Patentability of the biotechnological inventions in Poland

Rafał Witek, Warsaw July 2000

Law Condition

Regulations concerning the patentability which are included in pending Polish Patent Law (PPL) dated October 19, 1972 as amended on April 16, 1993 (Dziennik Ustaw 1993, No 26 item 117) are similar to the regulations defined by EPC.
Article 10 of the PPL defines a patentable invention as follows:
"Any new solution of a technical character which does not obviously result from the prior art and which is capable of practical application shall be patentable invention."
However, a such defined positive circumstance of the patentability is limited by numerous exclusions. Applied to the biotechnological solutions, patents shall not be granted:
a. under Art.12.6 of the PPL on "scientific theories and discoveries";
b. under Art. 12.2 of the PPL on "methods for treatment of diseases in the field of medicine and veterinary and in plant protection";
c. under Art. 12.3 of the PPL on "inventions whose exploitation would be contrary to law or public policy; this shall not apply were only the sale of a patented product or of a product obtained by means of patented process is limited by law";
d. under Art. 12.1 of the PPL on "new plant varieties and animal breeds as well as biological processes for the cultivation of plants or breeding of animals";

Examples of the typical categories of the biotechnological inventions which are patented in Poland

- **products**, e.g.: polypeptides (enzymes, antibodies), nucleic acids (primers, encoding sequences, vectors), micro-organisms, cell lines, kits, (e.g. diagnostic kits), compositions (e.g. medicaments, vaccines);
- **methods**, e.g.: methods for obtaining of the interesting product (e.g. fermentation, methods for isolation and purification), assays and diagnostic methods in vitro, laboratory methods;
- **uses**, e.g.: second medical indication;

The most frequent reproach during the examination procedure is the insufficiency of the disclosure and/or ambiguity of the claims. The Polish Patent Office (PPO) usually requires a strict structural definition (sequences, deposits). The functional features in claims are unwelcome.

Examples

Recently, we may observe some tendency to liberalise the PPO's approach. Frequently is admitted the functional and more general definition of the claimed matter.

Polish Patent Application No. P. 308 742 based on the PCT/FI93/00450 : WO 94/10325 (Polish Patent No. PL 178040 granted on 29.02.2000) relates to recombinant microbial host and a method for production of xylitol from this recombinant host. In the subject case, the PPO admitted to use a more functional definition of the claimed subject mater. The following claims have been patented:

1. A method for production of xylitol from a recombinant host, by genetic modification of native host organism, growing said organism and xylitol recovering characterised in that
a) an arabitol-producing microbial host is transformed with DNA encoding D-arabitol dehydrogenase (EC 1.1.1.11) and possibly with a DNA encoding xylitol dehydrogenase (EC 1.1.1.9) ;
b) a recombinant host obtained in step a) is grown using as a carbon source D-hexose like glucose, fructose, galactose, mannose, or a mixture thereof, or on a polymer or oligomer containing said D-hexose, or on D-arabitol, ethanol or glycerol, whereby xylitol is produced as an end product; and
c) a xylitol produced in step b) is recovered.
16. A recombinant host, characterised in that an arabitol producing host is transformed with a DNA encoding D-arabitol dehydrogenase (EC 1. 1. 1. 11) and possibly with a DNA encoding xylitol dehydrogenase (EC 1.1.1.9), thus enabling the recombinant microbial host to synthesise xylitol as an end product when grown on a D-hexose like glucose, fructose, galactose, mannose, or a mixture thereof, or on a polymer or oligomer containing said D-hexose, or on D-arabitol, ethanol or glycerol, as the carbon source.

Polish Patent Application No. P. 308122 based on the PCT/FR94/00851 : WO 95/02697 (Polish Patent granted on 08.05.2000) relates to novel adenovirus-derived viral vectors, the preparation thereof, and the use thereof in gene therapy. After a long examination process the PPO accepted as patentable the following claims:
1. A replication defective recombinant adenovirus comprising the adenovirus sequences, especially from a canine or a human group C adenovirus, and a heterologous DNA sequence encoding an therapeutic gene, antisense RNA or antigenic peptide, characterised in that as adenovirus sequence comprises: ITR sequences; an encapsulation sequence; E1 gene comprising deletion; E2 and E4 gene, wherein at least one comprises deletion

2. Defective adenovirus according to claim 1, characterised in that heterologous DNA sequence further comprises a sequence which permits expression of the heterologous DNA sequence, possibly promoter selected from the group consisting of an adenovirus E1A promoter, an adenovirus MLP promoter, a CMV promoter, and an RSV LTR promoter.
3. Defective adenovirus according to claim 1, characterised in that heterologous DNA sequence further comprises a signal sequence.
4. Defective adenovirus according to claim 1, characterised in that comprises: ITR sequences, an encapsulation sequence, a heterologous DNA sequence, and an E2 region.
5. Defective adenovirus according to claim 1, characterised in that comprises: ITR sequences, an encapsulation sequence, a heterologous DNA sequence, and an E4 region.
6. Defective adenovirus according to claim 1, characterised in that comprises: ITR sequences, an encapsulation sequence, a heterologous DNA sequence, and an E4 region, wherein E4 genes comprises a mutation outside of the E4 coding region.
7. Defective adenovirus according to claim 6, characterised in that E4 genes comprises a deletion of all or part of the promoter region for E4 transcription.
8. Defective adenovirus according to claim 6, characterised in that E4 genes comprises a substitution of at least one base in the E4 genes.
9. Defective adenovirus according to claim 6, characterised in that E4 genes comprises mutations within regions responsible for E4 gene expression or transcriptional regulation, or both.
10. A cell line for infection by a replication defective recombinant adenovirus, characterised in that comprises integrated into its genome, adenovirus genes necessary to complement a replication defective recombinant adenovirus comprising the adenovirus sequences, especially from a canine or a human group C adenovirus, and a heterologous DNA sequence encoding an therapeutic gene, antisense RNA or antigenic peptide, comprising as an adenovirus sequence: ITR sequences; an encapsulation sequence; E1 gene comprising deletion; E2 and E4 gene, wherein at least one comprises deletion and possibly at least one gene selected from the group comprising : late L1-L5 genes comprising deletion, E3 genes comprising deletion, L5 gene comprising deletion and functional E3 gene under the control of a heterologous promoter, and wherein one of the complementing genes is under the control of an inducible promoter.
11. The cell line according to claim 10, characterised in that comprises, in its genome, an E1 gene and an E2 gene wherein the E2 gene is under the control of an inducible promoter.
12. The cell line according to claim 11, characterised in that additionally comprises an E4 gene, wherein the E4 gene is placed under the control of an inducible promoter.
13. The cell line according to claim 10, characterised in that comprises, in its genome, an E1 gene and an E4 gene wherein the E4 gene is under the control of an inducible promoter.
14. The cell line according to claim 10, characterised in that further comprises a glucocorticoid receptor gene.
15. The cell line according to claim 10, characterised in that comprises E2 and E4 genes and the E2 and E4 genes are under the control of an inducible promoter.
16. The cell line according to claim 10, characterised in that the inducible promoter is an LTR promoter of MMTV.
17. The cell line according to claim 10, characterised in that comprises a gene encoding the 72 K protein of E2, wherein the 72 K protein encoding gene is placed under the control of an inducible promoter.
18. The cell line according to claim 10, characterised in that it is constructed from human embryonic kidney cell line 293.
19. The cell line according to claim 10, characterised in that comprises open reading frames ORF6 and ORF6I7 of E4, wherein the open reading frames are under the control of an inducible promoter.
20. A composition comprising an active agent and a pharmaceutically acceptable vehicle, characterised in that comprises as an active agent a replication defective recombinant adenovirus comprising the adenovirus sequences, especially from a canine or a human group C adenovirus, and a heterologous DNA sequence encoding an therapeutic gene, antisense RNA or antigenic peptide, which as adenovirus sequence comprises: ITR sequences; an encapsulation sequence; E1 gene comprising deletion; E2 and E4 gene, wherein at least one comprises deletion and possibly at least one gene selected from the group comprising : late L1-L5 genes comprising deletion, E3 genes comprising deletion, L5 gene comprising deletion and functional E3 gene under the control of a heterologous promoter.

Evaluation of the exclusions

Discoveries

a. unmodified microorganisms

Polish Patent Application No. P. 309 613 based on the PCT/FI93/00568 : WO 94/16091 (Polish Patent No. PL 177023 granted on 30.09.1999) relates to a process for producing a cyclosporin, especially cyclosporin A, by cultivating a strain of the novel Tolypoclodium species in an appropriate nutrient medium and, if desired, isolating and purifying the resulting cyclosporin.
The primary claim 6 concerns:
6. A biologically pure culture of strain Tolypocladium sp. LeA3 CBS 630.92.
During the examination proceeding the PPO states:
"The subject of daim 6 as presented in the Application P 309 613 is not patentable as it relates to a scientific discovery (Article 12.6 of the cited Law).
In the description, the Applicant has disclosed the information stating that the strain Tolypocladium 'has been isolated from a soil sample originating from Russia, close to Moscow.', hence being a phenomena objectively

b. use claims

Until now the use claims have been recognised as not patentable. But recently we may observe some new trends. The standpoint of the legislator expressed in the new Law of the Industrial Property which probably will come into effect at the first half of the 2001, unambiguously confirms patentability of the novel and inventive applications of the known product. As results from this new trend, several on inventions concerning second medical indication have been granted after long Appeal process. In the patents granted there have been used two types of wording of the claim.

- Medicament for use in the treatment of disease Y characterised in that it comprises the product X as an active agent

Decision of Board of Appeal : Odw.1407/97 dated 21.10.1998r. concerning patent application No. P.299814, granted patent No. PL177348;
and : Odw.1002/98 dated 21.10.1998r., P.301579, patent No. PL177349;
and : Odw.1691/98 dated 3.03.2000, P.303937

- use of product X for the manufacture of a medicament for treating disease Y

patent PL 180000.

It seems that "Swiss-type claims" will be recognised as the standard format. It should be cleared in the nearest feature since several next Appellations wait for the decision of the Board of Appeal.

Methods for treatment

Exclusion defined by the Art. 12.2 of the PPL encompasses only the inventions which are defined as the method claims. Unpatentable are only the methods for treatment and the stages thereof which are conducted *in vivo*. Thus, patentable are the pharmaceutical products, diagnostic methods *in vitro*, and even some conducted *ex vivo* stages of the methods for treatment.

Polish Patent Application No. P. 316 311 based on the International Application PCT/RU95/00047 relates to second medical use a trophoblastic ß-I-glycoprotein as a means for treating autoimmune diseases showing suppressors immunodeficit. In the primary set of claims have been defined the novel use and the invented method:
1. A use trophoblastic ß-I-glycoprotein as a means for the treatment of autoimmune diseases.
2. A method of treatment of autoimmune disease comprising the introduction of an immune correcting preparation, characterised in that the immune status is prestudied, and in case suppressors deficit is found, then as an immune correcting preparation trophoblastic ß-I-glycoprotein is introduced in the dosages of from 3 to 120µg per ml of blood.
3. The method according to claim 2, characterised in that trophoblastic ß-I-glycoprotein is introduced parentaraly.
4. The method according to claim 2, characterised in that trophoblastic ß-I-glycoprotein in the concentration of 60 µg/ml is cultivated with autoimmune cells isolated from peripheral blood, and introduced intravenously.
During examination proceeding claims have been reworded as follows:
1. A preparation for the treatment of autoimmune disease comprising a active agent and pharmaceutical acceptable carrier, characterised in that as said active agent comprises trophoblastic ß-I-glycoprotein is introduced in the dosage form of from 3 to 120µg per ml of blood.
2. A method for preparation of a intravenous preparation for the treatment of autoimmune diseases, consisting in an incubation of an immune correcting preparation with newly isolated lymphocytes of human blood wherein trophoblastic ß-I-glycoprotein in concentration of 3-120 µg per ml of blood of a patient is used, and from these cells the intravenous preparation is produced.
3. The method for stimulation of suppressor activity of lymphocytes characterised in that the blood from patient is taken, the immune status is prestudied in vitro, and in case suppressors deficit is found then the thropoblastic beta-1-glycoprotein in concentration of 3-120 µg per ml of blood is cultivated with the autoimmune cells isolated from peripheral blood.
4. The method according to claim 3, characterised in that the content of the suppresor T is studied.
5. The method according to claim 3, characterised in that trophoblastic ß-I-glycoprotein in the concentration of 60 µg per ml of blood is cultivated with MNC cells isolated from peripheral blood.

The PPO acting in the first instance refused to grant a patent to claims 1 and 2. The range of the protection provided by claims 3-5 (the treatment *ex-vivo*) was sufficient to the Applicant, and the patent has been granted only to this part of the invention.

Polish Patent Application No. P.315 659 based on the International Application PCT/FI95/00042 relates to a biological control of plant diseases and concerns: (1) a new method for screening effective control organisms from microbial strains isolated from soil, (2) new microorganisms (obtained in these method) belonging to the genus Nectria, as well their use for controlling fungal infection in plants. The PPO acting in the first instance refused to grant a patent to claim concerning the method of treatment reading as follows:
A method for inhibiting a fungal infection in a plant, which comprises:

"Public order" – transgenic animals

Certain Polish Patent Application relates among other things to a method for producing a transgenic non-human mammal comprising a introducing an expression system according to invention into a fertilised egg or cell of embryo of non-human mammal so as to incorporate the expression system into germline of mammal and developing the resulting introduced fertilised egg or embryo into an adult female non-human mammal. The transgenic animal has not been claimed as such.
The PPO acting in the first instance refused to grant a patent to that part of invention. In the refusal decision the PPO stated that:
" (...) An realisation of the claimed method would violate the social order in the sense of Article 12.3 of the PPL. An introduction of the transgenic organism to the natural environment could result in the infringement on the biological balance, whose results would be difficult to estimate. (...)"
In the opinion of the Applicant the PPO statement expressed in the Official Decision did not lead to the definite conclusion that the exploitation of the claimed method would seriously prejudice the environment an a as such is only a supposition. The filed Appeal has not yet been considered.
As far as I know the transgenic animal as such has not yet been patented in Poland.

Plant varieties - transgenic plants

The non-microbiological plant are not patentable as such, but this provision may be usually avoided by claiming an appropriate method comprising the appropriate, preferably microbiological, process or limitation to plant cells.

In the primary version of the Polish Patent Application No. P.314590 based on the PCT/US94/11837, which concerns the transgenic plant resistant to infection caused by a bacterial or fungal pathogen, has been claimed:
1. A recombinant, double-stranded DNA molecule comprising in operative sequence:
a) a promoter which functions in plant cells to cause the production of an RNA sequence;
b) a structural coding sequence that encodes for production of AGO; and
c) a 3' non-translated region which functions in plant cells to cause the addition of polyadenylate nucleotides to the 3' end of the RNA sequence.
2. The DNA molecule of Claim 1 wherein said structural DNA sequence is SEQ ID N0:1.
3. The DNA molecule of Claim 1 wherein said promoter is selected from FMV35S and CaMV35S promoters.
4. The DNA molecule of Claim 1 wherein said promoter is induced by a pathogenic infection.
5. A method of producing genetically transformed, disease resistant plants, comprising the steps of:
a) inserting into the genome of a plant cell a recombinant, double-stranded DNA molecule comprising
(i) a promoter which functions in plant cells to cause the production of an RNA sequence;
(ii) a structural coding sequence that causes the production of AGO;
(iii) a 3' non-translated region which functions in said plant cells to cause the addition of polyadenylate nucleotides to the 3' end of the RNA sequence;
b) obtaining transformed plant cells; and
c) regenerating from the transformed plant cells genetically transformed plants which express AGO in an amount effective to reduce damage due to infection by a bacterial or fungal pathogen.
6. The method of Claim 5 wherein said structural coding sequence is SEQ ID N0:1.
7. The method of Claim 5 wherein said promoter is selected from FMV35S and CaMV35S promoters.
8. The method of Claim 5 wherein said promoter is induced by
pathogen infection.
9. The method of Claim 5 wherein said plants are potato or wheat plants.
10. A genetically transformed, disease resistant plant comprising a recombinant, double-stranded DNA molecule comprising in operative sequence:
a) a promoter which functions in plant cells to cause the production of an RNA sequence;
b) a structural coding sequence that encodes for production of AGO; and
c) a 3' non-translated region which functions in plant cells to cause the addition of polyadenylate nucleotides to the 3' end of the RNA sequence.
11. The plant of Claim 10 wherein said promoter is selected from FMV35S and CaMV35S promoters.
12. The plant of Claim 10 wherein said promoter is induced by pathogen infection.
13. The plant of Claim 10 wherein said structural coding sequence is SEQ ID N0:1.
14. The plant of Claim 10 which is a potato or wheat plant.

The PPO refused to grant a patent on claim 10, since: "the genetically transformed disease resistant plant being a subject of claims 10 to 14 could be understood as novel plant variety, and therefore it is not patentable in Poland by virtue of Art. 12.1 of the PPL".
After several necessary changes, the patent (PL178652) has been granted on 03 November 1999 for the following claims:

1. A recombinant, double-stranded DNA characterised in that, comprises in operative sequence:
a) a promoter which functions in plant cells to cause the production of an RNA sequence, wherein said promoter is selected from FMV35S and CaMV35S promoters;
b) a structural coding sequence that encodes for production of AGO, wherein said structural DNA sequence is SEQ ID N0:1; and
c) a 3' non-translated region which functions in plant cells to cause the addition of polyadenylate nucleotides to the 3' end of the RNA sequence.