INTELLECTUAL PROPERTY PROTECTION OF PHARMACEUTICAL PRODUCTS AND PROCESSES

The role of intellectual property is significantly increasing within new international economic and commercial relationships. Intellectual capital is being increasingly recognised as one of the most important domains belonging to the greatest and the most powerful world companies. Intellectual property protection is a complex category and it comprises legal, technical and economical-financial aspects.

WORLD TRENDS

By establishing the World Trade Organization (WTO) and by controlling of international trade through ratified agreements, among which is the Agreement on the Trade-Related Aspects of Intellectual Property Right (TRIPs, adopted in 1994, in force since 1995), the patent protection of pharmaceuticals has been approached in a harmonized manner. TRIPs is an international multilateral contract obligating all member states of the World Trade Organization (WTO) to protect rights, not to liberalize their approach. WTO members are obliged, depending on the level and characteristics of social-economic, scientific and technological development, to introduce certain regulations in their legal and sublegal acts, making a balance between the minimum of the required standards of the TRIPS agreement and the benefit of their people. In addition to being a harmonized legal act, TRIPs also implies strict customs and inspection control which must be applied [1].

The elements of technologies can be protected as industrial property (patents, trademarks, models, samples and geographical marks of origin), can be kept as secret knowledge and experience "know-how" or protected as copyright, which, in total, is intellectual property.

The copyright and related rights law regulates the rights of the authors of literature, scientific, and artistic works (copyright), interpreter’s rights, phonogram producers’ rights, videogram producers’ rights, broadcast and databases rights as well as copyright-related rights (related rights). The author enjoys ethical and property rights from the moment of the emergence of the authorial work. The Internet and digital media, computer programmes and databases,\[...

inflict a serious problem and require the search for effective copyright protection. The new media have facilitated reproduction and dissemination, but also the anonymity of the distributor. On the other hand, copyright protection is aggravated.

For the field of pharmaceutical products, trademarks are of great importance, as elements of industrial property, and the pharmaceutical industry takes care of that. A trademark is the right which protects the mark which in commerce has the function to differentiate goods, namely the services of a natural or legal person of the same or similar goods, namely services of another natural or legal person. It can be individual or collective. A trademark lasts for 10 years, from the date of filing the application, and its validity can be prolonged endlessly. Becoming famous, relying on the steadiness of quality and good marketing, the trademark becomes one of the constitutive parts of the enterprise capital, sometimes even the main enterprise capital [2].

Patents are issued for inventions that are new and involve an inventive level and are convenient for industrial application. The subject matter protected by a patent can be a product (apparatus, substance, composition, microorganism, plant or animal cellular culture), a procedure, as well as an application of a product or a procedure. The invention has its inventive level if a solution of a certain problem does not obviously arise from the state of the art, for a person skilled in the art. An invention is new if it is not comprised by the previous art. Patent protection is permitted for new medical substances or compositions (formulated drugs), as well as for those comprised by previous art, and are applied in a surgical or diagnostic procedure or the procedure of treatment, with a proviso that their use is not comprised by the previous art. The protection is valid for 20 years.

Support and development of the patent system in the world framework provide monopoly to the owners of the rights and the achievement of significant revenue. The patent system influences the economical.
Following world trends, it may be noticed that our economy generally lacks the assessment of the market value of trademarks and patents, implied in the product price, as well as in the company price.

The Patent Cooperation Treaty (PCT) is an international agreement, signed in 1970, with the goal to join and simplify the application procedure for inventions, in more countries, through one international application, as well as to facilitate the procedure of the examination of the applications to the national patent offices. The patent procedure through the PCT is divided into two phases. In the first, so called international phase, an international patent application is filed with the ascribable patent office (recipient office). There is, also, a phase of submitting a request for international preliminary examination, PCT Demand, before the expiration of 19 months from the priority date. The second phase, so called national, starts from the moment when the indicated offices receives the copy of the international application and the report on international search, as well as, a translation of the application into the official language of the office [5].

Through the initiated reforms of the PCT, the WIPO is trying to harmonize the international patent system, simplify, reduce costs, and help the overloaded patent offices [6].

Graph 1 shows the increase of the number of filed international PCT patent applications (Request) and Graph 2 shows the increase of the number of filed International preliminary examination demands (Demand), indicating the use of facilities offered to applicants. The PCT Demand was used by approximately 80% of the applicants in order to save some time, and since 1. April, 2002 the deadline for entry into the national (regional) phase is 30 months of the priority date, regardless when the Demand was filed. On the other hand, data on the number of patent
applications, their richness and the amount of the costs of protection show that developing countries are excluded from any significant use of the international patent system.

Analysing graph 3, we can conclude that from the total number of applications in the world, using the PCT, 63% come from the USA, Germany and Japan, i.e. 85% of all applications are concentrated in the top 10 countries, and all other 105 countries participate with 15% of the total number of applications. (A similar configuration was noted in the distribution of benefits in the world economy). The reason lies in the fact that patent strategy is an integral part of enterprise strategy in developed countries. The WIPO plan for changes within the system, established as its goal a development that will provide that a greater part of the benefits remain for developing countries. [7, 8]

Recently, with the development of the pharmaceutical industry, special importance has been given to drug formulations and product in procedures in favour of use of the medical substance in the proper quantity, composition, and convenient form for respective use. Achievements in the field of pharmaceuticals would have not been at such a level without the support and development of the patent system in world settings, providing a monopoly to the owners of the rights and the realization of significant revenue. Pharmaceutical companies agree that 65% of the pharmaceutical substances would have not been developed or commercialized without patent protection permission, which is much more in comparison to any other industrial branch. [3]

The statistical data in Table 1 presented by the WIPO for 1999 confirm that the greatest number of patent PCT applications are from the field chemistry and metallurgy and human needs (40.2%), indicating that the largest number of research and new technologies are in this field, but also the realization of the inventors, owners, that these technologies are valuable and that they should be protected in the largest number of countries in the world. [7]

Table 1. Statistical data of the WIPO for 1999 – number of international PCT applications

| 1. | Chemistry and metalurgy                  | 21.1% |
| 2. | Human needs                              | 19.1% |
| 3. | Electricity                              | 16.0% |
| 4. | Physics, operating, transportation       | 15.9% |
| 5. | Mechanical engineering, lighting, heating, arms, explosion | 6.9% |
| 6. | Fixed constructions                      | 2.9%  |
| 7. | Textil and paper                         | 1.6%  |
HARMONIZATION OF REGULATIONS IN SERBIA AND MONTENEGRO

In the Strategy of industrial development of Serbia by 2010, the following strategic priorities are stated: supply of the domestic market with drugs of high quality, technology transfer and export to the world market. Prerequisites for emersion in the world market are, among others, the publication of an official document on a National policy of drugs, primarily, legal solutions, harmonized with the regulations of the EU: Law on Medicinal Products, Health Protection Law, Patent Law, Trademark Law. At that point, the state should have a defined strategy, not only for scientific and technological development, but also for the patent system. In addition to legal solutions, there are many other aspects, such as the composition of a positive list of drugs, the affordability of drugs, pharmaco-economics, drug supply systems, their rational usage. In our environment, it is still not used sufficiently for the purposes of development and research, namely the usage of patent information. Awareness of the importance and the influence of intellectual, particularly of industrial property on the reputation of the enterprise, institution, is still not predominant [6].

A valid Trademark Law in FR Yugoslavia has been effective since 1995. [9] The law on amendments of The Trademark Law was stipulated by: verification of the corresponding legal solutions in practice, compliance with The Treaty on Trademark Law (WIPO, 1994), ratified by the FRY in 1996, more rapid implementation with: the TRIPS agreement, the EU Directive for harmonization of the laws of the member states concerning trademarks, EU Trademark regulation, the WIPO Corporate resolution on the protection of the eminent trademarks (1999), a significant increase of the economic role of trademarks and the total intellectual property law in international correlations [10].

A valid Patent Law in the FR of Yugoslavia is relatively new, and has been effective since 1995. [9] However, its amendments are stipulated by the need to continue the initiated process of harmonization with the corresponding regulations of the European Union (EU), as well as with, in the meantime enacted, international conventions in the field of patents. In the same way, the enforcement of the corresponding legal solutions in practice, the rapid development of new technologies (genetic engineering, digital technologies and so on), significantly increased the economic role of patents, namely the total intellectual property law in international correlations, new economic and political prospects of our country, stipulated the need to amend the already existing law.


The Yugoslav Patent Law has permitted the protection of a new substance, since 1990, and since 1993 it has permitted the patent protection of medicines, and The Law from 1995 enabled protection and new usages. According to the subject matter, the accepted division of patents deals with a product patent and a process patent, which includes a use patent, which considers the following forms of patent claims, (within usual patent claims for a product, for process, and for use), for protection of: the product (substance), that is, the compound itself, the product defined by the process, composition, formulation, process (new or improved process) or analogous process, surgical, diagnostic or treatment process, or use. Pursuant to provisions of Article 7 of the Law, protection is given to the substance or composition for certain use, and it is not limited to the form of the product prepared for the use, protection is given to the substance or composition for use in procedures from Article 4.2 of the Law (12).

The special importance of patent information for corporate enterprises and development-research centres is reflected in the possibility of the fortification of positions and the development of more powerful strategies through: follow up of the competition; prediction of the development of particular companies and economic sectors; search for business partners; definition of the right starting position for future projects. The data on protected inventions, known trademarks of a company, its products and services, are a recommendation for business partners from the country and abroad, that they can, with less risk, establish business cooperation, to invest in development of the company or to grant a licence.

In order to obtain the adequate protection of an invention from the field of pharmacy and chemistry, it is necessary (in accordance with The Law) that the patent application is composed in acceptable form, i.e. to have a description of the invention and to define patent claims, in order to avoid likely consequences due to an inadequately presented invention in claims [13].

An issue of special interest is an infringement of patent rights by early working, when a pharmaceutical company, before the expiration of patent protection,
without asking for any permission, without asking for a license from the right holder, for the purpose of registration of the generic product, prepares samples, performs clinical tests and files an application with the corresponding state body, for putting the product on the market, in order to start commercialization of the product, immediately after the date of expiration of patent protection. The problem of the mentioned early work, still being discussed within the WHO, is based on the court decision in the USA, in the case of Roche Products Inc. vs. Bolard Pharmaceutical Co. (733 F.2d 868, Fed.Cir., cert. denied 468 US 866. 1984). For that reason is the case of stated derogation called the Roche–Bolard clause. "Bolard" was first introduced in the USA, by the following acts: US Drugs Price Competition and Patent Term Restoration Act (1984) and was immediately accepted in Canada, Australia, Israel, Argentina and Thailand. For its obvious usefulness, a number of countries consider the possibility for introducing similar legislation. The introduction of generic products improves the health protection level, because products with considerably lower prices are placed on the market.

Within the WTO a debate was conducted between Canada and the European Union. There is a indicated derogation of the "Bolard" type in Canadian legislation, but in addition to the tests, production and sale and stocking are also permitted, so that the generic product is placed on the market as soon as the patent protection expires. The EU opposed such a practice. After a panel discussion within the WTO, a stand was taken that early working is not antithetic with the TRIPS agreement and in the absence of a prolonged period of patent protection, but that production and stocking were not consistent with the TRIPS. (WT/DS114/R, 17 march, 2000). The World Health Organization particularly pleaded for the permission of early working right concerning the registration of drugs used for the treatment of AIDS (WHO, 1999; UNAIDS, 1999).

The practice is different in Europe, the opinion that research does not consider clinical examination which should show if the product is efficient and safe, still prevails – these activities denote patent infringement, while the science and research within these tests do not represent patent infringement. For that purpose the European Commission pressed upon is body National Economic Research Associates to compose a report on generic industry in Europe and it considered the possibility of altering of legal act in this sense, for its member states. France has already introduced "mini Bolard" clause through its Law on financing of social insurance. Hungary and Croatia have such a clause within the Patent law.

Introduction of the Roche–Bolard clause within the revision of pharmaceutical legislation in the EU would contribute to the creation of considerably more favorable conditions for generic companies and the improvement of health protection of the population. The standpoint of the Group of Pharmaceutical Producers of Serbia and Montenegro is to keep the legal possibility of early working on the development of new products within the Patent law, so that pharmaceutical manufacturers in Serbia and Montenegro can perform all the activities required for the registration of products and put them on the market at the moment of expiration of the valid patent [3,4].

EXAMPLES OF INTELLECTUAL PROPERTY PROTECTION

Research conducted at AD "Zdravlje" are completely within world trends in the fields of synthesis, extraction, biotechnology, pharmaceutical technology, preclinical and clinical research, so that its high-quality products, usually marked with trademarks, are placed on the domestic and foreign market. AD "Zdravlje" have 10 registered patents valid in the FR of Yugoslavia, 13 patents applications in the FR of Yugoslavia are pending, 7 of which are filed as international PCT applications, and for 3 of them a PCT Demand has been filed. AD "Zdravlje" has 161 registered trademarks which are valid, 11 applications are in pending, and 25 trademarks are internationally protected.

1. In the case of a patent claim for a new product – substance (compound), it should be composed in such way to clearly and completely determine the chemical compound for which protection is sought. It is defined by the chemical name and structural formula with indicated radicals the meaning of which should be determined.

Example: Yugoslav and international patent application P-769/00, PCT/YU 01/00031, WO 02/46241, named: "Polynuclear complex Fe(III) with pululan oligomers, procedure for its synthesis and pharmaceutical preparations thereof", by the following inventors: Ljubomir Ilić, Suzana Ristić, Milomir Caesar, Goran Nikolčić and Slobodan Staniković, with the priority date 7 Dec., 2000 [14]. The first independent patent claim which determines chemical compound is:

"Polynuclear complex of pululan oligomers of formula (I):"
wherein \( n = 100-8200 \), with iron(III) hydroxide of formula (II):

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\begin{array}{c}
\text{OH} \\
\text{Fe} \begin{array}{c}
\text{OH} \\
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\text{Fe} \\
\text{O} \begin{array}{c}
\text{Fe} \\
\text{OH}
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(II)

\[ n = 900^\circ. \]

2. In the case of the patent claim for a composition, the mentioned composition should be determined by its qualitative composition and quantitative ratio/amount of each ingredient. In compositions with the same active ingredient, the quantitative ratio of the ingredient may be expressed as the "effective quantity." Unexpected effects and advantages of the composition should be highlighted in the description of the invention. The analogous substitution of the ingredients does not meet the inventive criterion. If there is a synergism, it is explained in the description of the invention.

Example: Yugoslav patent application P-1675/83, patent No YU 42 873: Procedure for the decatetation of \( \alpha \)-acetyl-digitoxine*, by the following inventors: Slobodan Stanković, Sinisa Borojević, Miljko Stanković, Mijivoje Radelović, with priority date 9 August, 1983 [17]:

"Procedure for the decatetation of beta-acetyl-digitoxine denoted by the fact, that to 1 to 10 m\(^3\)/vol. %, optimally 1% solution of beta-acetyl-digitoxine in absolute ethanol, aluminium oxide impregnated with sodium hydroxide with a degree of impregnation of 0.1 to 0.5 g of NaOH/g Al\(_2\)O\(_3\) and activated at 300\(^\circ\) to 1000\(^\circ\)C, optimally for four hours at 800\(^\circ\) C in the weight ratio 4:1 to 1:2, optimally 2:1, towards beta-acetyl-digitoxine and, subsequently, heated at boiling temperature for 1–3 hours, optimally 2 hours.

5. In the case of patent claims for use in pharmacy there are certain deviations in comparison to acceptable patent claims from other fields of the art.

Pursuant to Law provisions dispensing surgical, diagnostic and treatment procedures, applied immediately on the human or animal body, are not acceptable patent claims directly referring to use, but the intention is that the new, inventive use of substances and compositions in the processes are protected indirectly and to provide the equal treatment of inventions, with inventions belonging to other fields of the art.

5a. In the case when an already known substance or composition, is involved for which medical use is found (so called "first medical use") in surgical, diagnostic or treatment processes, patent claims in the form of "product patent claims limited by their purpose" are acceptable.

Example: Yugoslav patent application P-309/01: "Procedure for the synthesis of amino acids and an iron complex" invented by: Slobodan Stanković, Danijela L. Stojarović, Ljiljana Pešić, with priority date 26 April, 2001 [18]:

"Amino acids and a metal complex, of the general formula \[ (\text{H}_2\text{N}-\text{R-COOH})\text{M}^{2+} X^{2-} \] ferrous glycine sulphate, for the prevention and treatment of sideropenic anaemia, obtained using the procedure according to claims 1 to 4."

5b. In the case when the new and inventive use of a known substance or composition in procedures is involved, the following form of patent claims is acceptable (so called: "second medical use"): "Use of
substance or composition X for the production of drug for therapeutic use Z".

Example: Yugoslav patent application P–308/01 “Pharmaceutical preparations on the basis of bivalent iron and medical plants and production procedures” invented by: Slobodan Stanković, Danijela L. Stojanović, Zora Stojiljković, Dušanka Mihajlović with the priority date 26 April, 2001 [19]:

“The use of nettle, yarrow and horsetail extracts for obtaining a pharmaceutical preparation for the prevention and treatment of sideropenic anaemia”.

CONCLUSION

Information on intellectual property and the utilisation of its achievements such as: world state of the art and world design fund; development strategy; technical solutions; patent protection of new, inventive, applicable solutions; trademark protection of original and new logos; model or sample protection of new and original design, skilled and creative marketing support concerning choice and utilisation, are cumulative conditions for total success, the acquisition of extra revenue and the most reliable investment.

LITERATURE

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tive preparations on the basis of uric acid sodium salt and medical plants and process for their obtaining”.

IZVOD

ZAŠTITA INTELEKTUALNE SVOJINE ZA FARMACEUTSKE PROIZVODE I POSTUPEK

(Stručni rad)

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Farmaceutska industrija je visoko profitabilna, ima poseban društveni značaj, visoke zahteve za kvalitet, posebne mere u proizvodnji i prometu lekova, izuzetno visoka ulaganja u istraživanje i razvoj. Većih multinacionalnih kompanija uvećao količinu patentne zaštitu u ovoj oblasti za potrebe otkrivenih sredstava, obezbeđe monopol, ostvaruje značajni profit i izuzetno poštaju zakonsku regulativu. Farmaceutske kompanije priznaju da 62% njihovih farmaceutskih supstanci ne bi bilo razvijeno ili komercijalizovano da nije dozvoljena patentna zaštita, što je mnogo više nego u bilo kojoj drugoj grani industrije. Međunarodna trgovina regulisana je sporazumima Svetske trgovinske organizacije (STO), među kojima i Sarjavom o tvornickim aspektima prava na intelektualnu svojinstvu (TRIPS). Srbija i Crna Gora svoje propise u ovaj oblasti harmonizovale su propisima visoko razvijenih zemalja u cilju pristupačnosti EU. U Strategiji razvoja industrije Srbije do 2010. u delu koji tretira farmaceutsku industriju značajno mesto dato je harmonizaciji zakonske regulativ, uz prelazni period od minimum 5 godina. Grupacija farmaceutske industrije Jugoslavije je proglasila za jedan od prioriteta programa razvoja interzvivnu i pravovremenu zaštitu intelektualne svojine.

Ključne reći: Intelektualna svojinstva • Farmaceutski proizvodi • Zakonska regulativa • Harmonizacija propisa

Key words: Intellectual property • Pharmaceutical products • Legal provision • Harmonization of regulations