Acta Biochimica Polonica
Vol. 40 No. 1 1993

Intellectual property in biotechnology

Tomasz Twardowski

Institute of Bioorganic Chemistry, Polish Academy of Sciences, ul. Z. Noskowskiego 12, 61-704 Poznań, Poland

Production of new bioproducts requires several time and money consuming steps: research, optimization, development, followed by marketing, design etc. A new project (e.g. biotransformation) needs investment of intellectual effort. The investor, most often a scientist, expects to gain profit. It is possible to protect intellectual property in the following ways:

- 1, patents, used mostly in industry (e.g. pharmaceutical industry, more recently applied also to living organisms and their parts);
- 2, trade secrets, used to safeguard some procedures (in this way, public opinion is not informed at all about their existence);
- 3, protection of plant and animal varieties (applied mostly in "classical" agriculture);
- 4, copyright, and
- 5, copy protection rights used mostly by writers, artists and authors (e.g. computer programs);
- 6, trade marks;
- 7, registered designs.

Ideas, theories and natural laws (e.g. $E = mc^2$) are generally excluded from patenting and from intellectual property rights protection.

Patents, trade secrets and (on a minor scale) plant and animal protection rights are used in the case of biotechnology achievements. A patent (not only in the case of biotechnology) can be characterized as follows: For a limited period of time the competitors are excluded from a precisely described area of technology. The legal right to exploit the invention belongs to the assignee (not to the inventors of the patent), but the royalties bring profit to the inventor. The public is informed about the invention and has a chance to control the use of the achievements; patent examiners (experts in the field) have to analyze the application of the patent. There are unquestionable advantages of patenting: 1, protection from exploitation by competitors; 2, royalties to be obtained from licensing; 3, stimulation of technical progress and exchange of information as well as protection against "double" invention. The scientific discoveries can be more easily transferred to the industry and commercialized due to patenting.

In the case of biotechnology some forms of supervision and controls are necessary for several reasons. We shall present here three of them:

- 1, to monitor safety precautions;
- 2, to allay public concern (e.g. from the point of view of ethics and morality);
- 3, to protect the intellectual property rights of the inventors.

A novel technology, such as application of procedures involving recombinant DNA engineering, may initially arouse anxiety in the scientific community, lay circles as well as among lawyers. However, there is no justification for extending special control beyond the necessary minimum. For example: the safety of a foodstuff (or pesticide, or any other product) is determined by its physical and chemical properties, and not by the technology used in its manufacturing. What is most important is the safety of the final products. Nevertheless, side products or contaminations of the nature during the manufacturing process also have to be strictly controlled. For modern biotechnology one of the key issues is to make all concerned understand the difference between *regulating the product or the process of genetic modification.*

Biotechnology can be considered a very old industry as well as a brand new one. I shall limit the scope of this article to the following

biotechnology areas: 1, all genetic engineering; 2, fermentation processes; and 3, manufacturing and the use of synthetic peptides and oligonucleotides (in general: oligomers) in the first two cases.

Present state

In Poland there are at present (September, 1992) no formal regulations concerning intellectual property, patent law, ethics, biohazard and bioinformatics in relation to biotechnology; however, not all new situations require new legislation. As Poland plans to join the European Community in a relatively near future, the Polish scientific community has to know (or has to learn) the regulations already well developed in the Western hemisphere. In this paper I shall focus attention on the comparison and analysis of present situation in selected "peripheral" aspects of biotechnology. (Several articles concerning these problems have been published, mostly in Polish, in the journal "Biotechnologia"[1 - 10]).

Objectives

Technology transfer may be defined as the movement of technical information and/or materials used for developing a product or process, from one sector to another; in the case of biotechnology mostly from the West to the East. Both sides (donor as well as acceptor) should be familiar with the *state of the art* not exclusively as it concerns technology but also in public opinion and legal terms. The popularization of the rules and regulations of the Western hemisphere in view of the forthcoming basic changes in Polish law, is crucial. Poland will probably join European Patent Convention and Budapest Treaty in 1993. The society should be well prepared for these events.

Importance and advantages

In anticipation of significant changes in geopolitics and rapid development of biotechnology as technology of the 21st century, information about new regulations is fundamental for the scientific community. The new regulations will affect not exclusively the transfer of products and technologies, but also the freedom and transfer of information - which is a key issue for scientific centers, for industry as well as for the society.

The leading principle of granting a patent protection [1, 10 - 13] is to secure the rights of the inventor. Several factors affect the final situation of biotechnology inventors. Bioinformatics in today's technological world is not free of charge and it is not cheap (on the contrary - it is very expensive). Biohazard should not be a term familiar exclusively to scientists. In elaborating and marketing new technologies which can affect human life, ethics should always be taken into account. Only the patenting system guarantees the transfer of information accessible in all these aspects. Combination of these factors is strictly related to the future development of biotechnology in Poland.

Unlike in Poland, we can observe in other countries several high level initiatives concerning future development of the legal status of biotechnology. For example [4, 8, 9, 14 - 18]: in the U.S.A., within the framework of the Congressional Office of Technology Assessment, the Congress initiated the report "Biotechnology in a global economy"; as the result Congressional Biotechnology Caucus has been formed. In Denmark and Germany the legal status of biotechnology was the subject of a plenary debate of the Parliaments, etc.

An enhanced level of commitment to biotechnology of the technologically leading states (the U.S.A., Germany, Japan, France) should encourage us to work on the legal status and, particularly, on protection of intellectual property in biotechnology in our country. The commercial fruits of research in biotechnology should be safe for the public and rewarding for the academic community.

Historical background

Traditionally, the field of biotechnology has been considered as belonging within the academic laboratory. However, the historical background of industrial importance of biotechnology is well illustrated by the claim made by Louis Pasteur in 1873: "a yeast free from organic

germs of disease as a manufactured article ". The milestones in modern biotechnology patenting are represented by:

-1. The Chakrabarty patent (issued in the U.S.A., on March 31, 1981, # 4,259,444). This patent claimed a microorganism having a foreign plasmid inserted to provide for degradation of hydrocarbons (e.g. oil). This was the first case of patenting of a living organism *per se*.
-2. In 1982 the U.S. Patent and Trademark Office decided that genetically engineered plants can be covered by patents.
-3. The introduction of polyploidy in oysters (April 1987) was the first patent related to genetically transformed animals.

The aim of a patenting system

The leading principle of granting patent protection is to secure the author(s) a compensation for their achievements by the allowance of an exclusive right. Another equally important function of a patent system is to inform the society about technological developments. The flow of technical information stimulates competition and prevents repetitions. Because of these three factors patents prove to be an essential part of the strategic planning for research, for industry and for national economy. The patent system plays a key role in technology transfer (on the know-how level and in investment). Only an efficient patent protection system guarantees publication of scientific achievements. The alternative is a company secret (*trade secret*).

By definition patents [1, 8, 10, 13] are granted for inventions which are: 1, new; 2, significant; 3, industrially applicable; 4, reproducible (by a person skilled in the art). Patents can be granted to: 1, products (e.g. a new microorganism); 2, compositions (e.g. a mixture which contains microorganisms and exploits their activities); 3, processes (e.g. production of a microorganism); and 4, methods (e.g. a way of preparing compositions or formulas). In the case of microorganisms only the deposition of their forms (standard samples) in a depository institution guarantees their reproducibility. The patent description should be descriptive enough for the procedure to be reproducible by the experts in the field. This characteristics should be examined by a "person skilled in the art". The term "state of the art" is defined by the European Patent Organization [8] as "everything made available to the public by means of a written or oral description, by use, or in any other way".

Patenting of living organisms and genetic data, those concerning the human genome, particularly, is highly controversial and emotion arousing problem [2, 7, 16, 17]. Patenting of animals [14] (excluding humans) and plants [12] is possible in the U.S.A. On the other hand, according to the German law [8], patent protection can be granted only to those plants or animals (or parts of them) which are essential for further biological processes for production of new plants or animals. The problem of patenting animals is a complicated issue and conflicting opinions have been presented [14]. It is important to note, that methods of production (e.g. microbiological methods) are protected by patent law (with the exclusion of protection under the Plant Varieties Protection Law). However, we have to stress the difficulties in drawing the borderline between patenting the product and/or the process in the case of modern technology. We have to expect that the number of patent applications concerning living organisms or their parts will be increasing. In several countries there are some restrictions concerning patenting, for example, medical devices [13].

Patenting in agriculture

Protection of a plant breeder's right is fully catered for under the Plant Varieties Protection Law [12]. For a plant variety to be eligible for protection it should be characterized by: *distinctiveness, uniformity and stability*. The plant variety right allows the producer (e.g. a farmer) to produce and sell the reproductive plant material of a given plant variety. The fundamental "farmer's privilege" is to save the seeds from the current crop for sowing next season. The plant variety protection does not concern the technology of breeding and its scope is limited to the physical and physiological properties of the material. In the United States plant breeding methods can be patented

and protection of plant varieties has been granted under the "Certificate of Variety Protection". Genetic engineering technologies, which are not covered by the plant variety system, have created a new situation. Since they can be described in similar terms as any standard technology and are applicable to many plant species. Two forms of protection of a plant variety can be granted: the plant variety rights and patent protection. Combination of these two systems can co-exist and provide full protection of the property rights. It is worth mentioning that this situation provoked a debate on property rights to local genetic resources (particularly in the developing countries) [11].

Microorganism

In Europe the term "microorganism" is defined by European Patent Organisation (EPO) as all microbiological entities capable of replication (e.g.: bacteria, fungi, viruses, mycoplasmae, algae, protozoa, cells) [13]. The European Commission of EPO suggests the patentability of all living matter (except human) or parts (of plants or animal varieties) which are protected under the plant protection law. Also the products of nature are patentable, if human intervention consists in more than selecting, cultivation or growing of biological species under natural conditions. Moreover, there is a fundamental patentability requirement to "deposit, access and redeposit" all forms of plasmids, microorganisms, fungi etc., in a depository institution under the conditions of Budapest Treaty [1, 10].

Differences in patenting systems

There are several basic differences between the United States, European Patent Organization and Japan [8 - 10, 13, 15].

The most important difference between national systems concerns the application of either the rule of *first to file* (which is the case in the EPO countries and Japan) or of the rule *first to invent* together with 1 year grace period (practiced in the U.S.A.). Publication of the patent application is released 18 months after its submission in Europe and immediately after patent granting in the U.S.A. There are significant differences in the extent of patent examination by the national patent office: checking exclusively the formal aspects or an analysis of *meritum* of the patent application. The periods of protection vary from 15 to 20 years. The expiry time of patents is as follows: in Japan - 15 years after publication, in the U.S.A. - 17 years after being patented, in Europe - 20 years after final application. The protection time is counted from different starting dates (from the date of application or the date of granting). The access to microorganism deposits is limited to a different extent (who and when is allowed to obtain a sample). In Japan a very narrow scope of protection is a standard; in some countries a "patent in addition" under the same date and issue number applied. The differences between "invention and nature", procedure and period of opposition are among most common differences. Practically in all countries the inventions which are incompatible with public order or morality are prohibited; however, the definitions of "public morality and order" differ largely. The explanation of the presented differences is evident: in particular countries the patent law was developed in a slightly different way in order to protect local achievements.

Application for a foreign patent is mandatory in each country where protection is required. In the case of important achievements, only global scale patenting really protects the rights of an inventor. The priority date is based on the first patent application. However, the local patent laws have to be observed as well as the language of the country has to be used. This explains why global patenting is so expensive and time consuming (the submission fee, preparation of application, consulting, translation costs, etc.). The European Patent Convention (EPC) (1973, Munich) allows for some uniformisation: since 1978, a European Patent Application at the European Patent Office in Munich results in granting limited protection for 5 years in 14 European countries (the EPC countries include: Austria, Belgium, Denmark, France, Germany, Greece, Italy, Liechtenstein, Luxembourg, the Netherlands, Spain, Sweden, Switzerland, the U.K.). In order to obtain patent protection the national patent application must be filled out and submitted. Similarly, a single application presented at the office of the

World Intellectual Property Organization in Geneva guarantees the priority, but in particular countries national patents must be obtained.

Complications

The difficulties of biotechnology inventions patenting can concern several aspects. Only a few examples are presented here to show the significance of the problem: Functionally identical enzymes can be isolated from different material (by different techniques) with significantly different structures (e.g. amino-acid sequence). Living organisms are extremely complex and difficult to describe; previously, the same preparations have been described in significantly different ways (e.g. without the knowledge of the primary structures of their genomes or genes). Time is also a crucial factor. In the U.S.A. it requires on the average seven to ten years to bring a therapeutic, drug or biological product, to the market-place. During this period, the description criteria may change. In many cases, a clear statement of what constitutes a "new molecule" is required for patentability [9].

Freedom of transfer of technological information and the question who is the owner of the test results, directs the problem towards ethics. "Technology" seems to have a clear meaning, but "ethics" may be interpreted in different ways. Moreover, ethical problems are charged with many emotions, which often have an economic background. For example, let us try to solve the problem, who is the owner of the data in the following case: a sample of blood was routinely tested before the donor's employment. Who owns the results: the donor of the sample, the future employer (who pays for the analysis) or the laboratory (where the test was made). Is the researcher allowed to make further analysis without permission? And the next question: who should be informed about the full spectrum of results: the donor of the sample, the researcher interested in the scientific aspects of blood analysis, the payer or the insurance company? There are also other difficulties: if the person concerned knows the result and buys the insurance, does he or she have to inform the insurance company and – on the other hand – is the insurance company allowed to test the sample and gain profit from the knowledge of the analysis results which might be unfavourable for the person to be insured?

In some countries the problem has been (at least partially) solved. In Denmark, for example, is forbidden to use genetic information (from DNA sequencing) when hiring people and selling life insurance.

The possible consequences of new development in biotechnology have become the subject of lively debates and great anxiety in many countries (not yet in Poland). Opponents concentrated not on the new achievements and future prospects, but on (potential) hazard and risk. An example could be the public concern with respect to genetically modified plants: is it possible, that the gene(s) which has been manipulated might be transferred to the environment? Speculations (not supported by any scientific background) point to the possibility of production of monsters by widespread gene transfers. Fortunately, nature itself with the integrity of species as well as the legal regulation of laboratory work [3 - 6] guarantee our safety. During the last 10 years plant genetic engineering steadily developed. Today, most of the major crops (and many vegetables and beautiful flowers) have been routinely transformed and numerous plants have already passed the field tests (potato, tobacco, sugar beet, oil seed rape, sunflower, soybean, cotton, flax, alfalfa, maize, rice). Field tests of transformed plants provide irrefutable evidence that new techniques of biotechnology are safe for the environment. Similarly, in the case of human health: the U.S. Federal and Drug Administration (F.D.A.) [9] has approved more than 400 biotechnology-based clinical products and about 1000 clinical tests are in progress and further more than 1000 clinical trials applications are under review. In fact, 50% of all new drug applications for biological preparations concern products made by monoclonal antibody or recombinant DNA techniques [9]. Not a single report suggesting danger for human beings or for our environment has been presented.

It is of importance to mention that the U.S. Patent Office is preparing to adopt world patent standards [15]. The European system is based on the already mentioned principle *first*

to apply, while the American one on the *first to invent* principle. In the U.S.A. and the Philippines all credit is taken by the person who first came up with an invention (this has to be documented, e.g. by a certified laboratory notebook). It seems from preliminary negotiations, that the principle *first to invent* will be given up and one year grace period will generally be adopted. Within this frame, an inventor could publish his results and fill a patent application within a year. Several other provisions are going to be unified: publication of a patent application after 18 months (in the U.S.A. the application remains secret until patent is issued), scope of claims (in Japan this scope is very narrow). Important issues include also the acceptance of applications written in English (patent offices in particular countries accept applications in the local languages) and unification of patenting costs.

Conclusions

Powerful tools of biotechnology have created myriad biomedical products useful for clinical diagnosis and therapy, including: tissue plasminogen activator, anti-clotting agent to recombivax HB, a second generation of hepatitis B vaccine. In the next century, we expect biotechnology to have even stronger influence on our every-day life. The frontiers of biotechnology shall expand so as to encompass not only new medications, but also new sources of energy, biomaterials and diagnostic tools for detection purposes in technology.

The future development of biotechnology depends on several factors, including financing, legal regulations, intellectual property rights and litigation procedure. The following priorities and future applications of biotechnology have been predicted in the report prepared for the United Nations General Assembly [11]:

- detoxification and water treatment,
- biological control of pests and diseases,
- crop biotechnology,
- freshwater and marine aqua culture,
- human health and well-being,
- industrial biotechnology.

The objectives of intellectual property promotion in biotechnology include economic and technological progress. From the inventor's point of view the following fields of activity are of importance:

- National and international cooperation to improve the organization, standardization and distribution of documents.
- Creating opportunities for inventors and innovators to meet with potential users.
- Giving advice and providing assistance to the governments and governmental agencies (at their request) to improve administrative procedures.

There is still a need to develop domestic (as well as international) competent and effective advisory boards which would exert a strict control, particularly over industrial biotechnology. The academic community should be responsible for the development of a workable scheme of practical guidelines. It is essential to include all interested parties in the advisory panel. Regulations can form a framework for assuring safe industry and possibly unpolluted environment, as well as the security of intellectual property rights of us all.

REFERENCES

1. Ilnicka-Olejniczak, O. (1989) *Biotechnologia* **3**, 13 - 32.
2. Twardowski, T. (1989) *Biotechnologia* **4**, 22 - 35.
3. Chmiel, A. (1989) *Biotechnologia* **5-6**, 86 - 90.
4. Kelman, A., Anderson, W., Falkow, S., Fedoroff, V. & Levin, S. (1989) *Biotechnologia* **5 - 6**, 90 - 105.
5. Houwink, E.H. (1990) *Biotechnologia* **8 - 9**, 17 - 23.
6. Chmiel, A. (1990) *Biotechnologia* **10**, 77 - 82.
7. Twardowski, T. (1991) *Biotechnologia* **12**, 10 - 14.
8. Schofield, G.M. (1992) *Biotechnologia* **17**, 6 - 11.
9. Hellmann, K.B. (1992) *Biotechnologia* **17**, 12 - 17.
10. Fiołka, J. (1992) *Biotechnologia* **17**, 18 - 26.
11. *"Our common future"*, a report prepared by UN World Commission on Environment and Development (1987) pp. 383, Oxford University Press.
12. Crespi, S. (1989) *Intellectual Property in Business* **1**, 15 - 18.
13. Directive on the Legal Protection of Biotechnological Innovation (1989) in *Intellectual Property in Business* **1**, 20 - 21.
14. McCormick, D. (1988) *Bio/Technology* **6**, 62.
15. Anderson, Ch. & Swinbanks, D. (1992) *Nature (London)* **356**, 645 - 646.

16. Genetics and the public interest (1992) *Nature (London)* **356**, 365 - 366.

17. Anderson, Ch. (1992) *Nature (London)* **357**, 618.

18. Anderson, Ch. (1992) *Nature (London)* **358**, 180 - 181.

Note added in proof:

The amendments to a bill of the Polish Patent Law has been introduced on October 30, 1992. This modification allows future unification of legal procedures in Poland and West European countries. A commentary concerning the new patent legislature will be published in the journal "Biotechnologia".