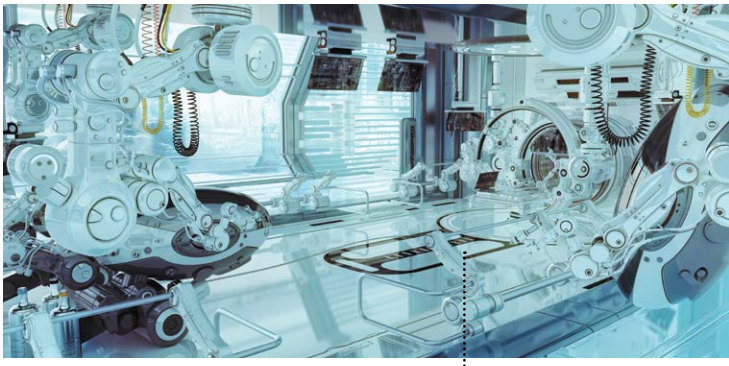


34 NEW ERA IN UKRAINIAN DIAGNOSIS

SCIENCE INSIDE
CORPORATE EDITION OF FARMAK JSC

Founder: Farmak JSC
Head of the project: Olena ZUBAREVA
Curator of the project: Yana CHERNIUK
Production: AMEDIA GROUP

Cover photo: from the archive of Farmak JSC

Adults and children from 2 months[1]

APSORBIN SACHET

Modern intestinal sorbent with unique properties [2]

- Absorbs and removes from the body exo- and endotoxins of various ORIGIN[1,2]
- Has a high sorptive capacity [2]
- Promotes the restoration of microbiocenosis and intestinal barrier function[2]
- The use of Absorbin sachet in complex therapy can reduce the duration of the acute period of allergic dermatitis and urticaria[2]

CONVENIENT DOSAGE FORM

PLEASANT TASTE

AFFORDABLE PRICE

[1] Package leaflet for dietary supplement Absorbin sachet
'Possibilities of modern enterosorption in therapy of children with syndrome of endogenous intoxication on the background of allergic dermatoses", O.M. Okhotnikova, Yu.R. Chernysh, 2017
It is not a medicinal product. Dietary supplement advertisement
UKR/PROMO/11/2017/APS/PB/004
Manufacturer Farmak JSC, 63 Frunze Str., Kyiv, 04080, Ukraine.
For additional information please call +38 (044) 496-87-87, e-mail: info@farmak.ua

The rapid development of the pharmaceutical industry requires constant development from all its participants. Farmak, which has taken the leading position in the Ukrainian market* since 2010, is constantly improving.

EXECUTIVE DIRECTOR OF FARMAK JSC VOLODYMYR KOSTIUK TELLS ABOUT SOLUTIONS WHICH BECOME THE MOST INNOVATIVE.

Stepping into the future

* In monetary terms, according to ProximaResearch.

PHARMACOLOGICAL AND ECONOMIC ASPECTS TO THE CORE OF THE SYSTEM MOVEMENT WITH THE TIMES

During a short period of time, Farmak made a transformation from a chemical and technical plant into an innovative company. A modern production was developed in Ukraine. The European-level medicinal products manufactured both for the domestic market and for more than 20 countries of Europe and CIS are the same high-quality medicinal products. Nowadays Farmak is a 7-hectare concentration of innovations that make up the arsenal of the modern pharmaceutical industry!

STRATEGIC PLANNING

Characteristic feature of Farmak is not just to track innovations, but also to implement them into its own production. It takes 4–6 years for a generic company to develop a medicinal product, so the planning step in Farmak is 5–10 years.

IMPLEMENTATION OF LARGE-SCALE PROJECTS

Currently, we have modern laboratories and R&D complex. These are intellectual clusters, which focus on creating new technologies, optimizing them, integrating quality with the use of modern analytical equipment. Each of Farmak projects is significant, that is whether they involve the global study of the original molecules for such medicinal products such as Amizon, Efial and other medicinal products, or cooperation with international companies.

OBTAINING NEW EXPERIENCE

Cooperation with foreign companies always results in new technologies and new knowledge. At the beginning of the 2000s, Farmak began to produce insulins using Eli Lilly (USA) technology. Farmak is the second company in the world to which the technology of insulin cartridges manufacturing, that is a complex of complicated technologies, was transferred. The company accepted the offer of European partners for development and production of the radiopaque contrast agent Magnegita in accordance with the European requirements 12 years ago. Farmak has rebuilt the main processes and fully adapted to new regulatory requirements. The product has been successfully launched in the European market, and now we are manufacturing another product — Dotagita using such model.

EXPANSION OF PRODUCTION

We felt the need to expand the production of finished medicinal products and active pharmaceutical ingredients (APIs). Therefore, it was decided to create a new department for the production of APIs in Shostka.

The new production was created on the basis of the Industrial Park "SVEMA" and occupies 4 hectares. Currently it is a modern complex that meets the requirements of GMP and contains manufacturing sites, quality control laboratories and logistics center.

The department has an autonomous and universal laboratory. All processes of chromatographic, analytical,

microbiological laboratories and the sector of stability are concentrated in one complex. The updated logistics station has 536 pallet places of 500 kg or 268 tons of different raw materials and substances. There is also an engineering and technical workshop with a steam generator, two powerful oil-fired compressor plants, an adsorption generator, an own power unit, water-heating boilers.

Modern water treatment systems are operated at the production facilities. We have even an aquarium with fishes, to which water comes after cleaning.

FARMAK IS THE SECOND COMPANY IN THE WORLD TO WHICH THE TECHNOLOGY OF INSULIN CARTRIDGES MANUFACTURING, THAT IS A COMPLEX OF COMPLICATED PROCESSES, WAS TRANSFERRED.

RATIONAL INVESTMENTS

Since 1995 Farmak has invested USD 239 million in modernization and innovation. In 2017, investments of Farmak JSC in development and modernization amounted to UAH 486 million. In 2018, their volume grew by more than a third — up to UAH 638 million. The main project of this year was «Solid medicinal products – 2».

Its implementation will make it possible to increase the total capacity for the production of tablet medicinal products by almost two times – up to 3 billion dosed units per year. In addition, the Company will continue to invest in modernization and equipment of active production, information technology, laboratories of the quality control department and biotechnology laboratory. We put special emphasis on the development of new medicinal products. In total, the Company has more than 10 serious capital investment projects at the various stages of implementation.

DEVELOPMENT OF BIOTECHNOLOGIES

To date, the Company has equipped a biotechnological laboratory that makes it possible to simulate the process of obtaining active substance — the main component of a medicinal product that has therapeutic properties. The amount of investments in this project is UAH 60 million.

We expand our competencies in biotechnology and are actively working on obtaining our own genetically engineered proteins for therapeutic purposes. We plan to thoroughly characterize these substances, make finished dosage forms from them, conduct non-clinical and clinical studies. Then we will be able to talk about view establishment of biotechnology production. This is a prospect for at least 5 years.

EXPANDING THE HORIZONS

Since 2017 Farmak has been a participant of the Horizon 2020 program and is involved in VAHVISTUS and ORBIS projects in Research and Innovation Staff Exchange (RISE). This is a unique opportunity to be familiarized with new developments of scientific laboratories of EU countries. In cooperation with the Institute of Organic Chemistry of the Academy of Sciences of Ukraine, the Department of Chemistry of the University of Helsinki (Finland), the Institute of Polymers, Composites and Biomaterials, Pozzuoli (Naples, Italy), Farmak has created VAHVISTUS Consortium. Its partners include the National Institute of Amazonian Research (INPA, Brazil), the University of Ibn Tofail (Kenitra, Morocco) and the University of Florida (Gainesville, USA). ORBIS Consortium, in addition to Farmak, includes the University of Poznan (Poland), the University of Warsaw (Poland), the University of New Jersey (USA), the University of Dublin, in particular the Trinity College (Ireland), Department of Pharmacy of the University of Helsinki (Finland). Zentiva pharmaceutical company (headquartered in Prague, Czech Republic) and Applaid Process Consulting (Ireland) became the industrial partners of the consortium. Farmak also cooperates with all the relevant universities in Ukraine. Currently, Farmak employs 35 candidates and 5 doctors of sciences.

EFFECTIVE MANAGEMENT

People are one of the Company's core values. First of all, we take care about our employees. The company provides the opportunity for constant development. Motivation Cafeteria operates at the company: everyone can choose an individual program. The company regularly sends employees for training, both in Ukraine and abroad.

We invite international experts to Farmak. In this way, we take care about professional and career development for employees. More than 80% of managerial vacancies are filled by own candidates.

PRESENCE IN THE INTERNATIONAL MARKET

The strategic goal of the Company is to increase the presence of Farmak in the European market. By 2020, we plan to increase the portion of exports to 40%. We consider the possibility of buying a pharmaceutical company in Europe. Poland was the first step, and now we are considering other countries.

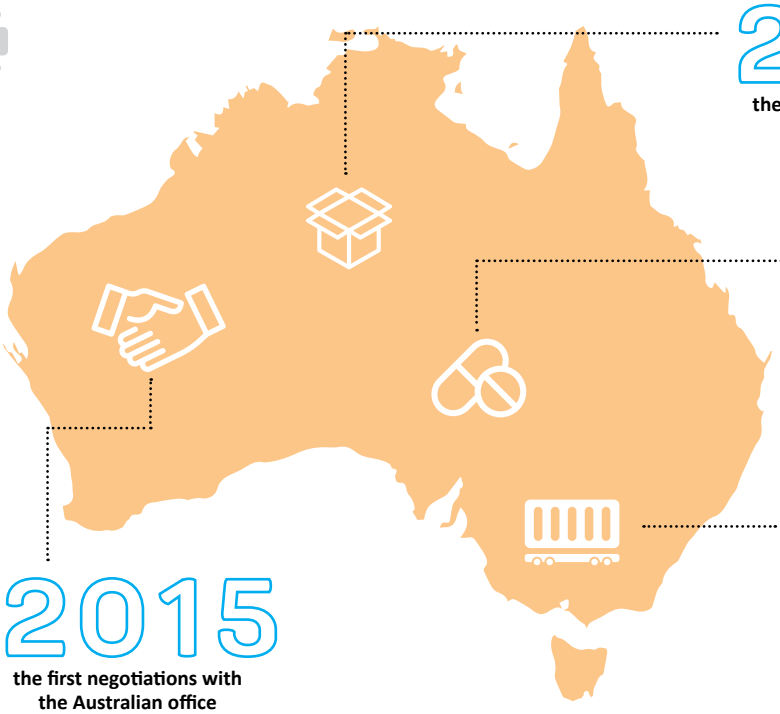
QCD Laboratory

Farmak is almost the only Ukrainian pharmaceutical company, which managed to establish trade relations with the state of the fifth continent. **THIS DIRECTORY IS THE LOWEST DEVELOPED IN UKRAINE.**

ENTRY INTO THE AUSTRALIAN MARKET:

Farmak expands the export map

The Australian market is well-regulated — at the level of the USA and EU. This entry has become a strategic step, because the certificate of this country contributes to the establishment of export relations with other countries.



2017
the first batch was shipped to Australia

2019
medicinal products for the total amount of more than USD 800 thousand were exported to Australia

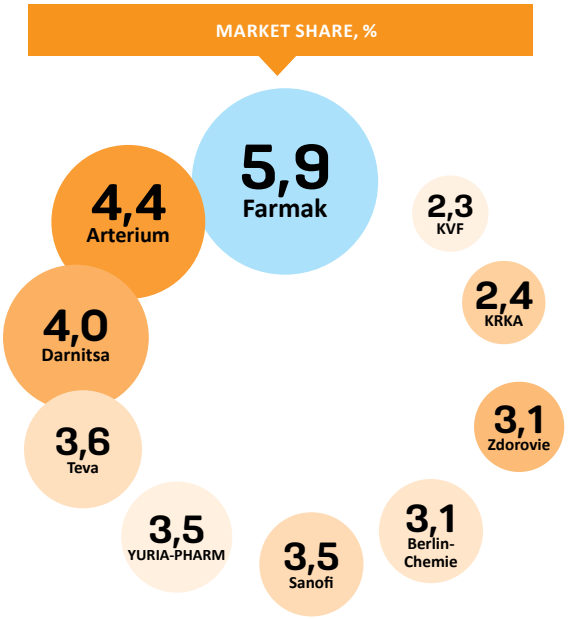
2023
the target is to boost the export to Australia up to 40%

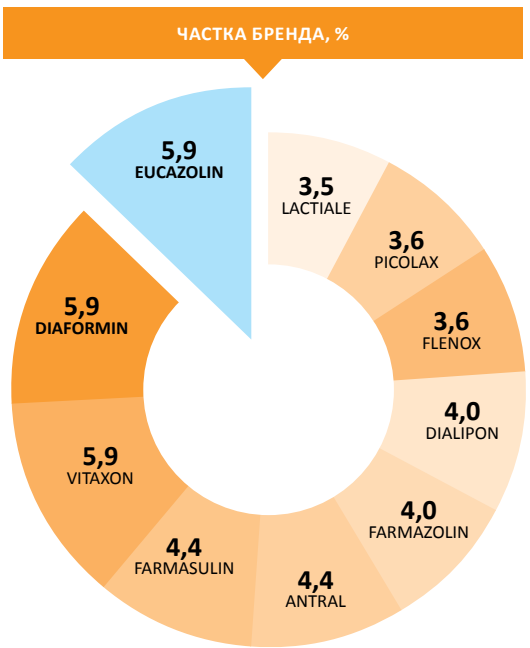
2015
the first negotiations with the Australian office

MOST OF ALL UKRAINIAN PHARMACEUTICAL MANUFACTURERS EXPORT TO CIS COUNTRIES. ABOUT 70% OF SALES ACCOUNT FOR THESE COUNTRIES.

RELATIONS WITH AUSTRALIA ARE LESS DEVELOPED. UKRAINIAN EXPORT MAKES UP LESS THAN 1%, SO NEW HORIZONS ARE OPENED TO FARMAK WHEN ENTERING THE NEW MARKET.

Leadership in figures





TOP 10

COMPANIES IN THE MARKET OF MEDICINAL PRODUCTS IN 2018

LEADERS ACCORDING TO AMOUNT OF SALES, MLN UAH

5 018 Farmak

3 704 Arterium

3 371 Darnitsa

3022 Teva

2 999 YURIA-PHARM

2 964 Sanofi

2 614 Berlin-Chemie

2 610 Zdorovie

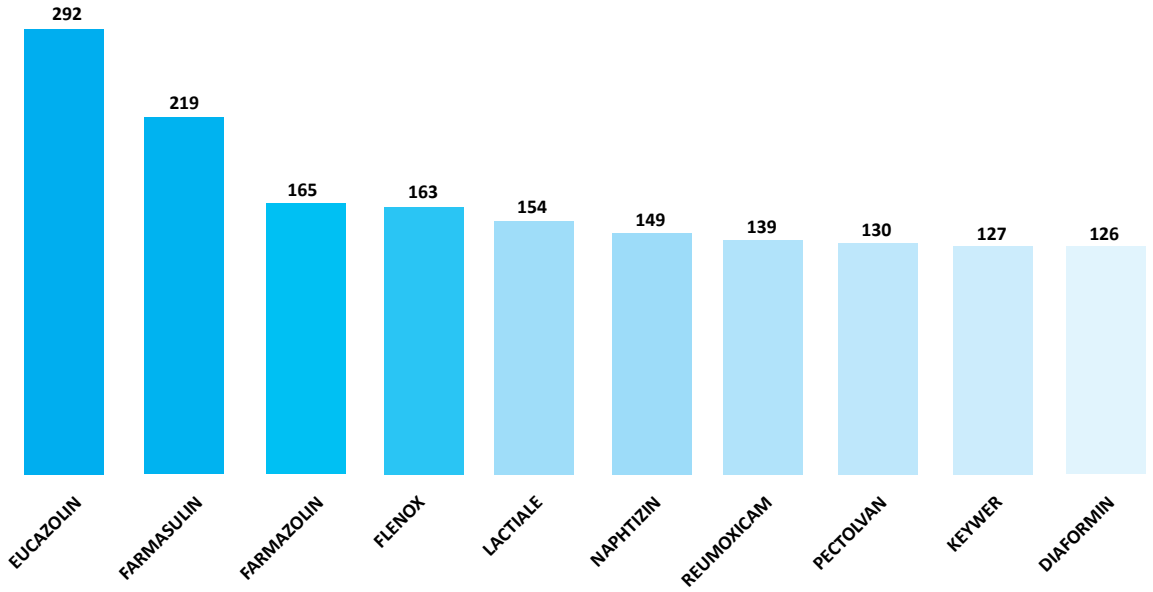
2 024 KRKA

1966 KVF

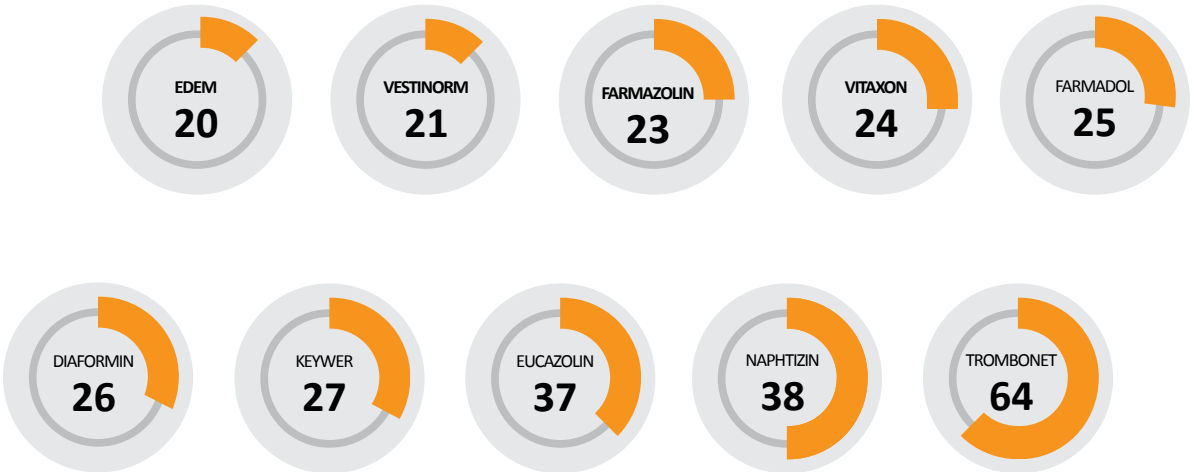
TOP-10

FARMAK IN THE PHARMACEUTICAL MARKET IN 2018

LEADERS AMONG MEDICINAL PRODUCTS ACCORDING TO AMOUNT OF SALES, MLN UAH



SALES GAIN, %



Conformity – proven!

Technical Director of Farmak JSC Andriy GOY is convinced that **BIOEQUIVALENCE AT FARMAK IS A STANDARD OF ETHICAL BUSINESS AND EXCELLENT EVIDENCE-BASED EFFICACY.** State authorities did not demand such studies 10 years ago, however the Company looked to the future, and now Farmak has a great experience in proving compliance with the original medicinal products

■ ***Please tell how relevant was the decision to prove bioequivalence and what was the reason for that?***

At that time, the need to confirm the bioequivalence of the generic to the original medicinal product through pharmacokinetic studies — the study of «conduct» of the active substance in the blood circulation system, became apparent in the West. In Ukraine, almost nobody knew about this. Then it was enough for the pharmaceutical company, which brought the generic medicinal product to the Ukrainian market to prove the equivalence to the original through clinical studies in several dozen volunteers by the method of symptomatic comparison. However, Filia Ivanivna Zhebrovska, Chairman of the Supervisory Board of Farmak JSC, always set a very high standard. The decision to prove the bioequivalence of new and existing medicinal products manufactured by Farmak was exceptional. It was a unique event for the whole industry — nobody had ever made a decision to invest in such a complicated and very long process, and the regulator had no such requirements. But our company has always differed with its far-sightedness. The step of planning in Farmak is 5–10 years. This makes it possible to maintain leadership positions in the Ukrainian market and be among the first to introduce modern technologies in production.

■ ***Looking back, what results of the bioequivalence project do you consider most important?***

This project became a driver that brought our technological skills in the production of solid dosage forms to the level of gold standards. A far-sighted decision has become an impetus for a technological jump and a rise in the culture of generic medicinal product development to a new level. After all, it is not just an analysis of the active substance on the background of excipients —necessary and complex bioanalytics, taking into account numerous variables, and very sensitive methods. For example, sometimes we work not with nanograms, but with trace amounts of substances!

We need to reproduce the entire target biopharmaceutical profile in the medicinal product that we offer. And

Farmak is a generic company, and due to bioequivalence, we can prove that our medicinal product has exactly the same effect as original. It also gets into the blood of the patient and has an identical effect on the body. 10 years ago, we became pioneers and today there are almost 30 medicinal products manufactured by Farmak with proven bioequivalence. No other company in the Ukrainian market can boast of such number.

this means that a lot of details must be estimated: not only the molecule itself, but also the construction of its crystals, the degree of shredding of particles, etc. And today, what was new to us 10 years ago became an everyday practice.

We are confident that we offer generic medicinal products that have been proven to have the same effect as the original. Doctors ascertain this each time and treat our products with great respect.

The project involved the proving of bioequivalence of both new medicinal products and those that the Company has already released. Were there any difficulties during such dramatic transformations?

There was situation when the processing of a medicinal product, that seemed to be known, required more efforts than the creation of a generic. In any case, bioequivalence studies make the process of developing medicinal products longer. It can take a year, one year and a half, or even more. It happened that in order to reach the final equivalence, dozens of batches were needed...

Fortunately, the process was smooth in about 80% out of hundreds of cases. However, the team is not ashamed of those 20% when the desired result could not be reached at the first attempt and it was necessary to improve the technology, make changes to the medicinal product composition or change the design of the studies. There were temporary failures and the fact

that we talk about them confirms the lack of falsifications, the transparency of our actions and the credibility of our approach. Until we received positive results with all the necessary statistical certainty, with full compliance with all European guidelines and criteria, we did not submit a medicinal product for registration.

Certainly, the changes affected not only the process of development of solid medicinal products, but also production capacities?

In order for the laboratory prototype to maintain all the necessary parameters in the batch production, the Company created a pilot site on which the technical equipment is presented in miniature. This makes it possible to simulate and develop the technological process in every detail. Further, compliance with the requirements on a commercial scale is ensured by GMP standards. So, another crucial parameter is added to the art of searching, science of modelling and practical orientation of engineering, — the reproducibility of the excellent result. Due to the modern equipment installed at Farmak, it is possible to manufacture 200 tablets per second – and each of them fully complies with the target profile.

And all these achievements became possible due to the efforts of the employees…

A team working on bioequivalence study is a really cool team!

Pass-through washing machine

Due to it, our Company has created a complete scientific and practical centre. Doctors, candidates of sciences — our employees, work in pure science and at the same time direct its achievements to the solution of applied issues. In comparison with all scientists who work on theoretical intelligence, our colleagues are distinguished by the skill of multidisciplinary thinking: the ability to design a technological process, manage the cost of components. And I am convinced that the potential of our team will grow in the future.

Farmak is a generic company. What gives reasons to call it innovative?

Currently Farmak has a powerful technological park, most of the modern processes used in the pharmaceutical industry are implemented at the industrial level. Therefore, its task is to be the leading centre of pharmaceutical technologies and to rapidly adapt innovations that are not protected by the patent, to reduce their cost due to sophisticated solutions and make modern pharmacological therapy affordable. This is a very significant contribution to the health care system of Ukraine, as well as those countries where Farmak is represented.

ESTESIFIN

TREATMENT OF FUNGAL INFECTIONS OF NAILS AND SKIN[1,3,4]

- **Wide spectrum of antifungal action on nails[1,2,3,4]**
- **Convenient application on the nail and under the nail due to the dropper[1]**
- **A big bottle that will provide a long course of nail fungus treatment[1]**

1 - Instruction for medical use of the medicinal product Estesifin solution.
2 - Naftifme: A Review" Aditya K. Gupta, Jennifer E. Ryder, and Elizabeth A. Cooper, 2008
3- Instruction for medical use of Estesifin spray
4 - Instruction for medical use of Estesifin cream
Name of the medicinal product: ESTEZIFIN
Naftifine
Pharmaceutical form: cutaneous solution, cutaneous spray, cream.
Active substance: naftifine hydrochloride. ATC code D01A E22.
INDICATIONS.
Topical treatment of fungal infections caused by pathogens sensitive to naftifine: fungal infections of the skin and skin folds; interdigital mycosis; fungal infections of the nails (onychomycosis); cutaneous candidiasis; tinea versicolor; inflammatory dermatomycosis with or without itching.
Posology and method of administration.
Apply to the affected skin surface once daily after cleaning, covering 1 cm of skin. Duration of treatment: in dermatomycosis - 2-4 weeks (if necessary - up to 8 weeks); in candidiasis - 4 weeks: in case of infections of nails - up to 5 months. In fungal diseases of nails it is recommended to apply it 2 times daily. Prior to the first application, remove the affected part of the nail. In mycoses of the external auditory passage - treatment for at least 14 days. Treatment should be conducted via insertion of cotton turundans into the ear, moistened with a solution, for 5-8 minutes 1-2 times daily. To prevent relapses, treatment should be continued for at least 2 weeks after the disappearance of the main symptoms of the disease.
Contraindications.
Increased sensitivity to naftifine or propylene glycol. The medicinal product should not be applied to the wound surface. Do not use for eye treatment.
Side effects.
In rare cases, local reactions may occur: dry skin, redness and burning sensation, erythema, itching, local irritation. Side effects are usually reversible and do not require the discontinuation of treatment.
For detailed information on the medicinal product, read the instruction for the medical use of Estesifin
Manufacturer.
Farmak JSC, 63 Frunze Str., Kyiv, 04080, Ukraine. For additional information please call: +38 (044) 496-87-87, e-mail: info@farmak.ua.
MA No. UA /14783/01 /01 dated 14.12.2015, MA No. UA /15944/01 /01 dated 28.04.2017 MA No. UA/15499/01/01 dated 03.11.2016.
UKR/PROMO/01/2019/EST/DM/001

Drug advertisement. Be sure to read the instruction and consult your physician prior to use it.

SELF-TREATMENT MAY BE HARMFUL FOR YOUR HEALTH

HOPE OF THE WORLD: healing innovations

Targeted fight against cancer, fundamentally new «objects» in testing medicinal products, the chance to withstand antibiotic resistance, **«SMART» TABLETS ARE ONLY SOME EXAMPLES OF HOW THE NEW TECHNOLOGIES WILL CHANGE THE PHARMACEUTICAL INDUSTRY.**

1 FIGHTING CANCER: HITTING THE TARGET

This is targeted therapy that gives hope for the facilitation of the fight against cancer. Such molecular targeted therapy is expected to be not only more effective than previous methods for cancer management, but also less risky for healthy cells. The key to the effectiveness of the method is the use of chemical substances targeted on a specific protein or enzyme responsible for the malignancy of a healthy cell.

Targeted therapy is a kind of pharmacological therapy for cancer. It can be used both independently and in combination with other therapies — in particular cytotoxic therapy. Targeted therapy, as one of the types of molecular medicine, directly affects the action of molecules that contribute to carcinogenesis. Thus, it is able to block the growth of malignant cells. Currently, targeted therapy has given promising results in the treatment of prostate cancer, breast cancer, lymphomas, melanoma and other oncological diseases.

The targeted accuracy of the effect is also important in the diagnostic aspect — it is about the emergence of a direction such as theranostics (from «therapy» and «diagnosis»). It means the creation of unique medicinal products, which will become the method of early diagnosis and at the same time — treatment. A new approach to the creation of pharmaceutical compositions is foreseen, which will be delivered «as targeted», in particular, by constructions based on the proteins of the superfamily of immunoglobulins or photoluminescent nanoparticles.

Laboratory of Farmak JSC

2 YOU ARE ON A CHIP: INNOVATION IN BIOENGINEERING

"Organ-on-a-chip" is the latest technology, which will allow investigating the course of the disease and testing new medical products without the involvement of animals and humans in the near future. But these are not all benefits. It will be possible to create the whole human body model, which will help to better understand the needs for nutrition and treatment, to anticipate possible allergic reactions. And the potentially significant role of innovation in the treatment of drug dependence is also mentioned.

The "organ-on-a-chip" technology is being actively studied at the Wyss Institute, an interdisciplinary institute at Harvard University specializing in bio-inspired studies. In fact, they develop bioinspiratory materials, which can be used further, in particular, in medicine.

"Organ-on-a-chip" is a tool for growing cell cultures, which simulates the functioning of organs or systems of organs of living creatures. The creation of models of lungs, liver, heart, kidneys, brain, as well as immune and reproductive systems on a chip has already begun. At the moment, researchers are working on developing models of human diseases that make it possible to identify new ther-

apeutic and clinical biomarkers, will help in the work on vaccines and will make a step forward in the development of personalized medicine.

Comparing the latest development with traditional research methods, its greater efficiency is obvious. The main disadvantages of traditional animal testing are: firstly, clinical studies last for a long time — often for years; secondly, a lot of money is spent, moreover, it is not always justified. But most importantly is, perhaps, the fact that the results of animal testing still cannot always be successfully projected to the human body. There are more disadvantages than benefits. Not to mention the ethical component of animal testing. Many of them become victims of long, expensive and not always effective experiments. Fortunately, the era of the latest technologies allows moving forward to more effective and ethical methods.

3 NEW ANTIBIOTICS: SEARCH FOR AN EFFECTIVE WEAPON AGAINST MICROBES

The end of the nineteenth century became a crucial point in the history of medicine: we began to use antibiotics. Pathogenic microorganisms, however, managed to "grow up": antibiotic resistance is increasing, so humanity requires new tools for fight. It's time for another revolutionary invention. The new type of antibiotics teixobactin, which was discovered several years ago, is potentially able to influence those gram-positive bacteria that are not influenced by traditional medicinal products.

FARMAK TOP INNOVATIONS

FARMAK HAS BEEN A LEADER IN THE PHARMACEUTICAL MARKET OF UKRAINE* FOR 9 YEARS, IN PARTICULAR DUE TO ITS PROGRESSIVITY. BASED ON THE CURRENT GLOBAL FOCUS AREAS, THE COMPANY ACTIVELY IMPLEMENTS INNOVATIVE TECHNOLOGIES. THE MOST IMPORTANT ACHIEVEMENTS ARE:

The principle of interchange: work on bioequivalence

Farmak guarantees the quality of manufactured medicinal products, from the development to their commercial production, each stage meets the standards of evidence of medicinal product therapeutic substitution.

The use of biotechnologies

Farmak pays much attention to the development of this focus area, which is important in the modern pharmaceutical industry. The Company has a unique biotechnological laboratory. Several active substances are currently undergoing approbations.

The newest laboratories: focus on R&D

Farmak creates the best conditions for scientific and technological works. The modern research complex includes laboratories fitted with equipment by leading global manufacturers. A team of 35 candidates and 5 doctors of sciences is working on the development of medicinal products.

Search for APIs: investment in the inventions

USD 39 million were invested in manufacturing of active pharmaceutical ingredients, due to which 20 own substances have been already obtained, and more than 20 will be ready for selling in the coming years. Farmak actively invests in its own production.

The sensationalism of teixobactin is due to its ability to influence the fatty acids involved in the formation of bacteria cell membranes, in contrast to traditional antibiotics, devoid of this ability. The new type of antibiotics undoubtedly has disadvantages. One of them is the limited influence of teixobactin on gram-positive bacteria and the inability to influence gram-negative ones. But, despite the shortcomings, the discovery of teixobactin is compared with the discovery of vancomycin in the 1950s, an antibiotic, the most powerful at that time in fighting against superresistant bacteria. Development of medicinal products based on teixobactin may become a sensation in medicine.

Another significant step undertaken recently was the discovery of malacidins, substances that replenished the class of calcium-dependent antibiotics in 2018. Like teixobactin, malacidins are able to effectively attack gram-positive bacteria, even such stable as staphylococcus aureus. The current task of malacidins is: to undergo a plenty of studies involving people. Many tests have been already conducted on animals, but this is not enough to track the effects on the human body.

After undergoing the testing, malacidins will have a chance to become a component of medicinal products. By the way, there have been no revolutionary events associated with the invention of antibiotics over the past three decades: the last thing to remember is the discovery of a group of lipopeptides in 1987.

* In monetary terms, according to ProximaResearch.

4 TABLETS WITH SENSORS: IT IS EASIER NOW TO KEEP IN MIND SOME THINGS

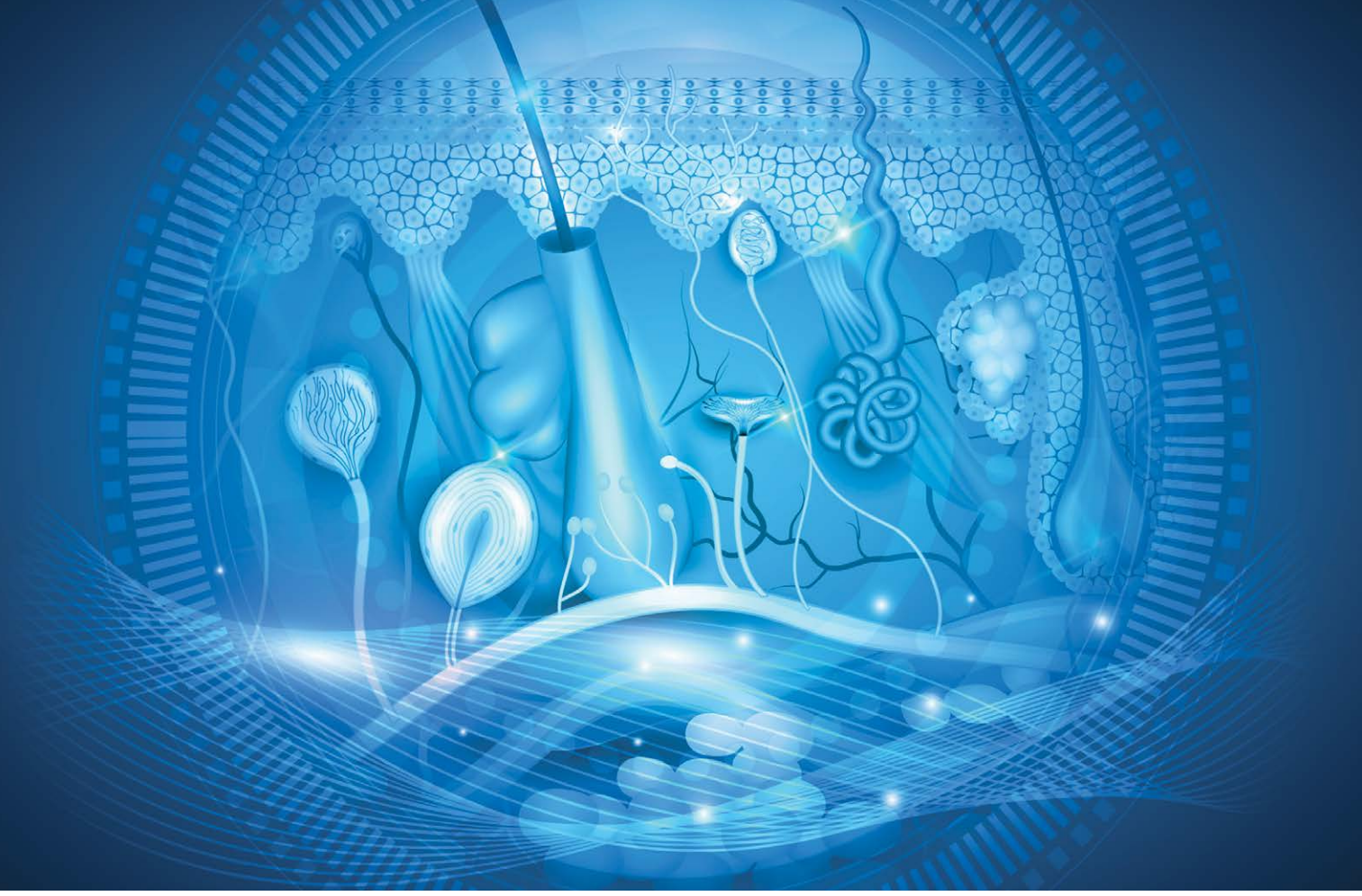
It is another interesting invention that became possible due to high technologies. To make it easier for patients and doctors to control the regularity of taking medicinal products, American researchers have developed tablets with sensors that transmit information about taking medications to digital devices. Tablets with sensors are easily swallowed, digested and removed from the body. Some of them are excreted undigested. None of the tablets cause harm to the body.

Sensors are made tiny using substances which are safe for the human body, such as silicon, magnesium or copper. The mechanism of action is as follows: the sensor in the tablet composition gets into the body and is activated on exposure to gastric acid. Information about the medicinal product is transmitted to the patch on the patient's body, and to the patient's smartphone. Then it is possible to transfer information to a doctor or trusted person due to a special application.

Similar technologies have already been used to control the number of analgesics in order to avoid the abuse of opioids. They helped doctors to track the state of patients with mental disorders. However, the technology is useful not only for people with mental disorders, but also for ordinary patients. Since anyone can forget to take medication at a clearly defined time, and compliance with the time frames is a fundamental component of the treatment of many diseases. So microchips in tablets can be a great tool for self-control. Abilify MyCite, approved by the US Food and Drug Administration in 2017, has become the first "digital" tablet. It was noted that it might be useful for the treatment of schizophrenia, bipolar disorder and depression.

Laboratory of Farmak JSC

In addition, a number of innovations will help to motivate patients. For example, instead of reading long and boring instructions for a medicinal product, a person will be able to view a mini-movie about the action of medicine in the body in the future. And taking the necessary medications will turn into an entertaining game for young patients — the idea of making tablets in a form of dinosaurs or octopuses using a 3D-printer has been already implemented.



To overcome burn wounds

LYOPHILIZED XENOGENEIC TISSUES THAT ARE USED AS SKIN SUBSTITUTES IN TREATMENT OF BURN WOUNDS (GRADES I-IIAB TO III), DONOR AND DEGLOVING WOUNDS, TROPHIC ULCERS BECAME A MILESTONE IN COMBUSTIOLOGY. The production was launched and the only bank of lyophilized xenogeneic medicinal products in Ukraine was created at Institute of Biomedical Technologies, LLC, which was founded in 1995 on the basis of I.Ya. Horbachevsky Ternopil State Medical University.

Photo from shutterstock.com

VOLODYMYR VASYLIOVYCH BIGUNYAK

honoured worker of science and technology of Ukraine, State Prize laureate in the field of science and technology, professor of the Department of General Surgery of I.Ya. Horbachevsky Ternopil State Medical University, founder of the Institute of Biomedical Technologies, LLC.

FROM THE IDEA CREATION TO IMPLEMENTATION

In 1976, the first burn unit was opened in Ternopil City Emergency Hospital, the need for which arose due to frequent domestic and industrial injuries of residents of the city and region. The current methods of treatment significantly differed from the modern ones; therefore, the efforts of doctors often did not give the desired effect, and burns of 30-40% of the body surface were considered an injury incompatible with life. Due to the efforts of combustiologists, in particular Professor M. Povstianyi, the chief combustistologist of Ukraine at that time, the strategy of treatment of burn wounds gradually began to change. The specialists of the burn unit of the Ternopil hospital and scientists of the departments of general surgery, histology, biochemistry of then Ternopil Medical Institute took an active part. It was found during the studies that the burn wound itself was the trigger mechanism for the development of all pathological changes in the patient's body: pain signals were generated there, because water, proteins, electrolytes were lost, it became a source of infection, and toxins entering the blood lead to dysfunction of all organs and systems. They came to the conclusion that treatment should be focused on the removal of dead tissues (necrectomy) as early as in the first days after the trauma with the subsequent closure of the wound with skin of the patient or its substitutes. But there were no high-quality skin substitutes. Thus, experts began to develop the technology of making a substitute from pig skin, since it most closely corresponds to human at the cellular level.

FEATURES OF THE TECHNOLOGICAL PROCESS

Long-term studies have confirmed the possibility of using pig skin preserved in liquid nitrogen in the treatment of superficial and deep burns. They began to use preservation of biological tissues using a lyophilization method, which involves drying of pre-frozen tissues in a vacuum, for prolonged storage and transportation of the material. According to the technology, the freshly cut surface layer of the pig skin 0.3-0.4 mm thick, processed in special solutions, is initially preserved in liquid nitrogen, and then lyophilized at low pressure and very low temperature. Subsequently, xenografts undergo special technological control and sterilization using the radiation method, they are packaged in sealed pack.

THE PRODUCTION OF LYOPHILIZED XENOGRAFTS, USED IN THE OPHTHALMOLOGIC CLINICS OF UKRAINE WAS LAUNCHED AT THE INSTITUTE OF BIOMEDICAL TECHNOLOGIES, LLC.

ADVANTAGES OF LYOPHILIZED XENOSKIN

There is no need to apply a bandage daily under anaesthesia after closing the burn wounds with lyophilized xenoderm grafts, transplanted xenoskin prevents infection and loss of water, proteins, electrolytes, accelerates healing, as well as positively affects the whole body, since it contains a large amount of amino acids, trace elements, growth factors and other useful components. Xenografts are especially effective in superficial burns of grade I to IIA. Wound epithelization under lyophilized xenoderm grafts takes 10-12 days.

FIGHT AGAINST SCARS

Patients who have suffered burns, injuries or surgery often have an associated problem — hypertrophic and keloid scars are formed, which can cause hyperemia, pain, peeling, ulceration, itching and psychological discomfort. In 2004, the Institute of Biomedical Technologies has developed a method for the manufacture and use of silicone plates. The main mechanism of their action is the delay of water molecules in the connective tissue of the scar, which reduces its density and changes the energy of the tension surface, which leads to the placement of collagen fibers in parallel to the surface of the skin, as in healthy areas. These changes prevent the growth of abnormal scar tissue in early use, help reduce the size of the scar and increase its elasticity at the stages of formation.

Rescuing the hearts

Nestor Mykolayovych SEREDIUK has dedicated over 50 years to medicine, during the last 30 of which he works in the field of cardiology. **TODAY'S CONVERSATION WITH A RESPECTIVE SCIENTIST IS ABOUT CRUCIAL MOMENTS OF HIS WORK AND THE LEVEL OF UKRAINIAN CARDIOLOGY DEVELOPMENT.**

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NESTOR MYKOLAYOVYCH SEREDIUK

therapist of the highest category, professor, Head of Department of Internal Medicine No. 2 and Nursing of Ivano-Frankivsk National Medical University, doctor of medical sciences, professor, honoured worker of science and technology of Ukraine, academician of the Academy of Sciences of Technological Cybernetics of Ukraine, ESC Professional Member, ACCA Silver Member, EHRA Silver Member, Member of Associations of Cardiologists, Arrhythmologists, Internists, Electrophysiologists, Association of Preventive and Anti-Aging Medicine of Ukraine. His achievements include more than 600 publications, 30 monographs, many textbooks and tutorials, almost two dozens of inventions, more than twenty improvement suggestions. The recent publications include The ECG Made Easy by British professor John Hampton in English, Ukrainian and Russian (Nestor Serediuk is a scientific editor of translation); 3rd edition of Internal Medicine; two-volume Internal Medicine in English, prepared and presented to the publishing house «Medicine» for publication (pending publication).

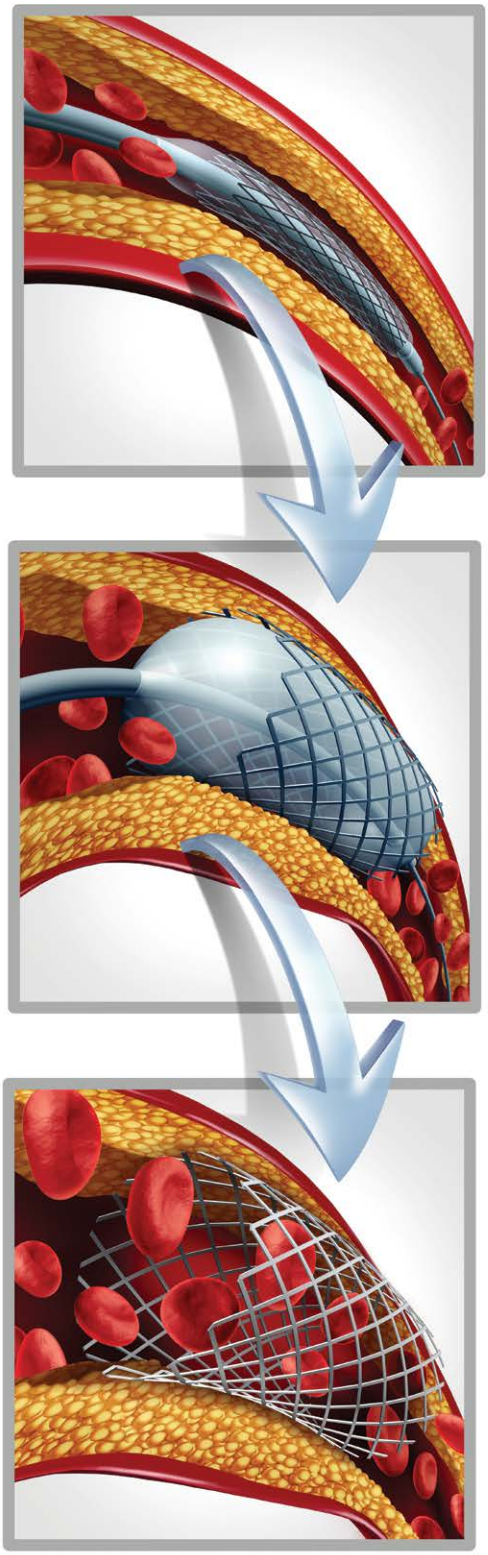
Nestor Mykolayovych, you are engaged in practical work, scientific activity, and teaching. You are going to create your own school of science, candidates of science who passed Ph.D. defense under your guidance, now work not only in Ukraine, but also in the UK, France, Germany, the USA... And which of the achievements do you consider the most important?

First of all, I would have probably mentioned one of my first serious practical intelligences, which at first glance may not seem to be very important, but its results have been gaining considerable popularity — every day they are broadcast on radio and on local television. It is about information on the medical consequences of weather changes. The medical and meteorological conditions have been classified and proved that the cardiological situation is calm under the first type of weather; the probability of strokes, heart attacks and other cardiovascular problems increases under the second, and especially the third one. In such periods, people who have problems should limit physical activity, in addition take the medicinal products prescribed to him/her by the doctor. Warnings about weather features are heard in the media (press, TV) for over 30 years and give a tangible result.

Also, I cannot fail to mention how we managed to achieve creation of cardiologic dispensary in Ivano-Frankivsk region on the basis of the former regional hospital — at that time it was the third, after Kyiv and Kharkiv, specialized institution in Ukraine. And today, in this regional clinical cardiological center (RCCC), equipped with a modern angiograph, devices for interventional cardiology (percutaneous coronary interventions — PCI), electrophysiological examination (EPE) of heart rhythm and conduction disturbances, telemetric diagnostics and control over the effectiveness of emergency care at the pre-hospital and after-hospital stages, high-tech coronary bypass surgery are being performed, which helps reduce mortality rate among those who have a heart attack from 20 to 5%!

THE PROBABILITY OF STROKES, HEART ATTACKS AND OTHER CARDIOVASCULAR PROBLEMS INCREASES UNDER THE SECOND, AND ESPECIALLY THE THIRD, TYPE OF WEATHER.

An important achievement was the fact that upon gaining independence we concluded agreements with the State Pharmacological Centre and leading scientific and medical institutions, companies, firms regarding conducting studies of the effectiveness of new medicinal products. Since our country



appeared, the studies began to actively develop, we have made it possible to become the basis of the Pharmacological Centre of the Ministry of Health of Ukraine for the study of medicinal products. The effectiveness of both domestic and foreign pharmaceuticals is studied. Our centre is involved in global projects. This gives the clinic the credibility of the international research centre.

THE POSSIBILITY TO REDUCE BLOOD FLOW IN THE THROMBOTIC (INFARCTION-DEPENDENT) ARTERY DRAMATICALLY REDUCES MORTALITY RATE. AND THIS IS A REAL REVOLUTIONARY TECHNOLOGY IN CARDIOLOGY.

■ ***With which domestic and foreign manufacturers do you cooperate?***

These are the leaders of the Ukrainian pharmaceutical industry, in particular, Farmak — we studied Trombonet (clopidogrel), an effective medicinal product well tolerated by patients. I should also note that small Ukrainian manufacturers also have prospective developments. I have "tested" some of the medicinal products by myself following coronary artery bypass grafting, i.e. I joined the experiment (rivaroxaban /xarelto at vasoprotective doses in combination with aspirin at small doses). The domestic pharmaceutical companies, we are co-operating with, include FarKoS, Darnitsa, KVF, Zdorovie, Borschagivsky CPP, and foreign ones - BAYER, SANOFI, Kusum, Novartis, PRO.MED. PRAHA. Online, KRKA.

■ ***It is no exaggeration to say that you are a witness of the rapid development of cardiology, and not without your contribution. Which of the modern technologies do you consider worthy of an excited exclamation: "This is fantastic!"?***

This is probably a coronary intervention. This technique is 40 years, and it began to be widely used in Ukraine somewhere 10 years ago. The possibility of restoring blood flow in the thrombotic (infarction-dependent) artery dramatically reduces mortality rate. And this is a real revolutionary technology in cardiology.

We open the affected artery, put the stent — and preserve life. But do we come out in the fight against heart disease as the final winners? No, because still small number (22-25%) of patients are hospitalized for "catheter treatment" later than in the first 120 minutes — the time when the PCI is most effective. Therefore, after the intervention, it is necessary to carefully monitor the situation so that the stented artery is not clogged up again

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or thrombosis is not developed elsewhere. It is important to ensure that the implanted stent is not tangled with tissue (so-called restenosis) etc. In addition, restoring blood flow does not still mean getting rid of the root cause of myocardial infarction. Therefore, I believe that the further development and improvement will depend on hybrid strategies, that is, combination of surgery with therapeutic measures and optimal medication.

FROM 20 TO 5%

coronary bypass surgery reduces mortality rate among those who suffered from a heart attack

■ ***What global developments do you consider effective in arrhythmology?***
Together with colleagues, we found a reference in the Japanese literature to a methodology that makes possible to identify some congenital anomalies (so-called additional pathways) and other causes that affect ways of circulation of heart impulses. Based on this, we have created a computer program that allows us to justify the diagnosis of arrhythmia and establish a violation of impulse transmission in a particular patient. We have now documented an application for utility model and sent it to the Patent Office of Ukraine. Another important area is the person-oriented approach to the treatment of a particular patient with his/her "bunch" of diseases, risk factors, etc.

WHICH STEPS ARE TO BE TAKEN IN UKRAINE FOR MORE EFFICIENT STRUGGLE AGAINST CARDLOGICAL DISEASES?

I am convinced that, besides the wide perfusion network in each region of Ukraine and participation in the European initiative «Stent for life», the State Register of percutaneous interventions, a new form of analysis of the results of the registry observations «Survey PCI», there should be diagnostic and medical electrophysiological laboratories in each region. Without this, you cannot move forward. Only electrophysiological studies provide an opportunity to establish exact cause of arrhythmia. This is extremely important, because it is arrhythmic disorders that cause mortality in more than 40% of cases of acute coronary syndromes.

■ ***We hope that improved diagnosis will be widespread in the near future! Undoubtedly, we are pleased with the development of domestic medicine. And in this connection, I would like to ask: is cardiology in Ukraine inferior to world science and practice?***
It is not inferior in any way! The only thing, in which we fail to keep pace with, is that our doctors cannot perform heart transplantations due to legislative aspects. We have excellent specialists (cardiac surgeons, interventional cardiologists, electrophysiologists, arrhythmologists, specialists in emergency cardiology and cardiac insufficiency), so we will hope that round-the-clock high-tech cardiology assistance will become more accessible to our citizens.

Access code to eternal life

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The term «biohacking» rapidly penetrated the lexicon of online communities, formed around the health topic. **WHAT IS IT — A SKILLFULLY OVERBLOWN EXCITEMENT, PIE IN THE SKY OR REAL ACHIEVABLE PANACEA?** Quite probably, only a little bit.

PHARMACOLOGICAL AND ECONOMIC ASPECTS TO THE CORE OF THE SYSTEM

As usual, let's try to outline concepts first of all. Everything seems to be clear with the first root "bio" in the term "biohacking". The multiple-meaning "hacking" is a bit tricky. The understandable analogue of the slang word "hack" is "to cut one's way". Initially hackers called programmers who, in a quick and elegant way, found the opportunity to bug errors in code. Subsequently, the word "hacker" has become firmly fixed as "computer cracker". Whatever the motivation of a hacker is, pure interest in the study of a system, or not a very pure interest in profit, in fact hacking is avoidance of the established procedures, increasing privileges for access to where it was not foreseen. When it comes to the human body, the search for ways to more efficiently management of the system is carried out in a variety of ways, from improved performance and to the use of digital devices in the body. What forms can acquire "power-leveling", when health and longevity are put at stake?

TREND HERALD

Not the greatest publicity around this topic was recently made by a resident of the Silicon Valley, an entrepreneur of Russian origin, Serge Faguet. He intends to live at least 120 years, and by that time, it is likely that such age will not be limited. At the same time, he plans to live with maximum efficiency, that is, aiming at influencing biochemical processes, to create those physical and mental states that they consider useful. After Mr. Faguet published a post entitled "I'm 32 and spent $200k on biohacking", it caused stormy discussion in the global network. It is noteworthy that the author's self-esteem became a separate issue of discussions not related to medicine. The only heading was interpreted as a manifestation of the position: "Look, I earned a lot of money — and could spend them not like everyone else!" However, considering that the wealth of a businessman is estimated at 45 million, his expenses for upgrading the body and the psyche is still cost-effective option.

THE ULTIMATE GOAL

The lion's share of funds was directed to diagnostic tests and consultations by doctors and psychotherapists. The justification of the principles on which Serge chooses the methods of self-improvement sounds like a real anthem of human rationality: they must be logical, scientifically sound, appraised by experts, optimal in terms of

OLEKSANDR KOLYADA

Research Fellow of the Laboratory of Epigenetics, Institute of Gerontology of the National Academy of Medical Sciences of Ukraine

The requirements of healthy lifestyle are in fact general. They fit millions, but do not indicate what to do specifically for you. Biohacking, if it is understood as a more targeted, compared to healthy lifestyle, prevention, is different in that it is based on personal data. For example, there is no need to take vitamin D in the event that the test results confirmed: it's quite enough. And the «correct» biochaker must have a lot of tests: biological, instrumental, genetic. The latter, by the way, are often idealized as if they can indicate what to eat or what not to eat, for example due to intolerance. In most cases this is not the case. However, competently conducted genetic tests help to assess the risks of diseases and to adjust lifestyle, including nutrition. Just adjust it — but not to describe it for you or your trainer or doctor.

Another possible aspect of the comparison: if healthy lifestyle is a compliance with the idea of nature, then biohacking is an attempt to improve this idea. And there are very good prospects in this ambitious intention. New works appear every year that show a successful attempt to «edit» the human genome. Gene engineering allows changing the sequence of genes in adults as well as in human embryos. The potential of these technologies is enormous, if everything goes as expected, then mankind will receive a significant number of medicinal products that will affect the root causes of the disease, and not the symptoms, in 20 years.

cost-effectiveness and feasibility, confirmed by objective and subjective indicators. The main points of the program, which are guided by the biochacker, seem to be a catechism of the Healthy Lifestyle at first sight.

- ***Sleep Hygiene*** – no specialist will argue here.
- ***Optimal Exercise*** – are beyond any doubt.
- ***Mental Health:*** psychotherapy and meditation — welcome, welcome and once again welcome.
- ***Optimal Nutrition:*** sugar as well as alcohol are poisons; cheap products of industrial origin - "no", organic - "yes"; cyclic fasting and dietary ketosis (maximum fat, minimum carbohydrates). At this stage nutritionists begin to point to certain distortions.
- ***Medical Testing.*** Control over the body is exercised by hundreds of indicators, from vital to "just interesting".
- ***In addition – taking supplements and drugs, literally bandful of them.*** In addition to vitamins and extracts there are hormones, nootropics, antidepressants, in general, a whole pharmaceutical guide-book.

The experimenter argues that the data of regular surveys and well-being indicate the success of his actions. However, commentators doubt the consequences that may have the use of such quantity of medicinal products, their interaction with each other and raise the question of whether "manual" control make the body overextend itself. As a result, doctors of almost all specialities — even to psychiatrists who emphasized excessive concern for own health got the opportunity to criticize individual points of the program and to fear the possible consequences of the use of almost hundreds of pharmaceuticals per day.

AN AGE-LONG DREAM — NEW TOOL

However, "blamestorming" of a millionaire-experimenter and evaluation of his prospects — this is not all the range of problems that arises when considering the phenomenon of biohacking. In particular, there remains the question of what it forces to distinguish this approach

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from other ways to longevity and talk about it as a new trend. After all, the guides for hunters for exceptional abilities are as old as the hills! There will be always those for whom general ideas of health will be not enough. There will be always those who believe that the mystery of the essence of the universe will guide the path to eternal life. "Hackers" of the body do not differ in this from, for example, Taoist alchemists who were looking for immortality, fiddled with elixirs or immersed in spiritual searches. What distinguishes today's contenders for exclusivity? If we leave aside the question of mastery in meditation and other psychophysical practices, then without any doubt: in comparison with other epochs, the science of the 21st century provided adherents of longevity with an enormous number of tools that enable them to control the organism and influence its condition.

However, the science is not yet sure about the consequences which attempts to use all together, simultaneously and immediately, will cause. Finally, the basis of the current scientific paradigm is the idea of the repetition of the experiment and the accumulation of statistically significant data — and in fact, there are not so many millionaires who are ready to consistently do experiments on themselves. If you look closely, the more difficult part to understand in the word "biohacking" is "bio" rather than "hacking" — the mystery of life is not explained in detail. All that is left to do is to observe, how the extreme actions of radical biohackers will end. In view of the seriousness of their intentions to live very long, it is worth not to get some popcorn ready while observing, but have own lifehacks that will allow making life longer and improving it.

And most of these tips, which (see above) are logical, scientifically sound, appraised by experts, are optimal in terms of cost-effectiveness and affordability and confirmed by objective and subjective indicators, after all, coincide with the general guidelines of the healthy lifestyle concept.

The main difference between the biohacking and the health care system and healthy lifestyle: health begins to be perceived as a measurable and managed resource. And it is the primary source of all life's achievements. More health — more energy to achieve the most ambitious goals. Also, due to the complexity of the approach, it is possible to cure diseases that have been interfering for a long time. And to prevent the disease by catching it in the early stages of progress.

Biohacking is focused on the creation of the most complete picture, which involves not only purely medical data, but also an analysis of lifestyle and necessarily mental health. The most expedient is the personalized, controlled, gradual and non-significant correction of lifestyle. Wellness procedures, if necessary, can include both pharmacological products and physiotherapy, manual techniques, and biotechnology, in particular the use of regenerative potential of stem cells.

If, however, to talk about the famous biohackers, the most illustrative example is the example of business icons of the 21st century — Elon Musk and Jeff Bezos. The mere look at their photos shows that their health parameters have not deteriorated with age, but have improved. We also see what success they have achieved in other areas of life. So, we are very grateful to Serge Faguet for the resonance he managed to create around the topic of biohacking, but his results cannot be called outstanding.

SVIATOSLAV KHANENKO

Co-Founder and Chief Medical Officer at Biohacking Clinic SQLAB

Required protection

NEW SYSTEMS FOR PROTECTION OF MEDICINAL PRODUCTS AGAINST FALSIFICATION ARE BEING INTRODUCED IN UKRAINE IN ACCORDANCE WITH EUROPEAN UNION DIRECTIVES. It's about serialization, that is, applying 2D code to each packaging of the medicinal product. Also, packaging will receive a new, more reliable protection that will indicate whether it was open.

AN APPARENT SOLUTION

Turkey was the first country to take decisive steps to protect medicinal products against falsification, for which the serialization of the national scale began in 2010. Thus, in the 2000s, many dissatisfied people appeared in the fact that the same packaging of medicinal products was repeatedly used during mutual settlements between end-user and insurance companies. Another problem was in the presence of black market of medicinal products. Unfortunately, this problem exists in virtually any country.

It became obvious that it was necessary to act, so the government worked on the necessary laws and began to implement security programs. As a result, it was in Turkey that for the first time in the world was fully implemented a system of tracking medical products.

THE SYSTEM OF SERIALIZATION OF MEDICINAL PRODUCTS PROVIDES MANUFACTURERS VERY REASONABLE ADVANTAGES:

- **Brand protection and a significant reduction in the risk of the release of counterfeit medicinal products**
- **Monitoring and analysis of economic indicators for each of the medicinal products, and hence — the opportunities for moreaccurate forecasting and compilation of release plans**
- **Optimization of workflows at all stages: production, logistics, distribution, retail sales**
- **Ability to track each batch and, if necessary, return the goods on time**

The essence of the system is that the manufacturer puts a unique packaging non-encoded labelling that allows you to track the product throughout the supply chain. And the consumer, using a mobile application, can make sure that the medicinal product is not fake and get all the necessary information about it. After Turkey, the countries of the EU, South America, the USA, China joined this program of medicinal product protection.

EUROPE: NEW REGULATORY REQUIREMENTS

In 2015, the European Union has adopted two directives on the protection of medicinal products. The first concerns serialization, which involves applying 2D code (matrix or two-dimensional bar code) to each package of medicinal product, which includes:

- ***GTIN number in accordance with the standard pro-***

posed by the international deratization of accounting GS 1, should consist of figures in the range of 8 to 14;

- ***unique serial number of packing;***
- ***number of batch within which the package was made;***
- ***shelf life.***

The second directive of the European Union obliges to protect the packaging from imperceptible openning. For this a special label should be applied or the packaging valves must be glued so that the consumer can see whether it has been opened before.

New requirements apply to all pharmaceutical manufacturers operating in the European market and should be implemented no later than February 9, 2019.

SERIALIZATION: FEATURES OF THE PROCESS

Construction of the serialization system, as well as any computerized system, is carried out in accordance with the requirements of the international standard ANSI / ISA-95. It declares the differentiation of systems by levels, and at the same time delegates a certain functionality to one or another level. Serialization codes are applied at I-II levels. At the III level — the level of the production area, there is the receipt of generated at the level IV serial numbers for the further formation, distribution and transfer of the volume of numbers to level II. Level III allows you to manage the basic data

configurable Manufacturing process data, recipes (set of parameters), orders for product manufacturing, audit trails. The IV level organizes the interfaces and channels of data exchange between the participants of the pharmaceutical market: contract pharmaceutical manufacturers, registration dossiers, national and European medicinal product testing organizations. At IV level, all information about the serialization process is transferred to the regulator, which is at level V.

ANDRIY KARDASHEV
Project Manager, Serialization and Aggregation System Implementation, Farmak

The introduction of the serialization and aggregation system involves a number of changes in the technologies and processes of pharmaceutical manufacturers and in companies that deal with the storage and distribution of medicinal products. However, this is a necessary step that contributes to their confident presence in world markets. Therefore, Farmak is actively working on implementing innovations to meet all the requirements of a dynamic and changing competitive environment.

The main European regulator (V level) is the European Medicines Verification Organization (EMVO), the organization responsible for the establishment and operation of the European Medicines Verification System. Its subsidiary, EU HUB, will receive all data from manufacturers wishing to be present in the European market for the serialization of pharmaceutical packages, as well as the implementation of a first-time control program.

The next step will be the development of a detailed scheme for the transfer of in-

The process of loading the package to the machine

SYSTEM OF SERIALIZATION OF MEDICINAL PRODUCTS IS PRIMARILY NEEDED FOR THE END CONSUMERS WHO SHOULD RECEIVE QUALITY TESTED MEDICINES, AND PHARMACEUTICAL MANUFACTURERS TO PROTECT THEIR RIGHTS TO MEDICINAL PRODUCTS.

formation on the serialization of medicinal products to wholesalers and retail distributors, as well as the creation of mechanisms by which consumers will be able to check the legitimacy of a particular package of medicinal product by sending a request to a European hub.

READY FOR CHANGES!

During the introduction of serialization of medicinal products, Farmak has already implemented a number of important preparatory stages.

- ***Clear planning.*** First of all, it was necessary to determine the algorithm for the introduction of serialization, to analyze the protocols on the information that will enter the system.
- ***Effective interaction.*** An important step has become establishing cooperation between employees from different departments, because everything is involved: production, quality, network, computer systems, logistics. Each employee must clearly see a range of responsibilities in order to contribute to the final result.
- ***Predictable choice.*** One of the requirements laid down by the working group in the preparation of a technical task for the choice of a potential provider of technical solutions was the possibility of serialization not only for European but also for other markets. The system that will be implemented by the Company will allow an entry of medicinal products also into other continents.
- ***The near future.*** After installation of the equipment, by means of which the code is applied to the packages and the quality of its application is carried out, start-up works will be carried out. Further — the final SAT-testing of the system. During these tests, prior to the release of the industrial exploitation phase, staff training will continue — it will be delivered by the technical solutions provider.
- ***Relevant issue.*** At the moment, focus is on generating serial numbers.

SERIALIZATION AND AGGREGATION

These concepts are related: the first, as already mentioned, implies the application of a unique code, the second — establishing the relationship between the primary packaging and each subsequent capacity or packaging. That is, the packaging of the medicinal product can be aggregated to the box, and it to the pallet. Aggregation is limited to medicinal products produced within the same batch. For example, if we have at least two series, but of the same medicinal product, they can not be aggregated to the box, and boxes to the pallets.

If a damage to a pallet or a box has occurred, it is necessary to «reaggregate» the boxes — to remove all the damage and to reaggregate the packages to the box, and new information about their connection «sew» in the logistics code To carry out the audit, we use hardware and software complexes, equipped with printers and scanners, which can reaggregate the palette of finished medicinal products. Aggregation is not currently mandatory for EU countries, but it allows you to significantly reduce the time for package packing to the box, and boxes to the pallets. Already in 2019, it will partially begin to be implemented in many countries of the world, but as a recommended application.

New era in Ukrainian diagnosis

OLENA BRIK
Head of Department
of Tender Sales,
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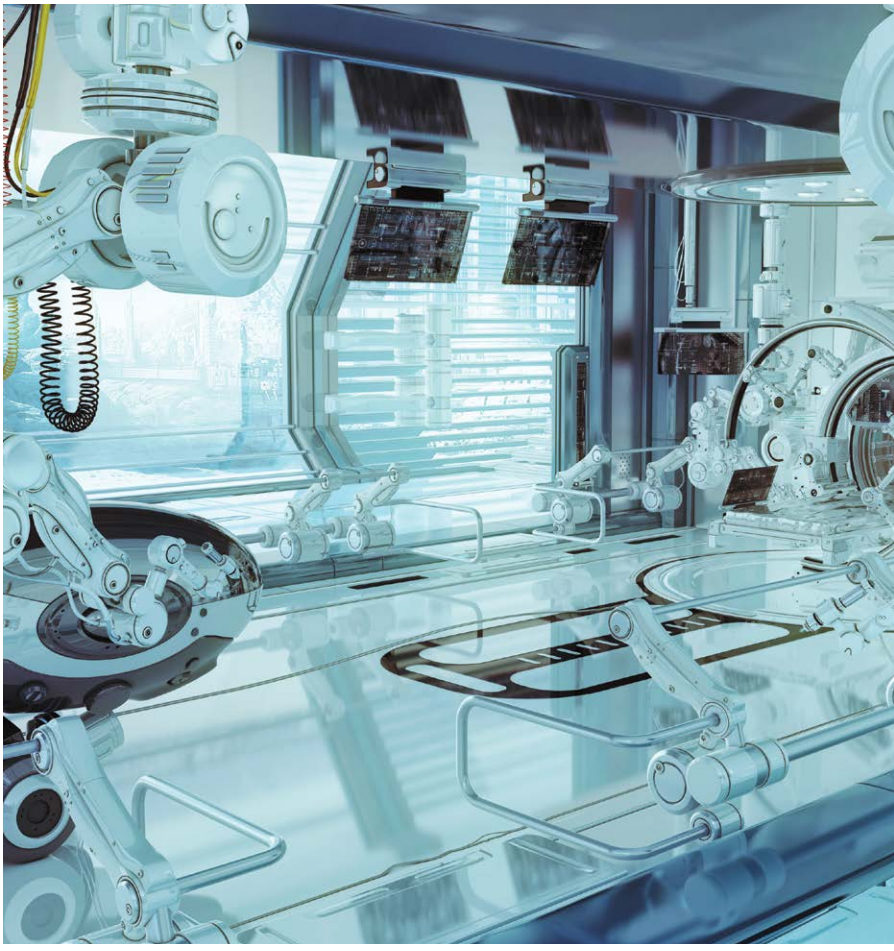

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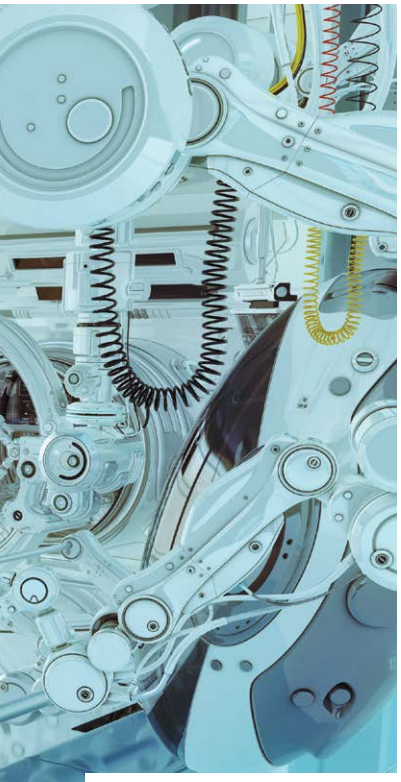
Given the high level of knowledge that requires the creation of contrast media for CT and MRI, there are no more than 30 manufacturing companies in the world. **FARMAK JSC, JOINED THIS LIST, CONTINUES TO CARDINALLY INFLUENCE ON THE MARKET OF THESE MEDICINAL PRODUCTS**

High-tech diagnostic methods — computed tomography (CT) and magnetic resonance imaging (MRI) — play a colossal role in modern medicine. On the barrier to the universal availability of such a diagnosis there is a significant cost of equipment, which can reach several million Euros. In addition, for diagnostic procedures in 90% of cases, it is necessary to use high-quality contrast medications that will enhance the clear visualization.

40%

in the natural equivalent was the total share of medicinal products "Tomogexol" and "Tomascan" in the market of medical products of the second generation for CT and angiography in 2018



PHARMACOLOGICAL AND ECONOMIC ASPECTS

The manufacturers of original and generic medicinal products face a daunting task. The product should contribute to the highest possible quality "image". At the same time, security is a specialist place, because even with the correct procedure and the high quality of the medicinal product, the likelihood remains of a number of side-effects. It depends on the generation of the agent.

And medicinal products for CT and angiography (containing iodine and working on the principle of X-ray irradiation) and medicinal products for MRI (which contain metal gadolinium that amplifies the visualization signal) are divided into two groups. They differ in security parameters. Also, there is a significant difference between them in the price. So, both generations are on the market. A budget diagnostic medicinal product for someone may be the only hope for timely diagnosis of serious diseases.

INVALUABLE EXPERIENCE

The addition to high-tech technologies for Farmak JSC started in Soviet times. At that time, the development and manufacture of the medicinal product "Triombrast" (diatrizoic acid dihydrate) allowed to get rid of the high-value import and provide X-ray contrast medicinal products throughout the Soviet Union.

NEW ERA IN DIAGNOSIS

Time is not in place! In 2007, Farmak JSC launched a tendering procedure for the production of a medicinal product for MRI on the basis of baptism in the bulk form for the EU market. Primary orientation the European market was due to its volumes and the presence of a sufficient number of MRI equipment. And already in 2008 it was decided to secure this medicinal product under the brand "Tomovist" in the Ukrainian market.

Over

245 000

magnetic resonance imaging has been already done using medicinal products manufactured by Farmak JSC and market share in natural equivalent in the market of these MRI agents in 2017 made up 73%.

In the same year 2008, Farmak JSC, based on its profound experience and competence in the production of X-ray contrast medications, launches on the market a second-generation agent "Tomogexol" (iohexol). Its quality was highly appreciated by physicians and radio-logs of state and private institutions of Ukraine, Kazakhstan and the Republic of Belarus.

LEADER POSITIONS

In order to provide all segments and to meet all the needs for quality diagnostics, in 2017 and 2018 in addition output of second generation means for CT and MRI: "Tomoscan" (iopamidol) and "Dotavist" (gadoteric acid).

Currently Farmak JSC holds a leading position in the market of contrasting medicinal products of Ukraine. The numbers speak for themselves —Farmak JSC in turn provides the Ukrainian market with high-quality and affordable medicinal products. Also, the presence of Farmak JSC positively influenced the pricing policy in the market of this group of funds. Importers got rid of the monopoly position and had to significantly reduce prices for their products.

MRI SCHOOL

Modernity requires high qualifications from manufacturers — and it also requires it from doctors. Realizing its social corporate responsibility and understanding the need for radiologists to continuously improve, Farmak JSC regularly invests in the training of doctors, which is carried out both in Ukraine and abroad. In 2010, in order to deepen knowledge and develop the skills of doctors, the Farmak founded a "MRI School". Every year it is visited by over 200 delegates from Ukraine, Belarus and Kazakhstan. The school focuses on the practical aspects of work. Its lecturers are the leading specialists of these Ukrainian and foreign clinics. In particular, among the foreign representatives were experts from Turkey, Serbia, Sweden, Poland and other countries. International cooperation of Farmak JSC continues throughout the European Congress of Radiologists.

MRI School: we are teaching doctors

ON 18-19 JANUARY 2019 FARMAK JSC HELD VII MRI SCHOOL FOR RADIOLOGISTS FROM FIVE COUNTRIES WITHIN THE «LEVEL» PROJECT. Advanced knowledge and world experience in the field of magnetic resonance studies were shared by the best experts from Ukraine, Turkey and Poland.

MRI School

IMPLEMENTING BEST ADVANCED EXPERIENCE

Farmak Company is not only the leader of the pharmaceutical market of Ukraine* and one of the largest domestic exporters of medicinal products to different countries, it is a socially responsible company that for many years has been implementing crucially important social projects to improve the quality of medical services, availability of medicinal products for socially vulnerable groups of the population, environmental and other programs. One such project is the MRI School, first implemented in 2010. At that time, it gathered 60 participants. But every year their number increases. Over 8 years, more than 10,000 doctors have upgraded their professional skills thanks to workshops and training activities organized by Farmak. Only in 2018, within the framework of the "Level" program, more than 4,000 specialists from all over Ukraine underwent training.

This year the MRI School of Farmak was devoted to practical aspects the use of X-ray contrast medicinal products in conducting MRI tests, MRI in oncogynecology, MRI diagnostics for endometriosis and adenomyosis, MRI-mammography in the complex diagnosis of mammary glands, the importance of clinical thinking in radiological practice, etc.

The main goal of the program is to maintain a high level of knowledge, to continuously improve and raise the professionalism of Ukrainian doctors and the level of domestic medicine in a qualitative way, drawing on world experience and current trends and practices in the field of provision of medical services. Participants of the VII MRI Schools had an opportunity to receive up-to-date information from the leading Ukrainian radiologists and specialists from abroad, discuss important diagnostic status issues and analyze the trends in radiology. Emphasis was placed not only on the theoretical basis, but also participants were able to enrich the practical skills.

* In monetary terms, according to ProximaResearch.

VOLODYMYR KOSTIUK

Executive Director of Farmak JSC

We want doctors not only to use European quality medicinal products of Ukrainian production in practice, but also to get skills of advanced approaches in the diagnosis and treatment of patients. We strive to ensure that the future specialists of the medical and pharmaceutical industry master advanced technologies even during their study at the univesity. We provide an opportunity to practice on up-to-date equipment for future doctors and pharmacists from seven universities in the country. In 2018, Farmak trained healthcare professionals in the field of obstetrics and gynecology, anesthesiology, surgery, neurology, diabetes, and traumatology. New directions launched in 2018 include gastroenterological training, school of nebulizer therapy for pediatricians and training of ambulance paramedics. It is very important for us, as a pharmaceutical company, that the medicine in the country has a high level and meets modern requirements and the needs of society.

SUSANA KHALILOVA

Marketing & Sales Director at Farmak JSC

The uniqueness of the MRI School is to gain primarily practical knowledge that doctors can use in their everyday work. In addition to the practical direction, the School also inspires physicians to develop and improve themselves. The speciality of a radiologist is now very relevant, because diagnosis is an integral part of medicine. Since we are a company specializing in the manufacture of X-ray contrast media, we could not stand by, and in 2010 we decided to launch activities for the professional development of doctors, in particular diagnosticians. We are pleased by the fact that the MRI School is becoming more relevant. This means that we are making a contribution to bringing our doctors closer to world information, to standards and approaches in diagnosis.

TETIANA KOBA

Advisor of the Acting Minister of Health of Ukraine

The MRI School and the «Level» project, as a whole, are investing in the medical community in Ukraine. It is very important that foreign lecturers teach at the MRI School. Because the international experts will share the world experience and improve the level of medical education of Ukrainian doctors. Such schools should be developed throughout Ukraine.

Farmak is a large pharmaceutical manufacturer, which, by its example, shows that it is a socially responsible company, not just a business entity. We are glad that we have such large companies that implement social initiatives. One of them is the MRI School. We are working on developing diagnosis, not treatment.

OLEKSANDR KOMARIDA

Director General of the Pharmaceutical Directorate of the Ministry of Health of Ukraine

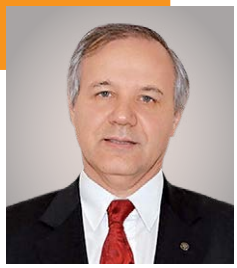
TETIANA YALYNSKA

Doctor of Medical Sciences, President of the Ukrainian Association of Radiologists

The MRI school is really of an international level. We are always ready to help and take an active part in these schools. Each radiologist who has attended a school will take a new method or new approach from it, and thus improves the diagnosis in the institution to which he/she will return.

The MRI School is an opportunity to share best practices and, accordingly, a chance for citizens to receive medical services of a significantly higher quality. I express my gratitude to Farmak, which is doing so much for the development of Ukrainian medicine. After all, everything that happens in medicine, and in pharmacy, is interconnected. And the Company takes the most active part in all changes.

I visited Ukraine for the first time in 2014 at a meeting devoted to issues of neuroradiology, and then I arrived a few more times. I want to note that in terms of neuroradiology, Ukraine is making great steps forward. You have become a leader in the Eastern European region in neuroradiology. In view of this progress, I hope that the country will join our Association and become its member soon.



TURGUT TALI

President of World Federation of Neuroradiological Societies

Manufacturing process, 1960

We are leaders

Corvalol entered the Ukrainian Book of Records as the most famous sedative medicinal product. Such an achievement was recorded during the celebration of the 60th anniversary upon the first release of the medicinal product.

Corvalol is 60!

IN MARCH, ONE OF THE MOST WELL-KNOWN MEDICINAL PRODUCTS AMONG CONSUMERS, CORVALOL HAS CELEBRATED ITS ANNIVERSARY. We will tell about the most interesting: who has developed the medicinal product and how it is manufactured today.

Manufacturing process, 1960

OUR KNOW-HOW

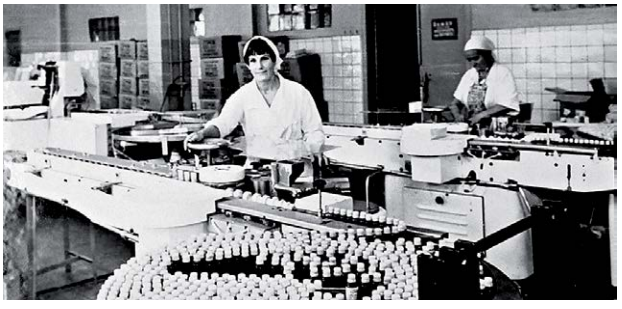
Corvalol began its long way in the domestic pharmacy in 1959 at Lomonosov Kyiv Chemical and Pharmaceutical Plant. Both now, and then cardiovascular agents were among the required medicinal products, so the specialists of the plant decided to develop technologies and create such medicinal products that would be an analogue of the German Valocordin. In 1959, the senior chemist of the plant V. Yakovleva settled down to this responsible work, and the first batch of Corvalol was released the next year. It was a real breakthrough of that time — the generic of the European sedative drug!

The production of medicinal products and in particular Corvalol was different from that of nowadays: the domestic semiautomatic line functioned, many functions were performed manually — bottling, closure and packaging, opening blister packs. For several years, an active reconstruction was initiated at the plant; German automatic lines were installed. In 1965 more than 6 million vials of Corvalol were released, and by 1975 they were marketed — 50 million vials per year. These medicinal products were unbelievably demanded among the inhabitants of the former Soviet Union.

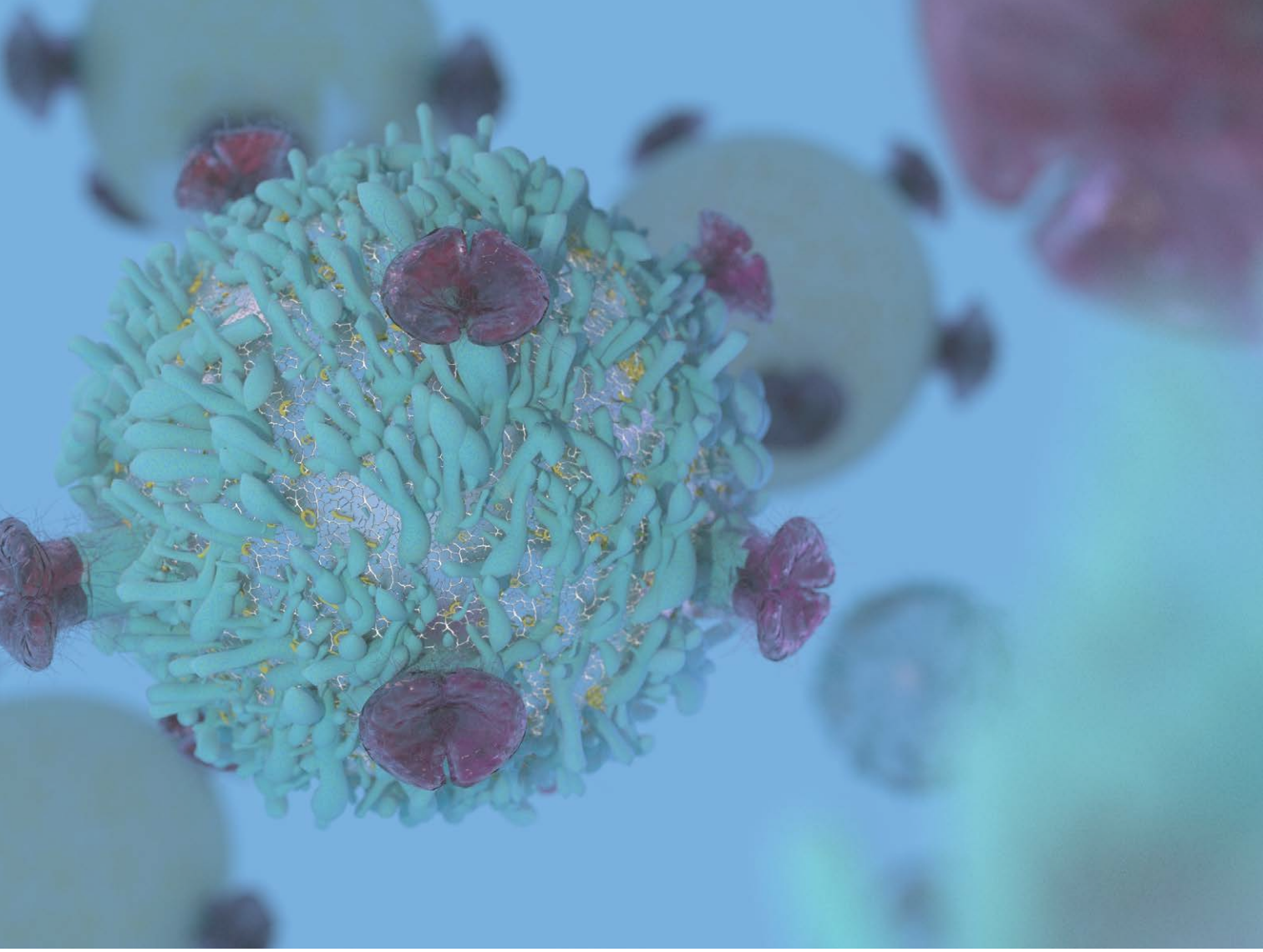
NEW EPOCH

After Ukraine gained independence, Farmak, which became the successor of Lomonosov Kyiv Chemical and Pharmaceutical Plant continued to manufacture all the medicinal products that were previously produced there, including Corvalol.

Currently, the production of all dosage forms of the medicinal product is carried out on a modern automation enterprise, where each stage is under strict control, observing national and international requirements and GMP standards.



The distillation of the medicinal product substance Corvalol, 1960



Will cancer be manageable?

The Nobel Prize in Physiology and Medicine was awarded for «discovery of cancer therapy by inhibition of negative immune regulation». **WHAT OPPORTUNITIES DOES IMMUNOTHERAPY GIVE TO ONCOLOGISTS — THIS ISSUE IS DISCUSSED BY DOMESTIC EXPERTS.**

Photo from shutterstock.com

For many decades, scientists around the world have been working on searching for effective therapy and effective medicinal products against the avowed enemy of humanity. Reliable and effective prophylactic measures against most types of cancer do not exist yet, as well as universal medicinal products that can completely neutralize malignant mass lesions and prevent relapses. Although attempts to achieve this have never stopped.

The undoubted achievement was the discovery made by professors James P. Allison and Tasuku Honjo, who independently of one another, in the United States and Japan, as a result of many years of research, have found out how the cancer cell succeeds in «cheating» the immune system and disabling the body's natural protection system. And finally, in the 90th of the last century, scientists at the same time managed to discover the first two proteins, which due to its structure dazzle the «guardians» of the immune system, T-leukocytes. Reactivation of the latter restores the ability of the immune system to attack cancer cells. Based on these discoveries, medicinal products have been developed that have proven effective in the treatment of certain types of cancers.

«Immune control stop therapy» has revolutionized cancer treatment and fundamentally changed the way in which it can be managed «, - as was noted in the Nobel Committee.

ABOUT LAUREATES

James P. Allison was born in 1948 in Texas, USA. He is a professor of M.D. Anderson Anti-cancer Centre at the University of Texas, and also collaborates with the Parker Institute for Cancer Immunotherapy.

Tasuku Honjo was born in Japan in 1942, since 1984 he is a professor at the Kyoto University.

BIO-BREAKTHROUGH

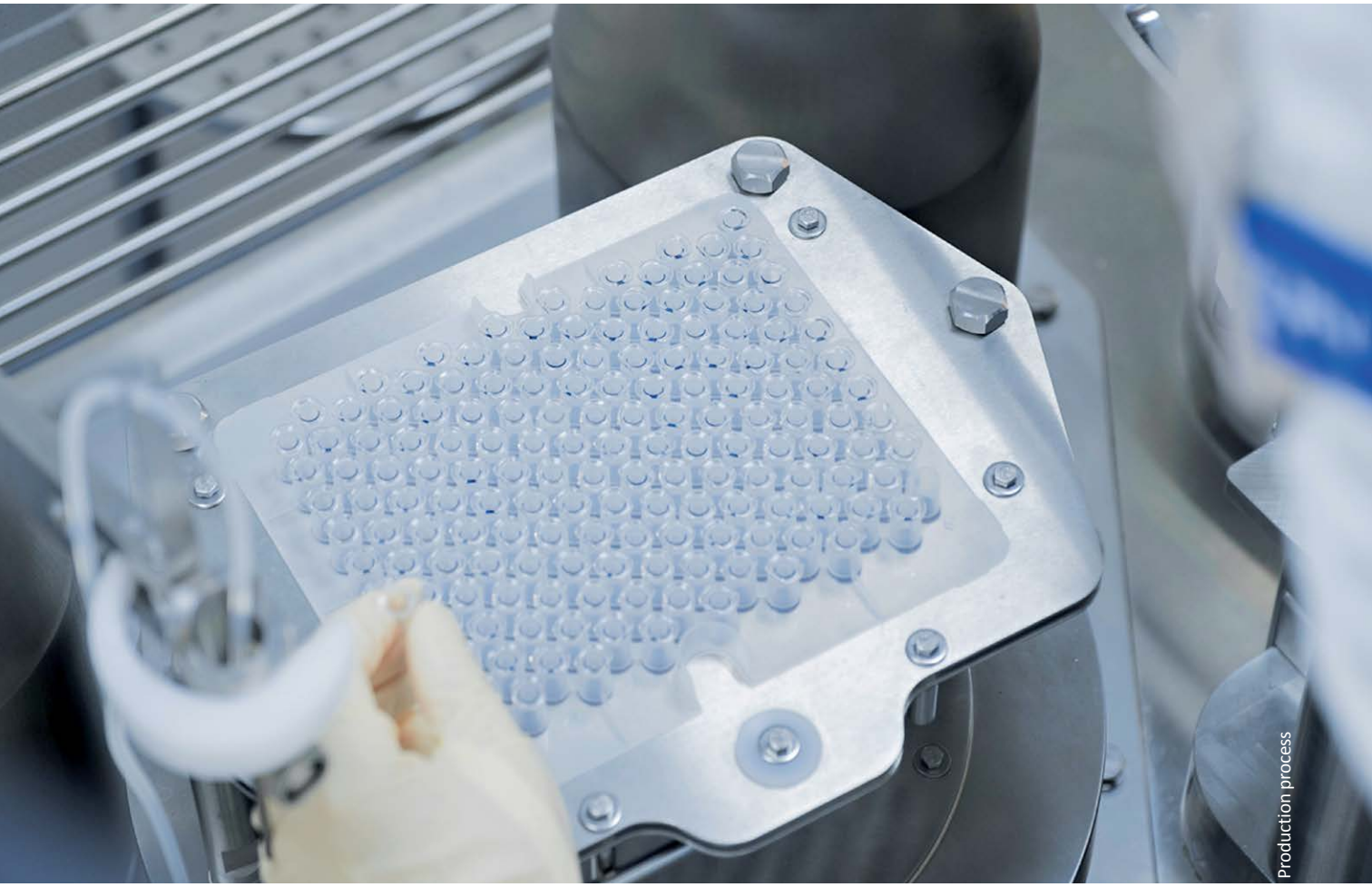
As it's known, most medicinal products used today in medicine are so-called small molecules, products of fine organic synthesis, - ***notes Oleksandr Rozbenko, Head of the physico-chemical research department at the Institute of Organic Chemistry of the National Academy of Sciences of Ukraine, Doctor of Chemistry.*** – Hundreds of billions of dollars is spent annually in the world for the development of new therapeutic agents. Modern achievements in the treatment of oncological diseases by means of chemotherapy can not be underestimated. They have essentially improved the selectivity of medicinal products for certain types of cancer and, therefore, increased the effectiveness of the treatment itself and greatly reduced the side effects. However, a significant disadvantage of small organic molecules as anticancer medicinal products is the rapid development of resistance to certain types of cancer cells. It's easy to understand: a malignant tumour cell is a much more complex biological system than a simple organic molecule created in a chemical laboratory. The development of new, promising anticancer medicinal products becomes with every year an increasingly difficult task: it requires the analysis and selection of an increasing number of "candidate" compounds and almost astronomical costs. This is forcing pharmaceutical companies to raise prices for finished medicinal products. And despite the progress in such newest branches of science as bioinformatics, combinatorial synthesis, and the introduction of rapid tests for bioactivity, it is now clear that the war against cancer can not be won by only chemical means. The use of biochemical approaches to treat many diseases, and especially with the involvement of our own body resources, has always been an attractive idea. In particular, on the verge of modern pharmacology are natural proteins and their synthetic analogues or homologues — polypeptides, the development of which became possible due to modern computer simulation of biochemical and biological processes and the emergence of new biochemical laboratory techniques. The complex biochemical phenomenon that accompanies the oncological transformation of a healthy cell is, in essence, a violation of the structure of cells synthesized by it. In addition, such cells launch a series of biomechanisms to combat the natural immunity of the body. Understanding the biochemistry of malignant cells can counteract such mechanisms of protection and destroy tumours at the expense of their own immunity.

IN PRACTICE

Research on anticancer immunity has been under way for a long time. Professors Allison and Honjo explained the mechanism of activation of anticancer immunity, which makes it possible to create the next generations of immunotherapeutic agents. The development of this year's winners has been an impetus for the introduction into the clinical practice of immunotherapeutic agents with a different mechanism of action, and as well as studies of a combination of two or even three immunotherapeutic medicinal products to enhance their effect and prevent the development of medicinal product resistance

In our country, such medicinal products are also used, they are registered and available to the pharmacy network, ***says Olga Ponomariova, an oncologist of the highest category of the Medical Network DOBROBUT, candidate of medical sciences.*** – In Kyiv, Dnipro and some other cities of Ukraine, international clinical trials are being conducted using these agents. In the Cancer Institute, the Kyiv City Cancer Centre, and in other institutions, both public and private, medicinal products are used in the daily practice of treating cancer patients.

Well subjected to immunotherapy are melanoma, lung cancer, malignant lymphoma, tumours of the head and neck, bladder, kidneys; the possibility of using immunotherapeutic medicinal products in the treatment of many other localizations of malignant neoplasms is studied. But in general we can speak about successful treatment and the final recovery only after a long observation, when at least 5 years have passed after the end of the therapy. This is a long-term remission, almost equal to a recovery.



Production process

OLGA
PONOMARIOVA

Being recently in the United States in a cancer centre where a person who just received the Nobel Prize is working, I became convinced how serious their attitude to the new direction is. Scientists who made this discovery, which will make a huge leap forward, are really genius. Work is in progress, science is developing. But nobody promises that it will be easy and simple. Everything is just beginning.

COMPLEX SOLUTIONS

Does this mean that the significance of immunotherapy is so great that it overrides all previously used techniques? In any case, explains Olga Ponomariova.

Chemotherapeutic medicinal products, despite the side effects and a number of other features, are very well studied and rescue a huge number of lives. They maintain their position also because often enough newest developments in the field of treatment of malignant tumours can not be applied due to the absence of biological markers of potential effectiveness. And for a number of localizations and cellular forms of malignant tumours, chemotherapy is still the only means of rescue.

Surgical treatment is widely used in oncology, which proved successful in early diagnosis.

Currently, a combination of different methods is used, for example, immunotherapy with chemotherapeutic or targeted medicinal products. For example, the efficacy of a combination of chemotherapy and immunotherapy in non-small cell lung cancer has been proved. Another method of anticancer conservative effect, radiotherapy also does not lose its position; currently, the object of the study is a combination of radiotherapy with immunotherapy with very encouraging preliminary results.

AWARD OF THE NOBEL PRIZEOF 2018 IS NOT ONLY RECOGNIZING PERSONAL ACHIEVEMENTS OF THE SCIENTISTS, BUT ALSO A SIGNIFICANT STIMULUS FOR ALL THE SCIENTISTERS OF THE WORLD, WHO DO THEIR BEST IN FIGHT OF HUMANITY AGAINST THESE INSIDIOUS DISEASES.

IN THE FURTHER SEARCHES

It is very important now that we do not fall into euphoria and take caution about the results of the introduction of this truly brilliant discovery. There is still a lot of routine work ahead. It is not the right time yet to say that a person was fully recovered after treatment by a new method. You should not forget about side effects that are likely to occur with immunotherapy. They are different than in chemotherapy, are not always obvious and usually more distant in time. But they are not excluded and are also dangerous. First of all, these are autoimmune reactions, which sometimes proceed extremely difficult.

How long will the effect of immunotherapy last? what does it depend on? How will the physico-chemical homeostasis of the body change due to the effect of immunotherapeutic medicinal products in the distant prospect? — these are just some of the issues that occur before the oncologists of the international scientific community.

There is a huge amount of clinical studies conducted globally, our oncologists are attracted only to a part of them. For each type of tumour, an optimal approach to treatment is being sought — various medicinal products and their combination, the search for new specific biomarkers that can predict the effectiveness of treatment and, if necessary, make the necessary adjustments to the therapeutic plan, if necessary. It is also impossible to forget that for some types of cancer, optimal approaches to immunotherapy have not yet been found. For example, pancreatic cancer is characterized by low immunogenicity and extremely rarely responds to immunotherapy, so decisions should be taken carefully. However, the database on the possibilities of immunotherapy treatment is dynamically replenished. Something that was considered impractical or risky yesterday can be quite real tomorrow. Secondly, it is imperative for the physician to expand their own knowledge in the field of immunotherapy and to responsibly analyze each clinical case. The question is how much the newest method of treatment can be effective for every person and whether there is a justifiable risk tu refuse an alternative, time-tested approach. In general, every step ahead generates a huge number of questions. The best representatives of humanity are looking for answers to them.

INTELLECTUAL PROPERTY PROTECTION: HOW TO PROTECT YOURSELF

TODAY IN UKRAINE, THE GREAT AMOUNT OF COMPANIES IS VULNERABLE IN TERMS OF PROTECTION OF INTELLECTUAL PROPERTY RIGHTS. Many companies behave in the Ukrainian market, to be frank, unfairly, grossly violating the rights of other market participants. To solve this problem, an integrated approach and interest of the state in improving the situation, both in the legislative field and in the independent control over the strict observance of the legislation, is necessary.

WHAT IS THE SITUATION WITH THIS ISSUE IN THE WORLD?

Each country has its own intellectual property protection system — copyright protection, industrial property, trademarks, geographic indications, etc.

It is important how the invention and its author are protected by the country. The legislation of developed countries provides for key protection mechanisms that allow the developer (author, inventor) to be more confident and secure.

Despite all ambiguity, European and US legislation still contains legislative principles that are lacking in Ukrainian legislation. In particular, the part that is important for pharmaceuticals — generics can enter the market the day after the patent expires on the original medicinal product. After all, manufacturers of generics have legal opportunity to carry out pharmaceutical development, process samples of APIs, conduct laboratory studies and prepare a registration dossier with the passage of all registration procedures during the validity of the patent. This greatly accelerates the access of generics to the market and increases the availability of medicinal products for people.

Generic medicinal products with similar therapeutic equivalence are much cheaper than the original. And with the entry of the generic into the market, the price of the original medicinal product is significantly reduced by price competition and the termination of the monopoly on the market, which benefits both the consumer and the country.

Effective mechanism for entering the generics market while respecting the balance of patent rights protection on the original MP (molecule, method of obtaining) is Bolar provision.

This rule is implemented in the legislation of developed countries and provides the opportunity for the release of the generic on the market immediately after the expiration of the relevant patent.

WHAT IS SITUATION IN UKRAINE?

Currently, such a mechanism is not in the legislation of Ukraine, but many steps have already been taken to implement it. In accordance with the State Strategy for the implementation of the state policy of providing popula-

VOLODYMYR KOSTIUK

Executive Director of Farmak JSC

«It is necessary to allow the national manufacturer to compete in the pharmaceutical market with a foreign manufacturer that is currently in a privileged position under equal conditions. Generic medicinal products of domestic production are high quality medicinal products. Over the past seven years Farmak has invested USD 184 million in innovative technologies and modernization of production.»

tion with medicinal products for the period up to 2025, approved by the resolution of the Cabinet of Ministers of Ukraine dated 05.12.2018 No. 1022, increasing the availability of medicinal products is one of the directions of the Government's activity, defined in the medium-term plan of priority actions by 2020.

The problem of ensuring the availability of medicinal products is to be solved by resolving the patentability of patents regarding inventions related to medicinal products. Namely, implementation of Bolar provisions into the legislation of Ukraine, according to which companies are allowed to apply for state registration of a generic before the expiration of the patent on the original medicinal product. After expiration of the patent, the company can immediately start the introduction of a generic into circulation. This reduces the time, as well as establishes the peculiarities of verifying the inventions whose objects are medicinal products for compliance with the requirements of patentability. That is, it will help to avoid the issuance of new patents for inventions that are not innovative, but only contain minor modifications to already existing patents, with a slight improvement in efficiency, so-called "evergreen" patents.

Also a draft law No. 9385 "On amendments to certain legislative acts of Ukraine regarding the implementation of certain provisions of the law of the European Union in the field of intellectual property" is under consideration of the Verkhovna Rada.

According to which Bolar provisions and a number of other mechanisms are introduced in order to eliminate an unfair patent monopoly on the Ukrainian market in the form of "evergreen" patents.

Adoption of these changes will lead to a significant reduction of the unscrupulous patent monopoly on the market of medicinal products in Ukraine and will open new opportunities for manufacturers of generics.

IN PRACTICE

The problem in protecting intellectual property rights is the ineffective mechanism for protecting rights for well-known TMs. For example, a major part of the Farmak history was the struggle for the medicinal product Corvalol.

In 1959, the first batch of Corvalol was released at Lomonosov Kyiv Chemical and Pharmaceutical Plant (since 1991 — Farmak). It was there that the name was created for the generic, the right to use that tried to assign another pharmaceutical company — Darnitsa.

Such actions are a manifestation of unfair competition, since it is about using the Corvalol brand. After all, it gives huge advantages to other manufacturers who try to immediately get without any efforts and use the same brand with the obtaining of uncompetitive advantages on the market.

Farmak advocates civilized competition and protects its rights to well-known TM Corvalol (Corvalolum).

EXPERT OPINION

SVITLANA MOROZ
lawyer, Candidate of Juridical Sciences, Managing Partner of Dictum Law Firm

In Ukraine, the violated rights of the owner of TM can be protected in several ways:

- **complaint procedure — addressing an offender with claims or demands;**
- **judicial protection of own rights;**
- **appeal to law enforcement agencies;**
- **appeal to the Antimonopoly Committee for unfair competition.**

In practice, to protect own violated rights, you must apply all of the above methods simultaneously, or several of them. The owner of TM can face the following problems:

1 The offender does not want to voluntarily stop the illegal actions. Moreover, sometimes the violator begins to resort to circuit mechanisms to mask the violation. For example, it records the rights to so-called dubbing of original TM, creates a series of fictitious business entities to hide the real offender, and so on. All this complicates the process of protecting the owner of TM.

2 Prolonged litigation processes. Judicial reform is still ongoing, courts remain overwhelmed, because of this the terms of hearing of cases are critically violated.1991 Instead of a few months, the hearing of a case can last for several years only in the first instance court. In addition, the opponents themselves contribute the prolonging of the process by abusing their rights: they initiate the appointment of optional expertises on obvious issues, appeal court orders, and so on. In the end, the general period of hearing of the case by all instances may last from two to five years. Meanwhile, business loses not only money for litigation, but also profits, as offenders may continue to violate the rights of the owner of TM.

3 Ineffective law enforcement agencies. Article 229 of the Criminal Code of Ukraine provides for liability for the misuse of TM. Consequently, the owner has the right to apply for a criminal offence. In Kyiv, one investigator can conduct simultaneously from 100 to 500 criminal proceedings. The question arises: will the investigation of the offence be carried out at all? Currently, the answer to it depends on the proactivity of the owner of the TM, since the main work will be performed by the lawyer instead of the investigating authorities, whose costs will be borne by the owner of the TM.

4 The Antimonopoly Committee, considering the issue of unfair competition, often approaches the case in a purely formal way, de facto not promoting the protection of violated rights.

In December 2018, Farmak launched a new production of solid dosage forms, which will allow to double annual production capacity and reach 3 billion units per year.

KEY PHASE OF THE PROJECT LASTED FOR TWO YEARS, ITS COST IS OVER EUR 10 MLN.

OPENING OF SDF-2 SITE: production capacities doubling

REORGANIZATION

During 2016-2018, specialists of Farmak turned the packaging site of SDF into large-scale production: 5 lines were placed, one of which is the most high-speed in Ukraine, established a system of raw material preparation, roller compactors and mobile containers. As a result of reorganization, the site is equipped with the process equipment necessary for all stages of the production of medical products.

PREPARATION: ANALYTICS

Working on a new site, Farmak listened to the consultations of leading European experts with many years of experience in organizing similar productions. The specialists carried out large-scale research and analytical activities, took into account both the Company's features and the main current trends in the industry, and eventually developed the best method of industrial technology for obtaining SDF.

BENEFICIAL WORK

Farmak cares about its employees being able to engage in a safe and mutually important business, getting a decent compensation. Thus, during the last 5 years the salary of Pharmacists has increased 2.4 times. Opening a new site will allow many people to

At the opening of the SDF-2 site

FILIA ZHEBROVSKA

Chairman of the Supervisory Board of Farmak JSC

«We have increased the salaries of our employees by an average of 15%, and in the last 5 years it was increased 2.4 times. Thanks to the new production, which will enable us to increase our capacities and make quality medicinal products manufactured by Farmak available to more people, both in Ukraine and around the world, additional jobs will be available. This meant that more families in Ukraine would look ahead with confidence, getting a stable and decent salary. We conduct business honestly and transparently and believe that such an approach will make our country independent, strong and free. And it will make people happy.»

join the work at the Company, as almost 100 additional positions will be created at the site.

THE NEWEST EQUIPMENT FOR THE NEW SITE

The entire cycle of the production of medicinal products, from the processing of raw materials up to the receipt of the finished dosage form, is carried out using the most advanced devices from the leading European brands such as Glatt, IMA, Marchesini, etc. These companies are recognized leaders in pharmaceutical engineering. There are also high-quality systems of energy supply, ventilation, air conditioning and design of "clean" premises at SDF-2 site, the air of which maintains a certain level of microorganisms, dust, aerosol particles and other important indicators are monitored.

TECHNOLOGICAL CYCLE

At the new site, all stages of the manufacture of medicinal products are implemented — from the preparation and processing of the initial components to the cleaning of equipment. Transferring raw materials and intermediates with different stages of production is carried out without contact with the environment, due to pneumatic transport and sealing systems. The automated control of the technological process enables the control of intermediates at all stages. Inventory of any size is qualitatively cleaned, as well as the premises in which processing of raw materials takes place.

CAPACITY GROWTH

Over the past two years, the total production of FARMAK has increased to 1.5 billion tablets per year. The site, which was reorganized into SDF-2, was built in 1998. Then it was not about such a level of productivity, but the updated technological scheme designed for maximum capacity growth.

ACTIVE DEVELOPMENT

This year Farmak will transfer to the new site the production of almost 30 products.

It is soon planned to increase the production capacity to 3 billion medical units. This will contribute to the further development of the export and the consolidation of Ukraine's position on the international scene. In addition, the Company, which is one of the top 100 taxpayers in Ukraine, will be able to replenish the state budget even more.

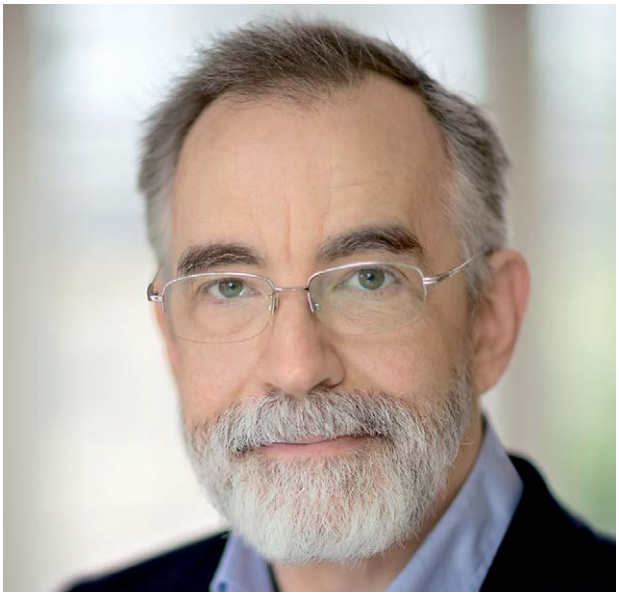
«One of the most important conceptual ideas for the new production of SDF-2 is the design of existing technological schemes in a complete and consistent series of batches, the size of which is scaled from an experimental few hundred grams to large-scale hundreds of kilograms. The implementation of such a philosophy has made it possible to unite the SDF manufacturing sites into a single flexible and universal production and economic complex with the launch of a wide range of modern medicinal products in tablets, capsules, sachets and dragees based on almost hundreds of therapeutic molecules.»

ANDRIY GOY

Technical Director of Farmak JSC

SDF-2 production site

Eric Drexler:



«THE FOUNDING FATHER OF NANOTECHNOLOGY» predetermined directions of modern science development for a decade.

The achievements of Eric Drexler make us believe that this person with the intelligence of the genius and the imagination of the artist in a fantastic way materialized in response to the aspirations of society, which believed in the inevitability and the good of progress, expanding the limits of human knowledge under the motto «to boldly go where no man has gone before».

- We will be able to harvest solar power a trillion times greater than all the power now put to human use. From the resources of our solar system, we will be able to create land area a million times that of Earth. With assemblers, automated engineering, and the resources of space we can rapidly gain wealth of a quantity and quality beyond past dreams. Ultimate limits to lifespan will remain, but cell repair technology will make perfect health and indefinitely long lives possible for everyone. These advances will bring new engines of destruction, but they will also make possible active shields and arms control systems able to stabilize peace.

What it is? The monologue of the science officer from the The Star Trek film series? No, this is a quote from Eric Drexler's first book, "Engines of Creation: The Coming Era of Nanotechnology". And this is not a fantastic novel. Drexler did not entertain the public with fabrications, he created a program for the future development of mankind.

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a human legend

IN THE SPACE ERA

Prior to the nanotechnology, Drexler came from the aerospace industry. Already in the first cource of the Massachusetts Institute of Technology, he joins the search for extraterrestrial resources. In 1975 and 1976, Drexler participated in NASA's researches regarding space settlements, developed high-performance solar batteries based on nanotechnologies. He also contributed to space policy, helping the non-governmental organization L5 Societ dealing with political issues of future colonization of space, to conclude an agreement on the activities of the states on the moon and other celestial bodies within the framework of the United Nations on December 18, 1979.

BASES FOR THE BREAKTHROUGH

The first article by Erik Dreksler on nanotechnology, which later developed into the concept of the development of an entire field of interdisciplinary research, was published in 1981 under the title "Molecular Engineering: An approach to the development of general capabilities for molecular manipulation". Based on the technique developed at that time for the design of complex protein macromolecules from simple molecular fragments, Drexler considered the possibility of creating a variety of devices — wires, motors, bearings. In the "Engines of Creation", his program work, published in 1986, he expands the scope of nanotechnology to all areas of human activity. From the utopian hymns of the advancement of progress in the selection of the authors of science fiction Drexler distinguished one thing: he was very well acquainted with advanced technological developments of his time and understood the prospects for their application. In the 1980s, there were two inventions that gave impetus to the whole development and variety of nanotechnologies of our time.

- Firstly, in 1981, a scanning tunneling microscope was created, which made it possible to see the singular atoms and connections never seen before. Already in 1989, he was successfully used for the manipulation of individual atoms. Microscope developers Gerd Binning and Heinrich Rohrer, researchers from the IBM Research Laboratory in Zurich, received for this invention in 1986 Nobel Prize in the field of physics. In the same year, the same scientists created a power atomic microscope.
- Secondly, in 1985, future Nobel laureates in chemistry, Harold Kroto, Richard Smalley and Robert Curl, have discovered fullerenes, molecules representing a closed sphere of 60 carbon atoms. Initially, no one expected the use of fullerenes in nanotechnology, but later, in the process of discovery and working with carbon nanotubes, fullerenes were used to create nano-sized transistors, nanowires, super-strong yarns and composite materials. The potential of fullerenes in biology and medicine also came into the spotlight very quickly.

WHAT CAN WE DO?

Professor Marvin Minsky summarized the best of all the theory of Drexler in the preface to his book. "Engines of Creation," Minsky wrote, "begins with the thought that our ability to do something depends on what we can build. This leads to careful analysis of possible ways to form atoms. Further Drexler raises the question: "What exactly could we build with using mechanisms?" For example, we could produce collection machines even smaller in size than living cells, and build more durable and lightweight than anything we have today. And as a result of this — the best spacecraft. And yet — tiny devices that will travel by capillaries and restore the living cells.

So, we get the ability to treat diseases, minimize the destructive effects of age, the ability to make our bodies faster or stronger than before. We could create machines that are similar in size to viruses that will work at speeds that none of us can yet appreciate (nano-assemblers. – E. Drexler). And as soon as we learn to do this, we could collect myriads of such tiny particles in intelligent machines, perhaps based on the use of quintillions of nano-

<60

types of therapies using nanoparticles exist nowadays

scopic devices that will work in parallel, make descriptions, compare them with previously recorded models, and then use the results of all past experiments (nanofabrics. – E. Drexler). In this way, these new technologies could change not only the materials and tools that we use to form our physical environment, but also the actions that we could make within any world we create."

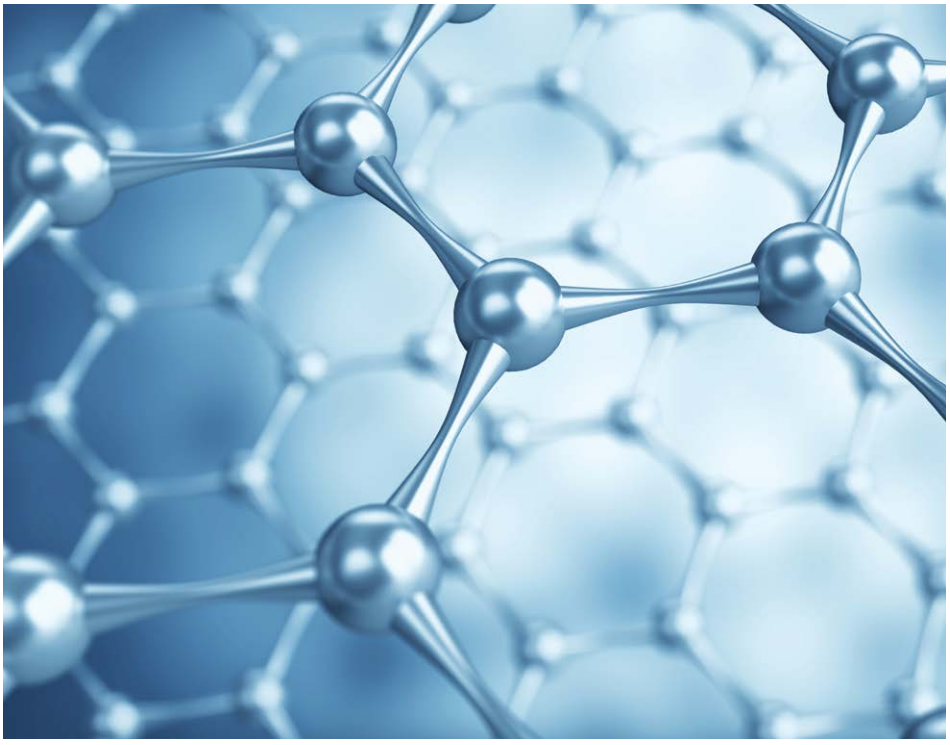

Photo from shutterstock.com

WHAT WE HAVE DONE?

Since the appearance of the first book by Drexler passed more than thirty years. Has humanity succeeded in this time, for at least to realize the bold forecasts of the American soothsayer, or they remained an unrealizable dream and went to the realm of science fiction writers, who, incidentally, repeatedly deduced the figure of Eric Drexler as a hero of utopia and space operas? Let's see!

Nanowires that have an atomic thickness, nanobatteries, capable of charging in seconds, tiny nano-data storage device that can store information in an amount equivalent to 1,000 DVDs — here are just a few examples of high-tech devices that have already been implemented. As for the nanomedicine, the vast majority of ideas are still at the stage of the projects. However, we can talk about specific inventions. So, for example, in the US, a nanocytometer was used — a pocket device that detects a disease with one drop of blood. Or we can mention the microsensor that is absorbed into the patient's body and analyzes the content of glucose and insulin in the blood. Already, the use of nanoparticles has increased the accuracy of MRI, ultrasound and brought DNA-sequence analyzers to a new level.

IN 2011 AT THE IV INTERNATIONAL FORUM ON NANOTECHNOLOGY DREXLER WAS ASKED: "DID ALL OF YOUR FORECASTS FROM THE PAST DECADE CAME TRUE? " "ALL THAT I FORECASTED WAS SUCCESSFULLY IMPLEMENTED", THE SCIENTIST ANSWERED. AND HE WAS RIGHT.

When it comes to the pharmacological aspects of nanomedicine, the unique possibility of "targeted" delivery of medicinal products directly to "destination" comes to the forefront. This creates the basis for the development of innovative medicinal products, as well as to increase the effectiveness of medicinal products available in the arsenal of pharmacists. The potential of such technologies lies outside the imagination — researchers are dreaming about nanodevices, which will independently gather in the necessary configuration, will highlight the pathology, evaluate it, treat it and report it to the doctor. Is it unrealistic?

An example of close to the implementation of the projects proves that we have every chance to witness the triumph of nanomedicinal technologies. So, it can be noted that a team of researchers from South Korea and the United States recently developed a prototype of nanopatch that can control the activity of the muscles of its owners and, if necessary, to inject medicinal products. And scientists from the University of York since 2013 are working on the creation of nanosystems that will be used to fight cancer. The nanoparticles covered with antigens are introduced into the body, where they are attached to cancer cells, giving the opportunity for targeted influence on the undesirable neoplasms.

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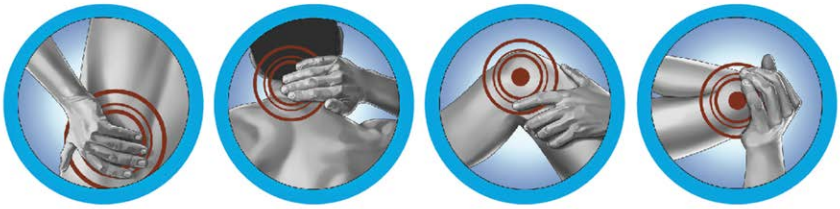

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OF JOINTS, TENDONS, LIGAMENTS AND MUSCLES, ACCOMPANIED BY PAIN

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Approved by Order of the Ministry of Health of Ukraine No. 453 dated May 18, 2016. Marketing Authorisation No. UA/15144/01/01
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Manufacturer Farmak JSC, 36 Frunze Str., 04080, Kyiv, Ukraine. Tel.: +33 (044) 496-87-87, HYPERLINK 'mailto:Info@farmak.ua' info@farmak.ua

1 - Instruction for medical use of the medicinal product
2 - Gürol Z., Hekimoğlu S., Demirdamar R., Sumnu M. Percutaneous absorption of ketoprofen. I. In vitro release and percutaneous absorption of keloprofen from different ointment bases. Pharm Acta Helv1996; 1(3)205-12
3 - Rother M., Lavins B.J., Kneer W. et al Efficacy and safety of epicutaneous ketoprofen in Transfersome (IDEA-033) versus oral celecoxib and placebo in osteoarthritis of the knee: multicentre randomised trial

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