PHARMACEUTICAL LAW
LEGAL FRAMEWORK

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Hardly any area of law has such a direct connection to human health as pharmaceutical law. This fact requires fulfillment of detailed and strict conditions which have to be satisfied before a certain drug or medicament is allowed for human use. Nevertheless, the area of pharmaceutical law extends beyond these issues. Equally important part of this area are the rules governing issues of drug advertising and corruption, the purpose of which is to prevent doctors from giving priority to interests other than improvement of patient health. It is of special importance for pharmaceutical companies to obtain timely, precise, correct and high quality legal advice with respect to various legal issues in pharmaceutical industry.

I Introduction

Pharmacy is the activity regulated in detail, with precisely specified rules for each stage a drug or a medicament shall pass through before it can be prescribed to patients. On the other hand, considering quantities of drugs prescribed every day, in addition to amount of money turned over in pharmaceutical industry, countries specify clear rules for purpose of making sure that doctors are not illegally influenced when rendering a decision which drug or medicament to prescribe. Finally considering the impact of drugs/medicaments on human health, the authorities set high safety standards for pharmaceutical companies. All these rules are specified in large number of acts and subordinate acts governing requirements to be satisfied before a drug is released on the market, granting licenses, patenting, testing, insurance, safety, efficiency and marketing. In order to avoid violation of these regulations, pharmaceutical companies need timely, reliable and high quality legal advice.

II Drug and Medicaments Agency

Serbian Drug and Medicaments Agency (hereinafter referred to as: the Agency) is given the task of regulating Serbian pharmaceutical market. Its competence is not limited only to issuance of the licenses and placing of drugs on the list, but the Agency also issues licenses for clinical testing of drugs and medicaments; monitors undesired reactions to drugs; approves advertising of drugs and medicaments; exercises quality control of drugs and medicaments; and engages in other tasks and assignments specified by the law.

III Clinical testing of drugs

In order for a drug to be given a license to be marketed it shall undergo pharmaceutical, pharmacological and toxicological tests. Before a drug is registered and placed on the market, thorough preparatory and research work has to be done (pre-clinical testing on animals and clinical testing on humans). A drug is tested in compliance with good production practice guidelines, good laboratory practice and good clinical practice. Clinical testing programs follow set of strict rules, set to ensure the testing procedure is adhered to and establishes positive balance between risks and benefits relating to therapeutical application of a drug in specific clinical practice.

The Agency receives applications from sponsors for carrying out clinical tests of drugs and medicaments. The applications are processed by the Agency experts, in cooperation with the Commission for Clinical Testing of Drugs experts.
When a license for clinical testing of drugs and medicaments is granted, a very detailed and highly professional assessment shall be made with respect to a proposed clinical testing, in order to ensure safety of patients participating in the clinical testing.
Also, a detailed control is conducted during the course of clinical testing for the purpose of both minimizing negative effects on patients and ensuring objectivity of the test results.

IV Drug marketing license

The process of drug registration and granting of the license for a drug is defined in the Act on Drugs and Medicaments and in other subordinate acts, in compliance with appropriate procedural rules applicable in the EU countries. The marketing procedure for a drug is a long process requiring submission of detailed documentation for the purpose of preventing drugs that do not satisfy strict quality, efficiency and safety criteria from reaching Serbian market. A drug shall be registered only if its quality, efficiency and safety have been demonstrated, which also includes striking positive balance between the risks and benefits of a drug at the moment of registration..
The Agency shall decide whether to grant a drug marketing license. As a rule, a drug is placed on the market on the basis of being granted the drug license. The exception are the drugs for which no license is granted, such as drugs made in pharmacies, drugs intended for testing during a research and other types of drugs explicitly specified by the law as eligible for being placed on Serbian market without the license.

The applicant for the drug license may be a local drug producer or its representative, foreign producer representative, and representative of a legal entity which is a drug license holder in the EU countries. Also, the applicant may be a legal entity with headquarters in the Republic of Serbia, to which a local producer has assigned its drug license.

The application for the drug marketing license shall be submitted to the Drug and Medicaments Agency along with documentation specified by the law, with the Agency being entitled to request additional documentation (the term for providing additional documentation is 30 days). The documentation required for obtaining the drug marketing license is made up of data relating to characteristics of a drug; data on pharmaceutical – chemical – biological tests; pharmacological – toxicological tests and data relating to clinical tests of a drug.

The license for a drug can be obtained through the procedure with either full or abbreviated documentation. The type of procedure itself is conditioned by a drug type.

The application for placing a drug on the market with full documentation shall contain all data specified by the law and other data of importance for obtaining the license which might be requested by the Drug and Medicaments Agency. The application shall also be accompanied by samples of the drug. The application with abbreviated documentation shall be submitted for generic drugs, generically hybrid drugs and biologically similar drugs.

The Agency shall, no later than 210 days following the receipt of full application, render its resolution on granting the license with 5 years validity or a resolution on rejection of the application, subject to the Agency Commission's opinion and assessment of documentation in terms of quality, safety and efficiency of the drug. The license shall be renewed following expiry of the license validity term, subject to the Agency's re-assessment.

Also, the Agency may grant the drug license with unlimited validity term, provided it has established that a drug which has been granted the license is safe, subject to the data relating to collection, discovery, assessment, understanding and prevention of undesired reactions to the drug during the five year period from the date of granting or renewal of the drug license.

The validity of the license shall terminate:

1. by expiry of the validity term (if not extended) or
2. upon request of the drug license holder. Also, the drug license shall terminate if the Agency establishes that
3. he drug is detrimental under normal conditions of use;
4. the drug lacks therapeutical efficiency;
5. the drug does not yield required therapeutical results;
6. the drug license has been granted on the ground of insufficient and incorrect data, or if the data has not been amended in compliance with the law;
7. the license holder no longer satisfies requirements specified by the law.

The Drug and Medicaments Agency may, against the previous agreement with the applicant, grant a conditional license for the drug, requesting from an applicant to meet some specific obligations, which shall be verified by the Agency once in 12 months as of the date of granting of the conditional license.

The Agency shall reject the drug license application if it has established that (i) the risk-benefit balance is not favorable under the normal circumstances of use; (ii) the drug lacks therapeutical effect or therapeutical effect has not been sufficiently proven by the applicant; (iii) the composition of the drug, in terms of quality and quantity is not in compliance with the data contained in attached documentation, or the documentation is not in compliance with regulatory requirements.

V Marketing license for foreign drugs and medicaments

The drug license may also be obtained under special conditions, provided a drug has the license granted subject to the centralized system of procedures applicable in the EU countries. In the Republic of Serbia, the drug license shall be granted in the expedited procedure when a drug has the license in compliance with the centralized system of European Medical Evaluation Agency.

In that case the Drugs and Medicaments Agency shall, no later than 150 days following receipt of the full application, render the resolution on granting the license or rejecting the application, subject to the opinion on and assessment of the documentation in terms of quality, safety and efficiency of the drug.

When the application is filed for obtaining the license with well known application of an active substance, the applicant is not obliged to provide data on pre-clinical and clinical tests, but might, instead of its own data, submit data published in a professional publication.

Since Serbia is not an EU member, at this stage of development of the pharmaceutical regulatory system, granting of the centralized license or the marketing license on the ground of bilateral recognition is still not possible.

VI Drug market and drug safety monitoring

On the drug market there are drugs issued under prescription and paid from the mandatory insurance funds, and drugs which are not on the presription list of the free of charge drugs.

When a drug is placed on the free of charge drug list, the criteria specified in the Rulebook on conditions, criteria, method and procedure for placing drugs on the Drug List, amendments of the List and taking a drug off the list shall all be observed.

The general criteria, subject to which the drugs are placed on the List are:
1. pharmacological and therapeutical justifiability of a drug;
2. pharmacological and economical justifiability of a drug; and
3. financial funds provided in the Financial Plan of the Republic Fund for Health Insurance (RFZO).

The special criteria include:
1. the special agreements (the Agreements executed between RFZO and a producer or the drug marketing license holder); and
2. drugs having priority in placement on the List.

The priority in placement of drugs on the List is applied when RFZO financial funds intended for drugs are insufficient for placing all drugs which have satisfied the general criteria on the List.

The priority in placement of a drug on the List shall be established by the Central Commission for Drugs on the basis of following criteria:
1. the List of Drugs does not contain any drug from the same pharmacological and therapeutical group;
2. public and health significance of the drug;
3. ethical aspect.

In terms of monitoring of safety of drugs, it should be pointed out that following the registration, a drug is placed on the market and begins to be applied in daily clinical practice on large number of patients, under the rules which are not at as stringent as during the clinical testing period.

Following placement on the market, the total safety profile of a drug is not yet known, meaning that information is still insufficient or is not available at all, relating to rare undesired reactions to a drug; reactions after a long exposure to a drug; interactions; potential errors; abuse and incorrect use and application of a drug on specific categories of patients.

For these reasons and the difference between the clinical testing under strict rules and daily, routine practice, the awareness of the safety profile of a drug is limited and shall be expanded. That is why monitoring safety of all drugs on the market, as well as gathering, discovering, assessing, understanding and preventing of undesired reactions to a drug is of prime importance.

VII Advertising and labeling of drugs and medicaments

Labeling of drugs

The regulations define in detail the method of labeling of drugs in order to ensure best possible information to its beneficiaries. The exterior packaging of a drug shall be in Serbian, in both Cyrillic and Latin alphabet, containing brief characteristics of the drug. The data printed on both exterior and interior packaging shall be legible, understandable and indelible.

The exterior packaging of a drug shall contain at least the following data:
- drug name and the international unregistered name of the active substance, if any, or generic or chemical name;
- active substances – in quality and quantity per dosage unit, pharmaceutical form, intensity and packing;
- the list of auxiliary substances having a confirmed effect;
- and for the drugs in the form of injections, the drugs for local application and the drugs for eyes, it is obligatory to specify all auxiliary substances;
- manner of application;
- warning that a drug shall be held beyond reach of children and other necessary warnings; expiry date; special measures for disposal and destruction of a drug;
- if required – name and address of the drug license applicant; license number, drug batch number and EAN – code;
- the manner of use for drugs sold without prescription;
- anatomy – therapy – chemical classification (ATC);
- and for veterinary drugs ATC-vet and other data in compliance with the regulations.
- The name of the drug shall also be written in Braille alphabet.

The interior packaging of a drug on the market shall contain at least the following data:
- drug name and the international unregistered name of the active substance, if any, or generic or chemical name;
- intensity and pharmaceutical form;
- name of the drug license holder; expiry term (month/year);
- batch number and other data in compliance with the regulations.

Advertising of drugs and medicaments

Advertising of drugs shall be deemed to include all measures aimed at promotion, prescription, issuance, sale or use of drugs. Additionally, advertising of drugs and medicaments also aims to assist its application by presenting properties of a product truthfully, fully and without exaggeration, in a manner and under conditions defined by the law.

There are several avenues for drug advertising: through the public media including the Internet; advertising in public places; and visits by drug agents to persons entitled to prescribe or sell drugs.

In that sense, it is prohibited to advertise the professional and medical procedures, methods of health protection including methods and procedures of traditional and alternative medicine in the public media, subject to the laws governing health protection.

Also, the results on application of the professional and medical procedures and methods of health protection shall be presented only at professional and scientific gatherings and published in professional and scientific magazines and publications, in compliance with the laws governing health protection.

Apart from the freedom of drug advertising in line with applicable procedural rules, there are certain restrictions with respect to drugs which shall not be advertised. The following drugs shall not be advertised to the general public: the drugs issued under prescription, the drugs for tuberculosis, the drugs for sexually transmitted diseases, chronic insomnia drugs and drugs without the drug license.

The advertising shall be objective and the public shall not be mislead. The list of drugs which may be advertised shall be prepared by the Drug and Medicaments Agency. Also, any form of advertising for drugs and medicaments shall receive prior approval by the Agency.

It should be noted that there is a difference between advertising of the drugs to the general public and to the professional public. The general public covers citizens of the Republic of Serbia, while the professional public includes medical and veterinary personnel prescribing drugs and medicaments, graduated pharmacists and other professionals in field of production, wholesale and retail sale of drugs and medicaments, as well as professionals employed within organization of the mandatory health insurance.

The difference is made for the sake of establishing more stringent requirements for advertising drugs and medicaments to the general public than to the professional public. So, when advertising to the general public, it is not permitted to show children taking drugs or medicaments without adult presence. Advertising of drugs or medicaments to the general public shall not be exclusively or primarily directed towards children.

Also, advertising to the general public shall not include names of pharmacies, private practices, specialized shops or legal entities dealing with wholesale trade of a drug, including location where a drug or medicament may be purchased. For the purpose of data protection it is not allowed, when advertising to the general public, to gather and present personal data on medical condition of a specific person, diagnosis, therapy procedures applied during a treatment, or a drug/medicament used in medical treatment of certain person or a group of persons.

Special rules apply to advertising of a drug to the professional public. The advertising materials intended for the professional public shall be marked with the term “Only for professional public” and shall be approved by the Agency.

Promotion of a drug to the professional public shall include principal data on a drug as contained in the drug license. This includes the data corresponding to brief characteristics of a drug, as well as data on the drug selling regime. The data shall be correct, updated, confidential and sufficiently complete, so that a recipient may be able, on such basis, to form an opinion on therapeutical value of certain drug. The data shall also contain the date when a drug was made or when a drug was last tested.

Promotion of a drug to the professional public shall be made by professional associates of an advertiser, who have graduated from medical, dentistry, pharmaceutical or veterinary medicine faculty. These persons shall be specially educated in the field of clinical and pharmacological characteristics of drugs they promote, and an advertiser shall be obliged to ensure continuous education of professional associates promoting drugs, verifying their knowledge in order to ensure full, precise and correct information on a promoted drug.

For the purpose of providing information to the professional public on characteristics of a drug or medicament being introduced to the market, it is permitted to present professionals with one sample of a drug or medicament, with the special note on packaging: “Free of charge sample, not for sale”.

VIII Corruption in pharmacy

In the world of pharmacy, there has been a growing criticism of lobbying attempts and impact on doctors by way of promotional gifts and by way of delegating doctors to attend various specializations and seminars. The question arises as to the limits of acceptable gifts and activities crossing beyond the promotion and education threshold into the sphere of illegality.

The laws and the subordinate acts explicitly define which gifts are deemed allowed. For example, an advertiser may sponsor professional gatherings only up to the level of covering necessary costs of travel, accommodation and meals, as well as costs of mandatory participation at a professional gathering and costs directly relating to organizing such professional gathering.

Besides there are restrictions relating to type of allowed costs to be covered by an advertiser; there is a time limit for covering such costs which is for duration of a professional gathering and for maximum of two (2) additional days for related “to” and “from” travel expenses. There is an additional restriction prohibiting sponsorship of accompanying events, such as tourist tours, sporting events and similar events not having the character of a professional gathering.

Sponsoring of professional gatherings shall not be conditioned by requesting or rendering any material or non-material counter-services by the professional public organizing the gathering or by an advertiser. The advertiser shall not influence the content of professional gathering organized by the professional public, but shall be entitled to, at special location points specified for such activities, beyond the area of principal event, to provide information on a drug or medicament in compliance with the laws governing drugs and medicaments.

An author, or a person making presentation at a professional gathering organized by the professional public (or a professional gathering at which the professional public participates), regardless of whether the gathering is sponsored by an advertiser or not, shall, before the beginning of a presentation (at the first slide or in another manner which is appropriate, clear and unambiguous) provide the statement on whether such presentation is sponsored by an advertiser.

The advertiser shall be obliged, on its web site in the Republic of Serbia, or on the official website abroad, or on other appropriate website, to place the data on professional gatherings it has sponsored (continuously for the current year, as well as for the previous year), including the total amount of funds used for sponsoring each professional gathering, informing the Ministry in charge of the web site at which it has placed the data, and providing, upon request, such data to the inspection in charge.

Professional associates of an advertiser, engaged in promotion of a drug, shall be allowed to provide to the professional public, as a gift, only the items which do not have a substantial value, i.e. items with symbolic value relating to medical, dental or pharmaceutical practice, or activities of an employer where the professionals are employed (e.g. pencil, notebook, calendar and similar small value items), which, pursuant to the law are not deemed to be advertising.

Promotion of a drug to the professional public shall not include encouraging to prescribe, issue, supply, recommend use or purchase a drug, by offering and giving an award or incentive by way of money or gifts, or by giving or procuring any other property or non-property gain, benefit or award.

Also, it is not allowed without a clear medical indication to encourage the professional public to replace one drug from the same therapy group by another; to present claims or conclusions on the effectiveness of drug being the subject of clinical testing in the country and abroad, except in case of post-marketing, non-intervention clinical testing; and providing information through the media, for purpose of advertising of medical institutions, private practices, veterinary organizations and specialized shops.

It is not allowed, when promoting a drug or medicament, to diminish the importance of warnings on precautions or undesired reactions to a drug, specified in brief information covering drug characteristics in the instructions for use; to diminish therapeutical value of another drug having the drug license; or in any other way to encourage doubts with respect to value of another drug; to use the material protected by any form of the intellectual property protection, without previous consent of the owner; to use postcards, or any other form of written consignments (the contents of which might be available or readable to other persons apart from the professional public), and use telephone numbers or e-mail addresses of the persons within the circle of the professional public, which advertise or provide information on their work in such a manner, without their previous explicit written consent.

IX Production and wholesale license

The drug production includes the complete drug production process or certain parts of the production process, active substance production, raw material procurement, drug quality control and market release of the drug batch, drug storage and distribution. The production process is any procedure applied in the drug production, from the receipt of raw materials, production, packing in interior packaging, up to the labeling and exterior packaging.

The drug production may be performed only by a legal entity meeting requirements with respect to space, equipment and staff, in addition to other requirements specified by the law, i.e. only a legal entity having the drug production license granted by the Ministry in charge, irrespective of whether a drug is intended for local market, or for exportation.

The drug producer is obliged to perform drug production and quality control in compliance with the law, provisions of the Rulebook, the production license, the guidelines of good production practice and the guidelines of good distribution practice.

One of the principal obligations of drug producers is keeping documentation on each produced drug batch for at least one (1) year following expiry of the term of use of the drug, or five (5) years after release of the drug, while the documentation on each batch of the drug intended for clinical testing shall be kept for at least five (5) years after the last clinical testing in which the batch of the drug has been used.

In addition, a drug producer shall have the plan for an urgent withdrawal of a drug from the market, such plan shall ensure efficient withdrawal of a drug from the market upon request of the Ministry in charge. For purposes of performing and coordinating the withdrawal procedure of a drug from the market, a drug producer shall nominate a person in charge, independent from sales and marketing department, who shall be available at all times.

The unlimited term drug production license shall be issued under a resolution of the Ministry in charge, such resolution specifying production location and pharmaceutical form produced at each particular point of production. The Ministry in Charge shall, ex officio register the drug production license holder with the issued Drug Production Licenses Register, following issuance of the drug production license.

The Serbian Drug and Medicaments Agency, when granting release of drugs to the market shall observe the provisions of international agreements covering obligations relating to market release of high quality and efficient drugs; increased worldwide trade in false drugs and the resulting necessity of its prevention, as well as international obligations relating to illegal trade in unregistered drugs.

In order to ensure that Serbian population and medical personnel have best possible conditions for prevention, diagnostics, treatment and rehabilitation, it is necessary that a wide range of high quality, safe and efficient drugs be available on Serbian market.

The Agency shall grant approval for market release of the non-registered drugs, when it is medically indicated and legally permitted.

The legal entity which has been granted the drug and medicaments marketing license for wholesale (Wholesaler) shall only sell drugs and medicaments having the drug license or the resolution on registration with the Medicaments Register, issued by the Serbian Drug and Medicaments Agency, as well as drugs and medicaments not having the marketing license, but their importation having been approved by the Agency.

The Wholesalers shall procure the drugs and medicaments only from legal entities in possession of the production license, wholesale drugs and medicaments license, and drugs and medicaments import license issued by the Ministry in charge. The Wholesalers shall be obliged, in case of an emergency, upon request of the health institution/private practice, or veterinary organization, to deliver required drugs and medicaments on wholesale and in shortest term possible, such that lives and health of population are not put at risk.

The Wholesalers shall be obliged, for the sake of continuous supply of drugs and medicaments for which they have been granted the drug and medicaments wholesale license by the Ministry in charge, to ensure required stocks, timely supply, import and analysis certificates issued by the Agency, so that there is no interruption of market supply for drugs and medicaments for which they have been granted the drug and medicaments wholesale license by the Ministry in charge.

The Wholesale may be performed only by legal entities which satisfy the requirements with respect to space, equipment and staff, as well as other requirements specified by the law.

X Intellectual property

The innovative activity in pharmaceutical industry relates to development of new and improvement of existing drugs, as well as development of existing medical equipment. The companies basing their operations on research and development tend to protect their intellectual property in order to ensure profit from their inventions and return on their investments during research and development phase. Being familiar with the intellectual property protection system is of key importance for pharmaceutical industry operations.

The patent registration for drugs is different from the patent registration in other industries for two principal reasons:

- Development of a drug requires a very long period of time
- Costs of developing a new drug are very high

For these reasons, a strong patent protection is necessary in order to ensure return on investment in developing a new drug. Having in mind these specific features, pharmaceutical companies protect their intellectual property in two ways:

1. Classic intellectual property protection in the form of patent, trade mark, business secret or in some other form, by which companies acquire exclusive exploitation rights over new drugs and other types of creative work. This protection is exercised through the Intellectual Property Protection Bureau and is the usual mechanism of intellectual property protection applied by all industries.
2. By registration of the data in form of exclusivity of the data, i.e. the market exclusivity; it ensures that no other pharmaceutical company is entitled to file the application for registration during the registered period. This registration shall be performed through the Drugs and Medicaments Agency and represents the additional system of intellectual property protection in the procedure of new drug registration.

The pharmaceutical company filing the patent application shall also submit clear and complete data on its discovery, so that persons in charge of assessing the documentation are able to render a technically complete decision.

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