

Patents on Genes: Recent Practical Experiences and Case Studies



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Content of the presentation



- Regulation
- Specialities
- Legal practice
- Case studies

Hungarian Patent System



History

- First Patent Act enacted in 1895
- Next Act 1969
- Present Act 1995 (harmonised with EPC)
- Amended 2002 (Directive 98/44/EC implemented)

Hungary Member of

- Paris Convention for the Protection of Industrial Property since 1909
- EPC since 2003

<http://www.hpo.hu>

Hungarian Regulations



- Act XXXIII of 1995 on the protection of Inventions by Patents
- Decree No. 20/2002 (XII. 12.) IM of the Minister of Justice on the detailed formal requirements
- Decree No.19/2005 (IV.12) GKM on the Fees for Administrative Services in Industrial Property Procedures before the HPO

Legal practice



- There is not any binding precedent case law in Hungary
- There are not any court decisions about the patentability of genes or biotechnological inventions in Hungary yet
- In practice the case law of the EPO's boards of appeal is taken into consideration
- Examiners are supported by the guidelines of HPO *
- Special chapters for biotechnological inventions

* http://www.mszh.hu/szabadalom/szab_modszertan/
(Hungarian only)

Examination procedure



- Formal examination
- Written opinion
- Search report
- Substantial examination

Search/examination is supported by

- Sequences in computer-readable
- EPOQUE
- STN
- Internal database

Specialities

Sequences in electronic form



- Nucleotide/amino acid sequences in computer-readable form, on an electronic data carrier shall be submitted*
- Stored in the internal database of HPO (ENyV**)
- Used by examiners for search
- Novelty search of unpublished sequences only via secured connection (STN database)
- After publishing/granting available for public in electronic form through public database of HPO (PIPACS***)

* Decree on the detailed formal requirements, Article 8

** Uniform Record System

*** Public Hungarian Industrial Property Database

Specialities

Written opinion



- At the request of the applicant a search report supplemented with a written opinion is provided*
- An early establishment about novelty, inventive step and industrial application
- Is sent to the applicant within six month from the accorded filing date
- The costs are about 100 €

* Article 69/A Patent Act;

Specialities

Filing and search fee



- The filing and search fee is increasing with the number of claims and not by the number of the inventions
- Biotech inventions relating to genes frequently comprises set of sequences in one claim
- The set of sequences is not necessarily in unity

Specialities

Extra service



- express novelty search
- for public
- provided in 30 days
- the costs are about 450 €

Patentability requirements

In all technical fields....



The invention must be

- new
- involve inventive step
- capable of industrial application
- clear and supported (disclosed in sufficient manner)
- in unity

The most important provisions are

For biotech inventions...



Patentable biotechnological applications Article 5/A

- inventions which are new, involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.
- biological material, which is isolated from its natural environment or produced by means of a technical process may be subject of an invention even if it previously occurred in nature

The most important provisions are

For biotech inventions ...



- the human body at the various stage of its formation and development and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
- an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

The most important provisions are

For biotech inventions ...



Disclosure of invention Article 60(1)-(4)

- The disclosure of patent application shall be clear and detailed in sufficient manner
- the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application
- For the public not available biological material has to be deposited
- The characteristics of the biological material, the name of the depositary institution and the accession number has to be disclosed
- The claims shall define clearly the scope of the protection sought, in accordance with the description

Patentability of genes



Genes origin of

- Human
- Animal
- Plant

Problems arises with

- Inventive step
- Industrial application
- Clarity
- Support
- Unity

Patentability of genes



Only by certain limit does take part of granting procedure*

- Assessing moral and ethical questions
- Taking into consideration of suffering of transgenic animals and medical benefit for humans
- Environmental risks of transgenic plants

*Possibly such a questions could be decided in revocation procedure eventually on court level; special regulation (authorities) to place these products on the market or into the public production (growing)



Patentability of genes

Products of nature invention *contra* discovery

Isolated and purified genes (with disclosed function) are patentable, human intervention is required

„To find a substance ... occurring in **nature** is...mere **discovery**, and ...**unpatentable**.... if a substance... has first to be **isolated** .. that process is **patentable**.
...if the **substance** can be ...**characterised**.., and it is **new** in the absolute sense then the substance *per se* may be **patentable**. „

EPO Guidelines for Examination, Part C, C:IV.2

Patentability of genes

Products of nature invention *contra* discovery



- Products of nature are patentable
- *Human intervention* (isolation, producing) is required
- Isolation and method of production are features of *technical character*
- Isolation and method of production have to be *disclosed* (supported)
- (Special) *function* has to be disclosed (supported)
- Claims have to be not limited to *isolated/produced* products and (special) *function*

Patentability of genes

Products of nature invention *contra* discovery



Claim as originally submitted:

Protein which comprises the sequence MSR KDGVLALLVV
VVWGLNFVVI KVGLHNMPRL MLAGLRFMLV (SEQ. ID NO: 1) or
a sequence with sequence homology larger than 50 % to SEQ.
ID. NO: 1.

Claim as acceptable (granted):

(Isolated) protein *enhancing the preparation of L-cysteine* which
comprises the sequence SEQ. ID. NO: 2 or the *functional* variant of the
sequence.

Patentability of genes



- absolute product protection can be permitted for sequence-related products
- not required in the claims to limit to the use or to the function of a nucleotide sequences or partial sequences
- in the application required to disclose the use or function of the sequences or partial sequences for which protection is sought
- the examiners check very strictly to ensure that the disclosed function is not speculative but real

Patentability of genes

Novelty



- Invention is new if does not form a part of the state of the art
- Expanded prior art is examined
- Novelty and inventive step are examined independently and with the same weight

Patentability of genes

Inventive step



- not obvious to the person skilled in the art
- obviousness from the viewpoint of the skilled person is examined before the contribution of the applicant
- problem-solution approach is used, but it is not compulsory

Patentability of genes

Person skilled in the art...



- .. is the following: In addition to the general knowledge relating to the state of the art, he has
- an average combinative and problem solving capability
 - good skills and experience for the professional work without creativity and imaginative ability
 - knows the basic solutions close to the relevant field

Patentability of genes

Inventive step



Typical problem of patenting of sequences is that

- DNA showing a high homology with known DNA *without unexpected function or surprising technical effect* is *not* patentable

Patentability of genes

Industrial application



- The industrial application of genes must be supported by description
- Concrete and real industrial applicability (function) has to be disclosed
- Theoretical or speculative function is not accepted (support)
- Any real function is acceptable
- A mere DNA without specific function is not patentable

Patentability of genes

Industrial application, clarity



Claim as originally submitted:

37. Human DNA sequence according to claim 17 used for diagnosing a congenital deficiency in delta-5,7 sterol delta-7 reductase.

Claim as acceptable:

37. Human DNA sequence according to claim 17 used for *in vitro* diagnosing/*as a probe* for diagnosing a congenital deficiency in delta-5,7 sterol delta-7 reductase.

Claim 17: DNA sequence

Patentability of genes

Clarity, support



Question of too broad (undefined) claims

- unclear scope
- novelty search

Homology

- 90-95 % acceptable
- functional feature

By structure and function defined scope of claims is required for

- homologs
- variants
- mutants

Patentability of genes

Clarity, support



Claim as originally submitted:

4. DNA sequence coding for a delta-5,7 sterol delta-7 reductase protein and which hybridizes with the sequence defined claim 3 under average or high stringency conditions or which has a sequence identity of approximately 60% or more with this sequence.

Claim as acceptable (granted):

4.approximately 90% or more with this sequence.

Claim 3: cDNA sequence

Patentability of genes

Clarity lack of functional features, products of nature



Claim as originally submitted:

6. Protein which comprises the sequence MSRKDGVLALLVVVW
GLNFVVI KVGLHNMPRLMLAGLRFMLV (SEQ. ID NO: 2) or a
sequence with sequence homology larger than 50 % to SEQ. ID.
NO:2.

Claim as acceptable:

6. *(Isolated) protein enhancing the preparation of L-cysteine which
comprises the sequence SEQ. ID. NO: 2 or the functional variant of
the sequence.*

Patentability of genes

Clarity, lack of well defined functional features



Claim as originally submitted:

4. A coryneform bacterium in which said DNA sequence coding for a diaminopimelate decarboxylase, and said DNA sequence coding for a diaminopimelate dehydrogenase are enhanced.

Claim as acceptable (granted):

4. (An isolated) coryneform bacterium containing DNA sequence enhancing the expression a diaminopimelate decarbocylase and a diaminopimelate dehydrogenyse *by increasing a copy number of the DNA sequence coding for said enzymes using a strong promoter or combination thereof.*

Patentability of genes

Clarity lack of structural features



Claim as originally submitted:

6. A megakaryocyte differentiation factor having an amino acid sequence the same as the native amino acid sequence of a megakaryocyte differentiation factor according to claim 1, an amino acid sequence wherein one or more than one amino acid residue in said native amino acid sequence is deleted, an amino acid sequence wherein one or more than one amino acid residue in said native amino acid sequence is replaced with other amino acids, an amino acid sequence wherein one or more than one amino acid is added to said native amino acid sequence, or an amino acid sequence including a combination of said amino acid modifications.

Claim as acceptable (granted):

6. A megakaryocyte differentiation factor according to claim 1 characterised by having *the* amino acid sequence *shown in SEQ ID No:30 with one or more of the following modifications*

- (a) *from 1 to 30 amino acids of the sequence shown in SEQ ID No:30 are deleted;*
- (b) *from 1 to 30 amino acids of the sequence shown in SEQ ID No:30 are replaced with other amino acids*
- (c) *one or more amino acids are added to the sequence shown in SEQ ID No:30 .*

Claim 1: A megakaryocyte differentiation factor

Patentability of genes

Unity, inventive step



Claim as originally submitted:

1. A DNA encoding aspartokinase III of bacteria belonging to the genus *Escherichia* and having in the encoding region one or more mutations which release the feedback inhibition by lysine of said aspartokinase III, said mutation being a mutation by which the 318th methionine residue of aspartokinase III is substituted with another amino acid residue and the 323rd glycine residue with another amino acid residue, a mutation by which the 325th leucine residue is substituted with another amino acid and the 347th valine residue with another amino acid residue, a mutation by which the 323rd glycine residue is substituted with another amino acid residue and the 347th valine residue with another amino acid residue, a mutation by which the 325th leucine residue is substituted with another amino acid residue and the 345th serine residue with another amino acid residue, a mutation by which the 323rd glycine residue is substituted with another amino acid residue and the 358th serine residue with another amino acid residue, a mutation by which the 344th threonine residue is substituted with another amino acid residue, a mutation by which the 250th glutamic acid residue is substituted with another amino acid residue, a mutation by which the 346th glutamic acid residue is substituted with another amino acid residue and the 347th leucine residue with another amino acid residue, a mutation by which the 250th glutamic acid residue is substituted with another amino acid residue and the 364th threonine residue with another amino acid residue, a mutation by which the 202nd aspartic acid residue is substituted with another amino acid residue and the 321st serine residue with another amino acid residue, a mutation by which the 283rd arginine residue is substituted with another amino acid residue, the 333rd alanine residue with another amino acid residue, the 338th serine residue with another amino acid residue, the 346th glutamic acid residue with another amino acid residue and the 414th asparagine residue with another amino acid residue, or a mutation by which the 318th methionine residue is substituted with another amino acid residue, the 321st serine residue with another amino acid residue, the 328th valine residue with another amino acid residue, the 349th valine residue with another amino acid residue and the 405th glutamic acid residue with another amino acid residue.

Patentability of genes

Unity, inventive step



- The linking feature of the sequences has already been disclosed in the prior art
- The claimed mutations are considered as independent preferable embodiments of known mutations (which are not even inventive)
- Unpredictable effect of new mutants is not disclosed
- The claimed mutant can occur in nature without human intervention

Patentability of genes

Unity, inventive step



- Applicant argued that the unexpected feedback inhibition is the common linking feature
- Office said that the application involves only selection based on well known feature
- Applicant restricted the claim to special mutant, the unexpectedly good effect of this special mutant has been originally disclosed (supported)
- Office accepted the arguments of applicant (no further details arose to refuse the application)

Patentability of genes

Unity, inventive step



Claim as acceptable (granted):

2. *Isolated* DNA encoding aspartokinase III of bacteria belonging to the genus *Escherichia* and having in the encoding region (one or more) mutation which *mutate* release the feedback inhibition by lysine (of said aspartokinase III) said mutation being a mutation

by which the 318th methionine residue of aspartokinase III is substituted with another amino acid residue and the 323rd glycine residue with another amino acid residue.

Patentability of genes

Unity



- The set of sequences is not necessarily in unity
- The same origin of the DNAs itself does not assure the unity of the application

Patentability of genes

Transgenic plant patents



- Non-human organism (host)
- Not plant-varieties but plants
- Seeds, transformed plants characterised by well-defined technical features (e.g. genes) not by process of production (e.g. crossing or selection) and not by origin

Patentability of genes

Transgenic plant patents



Claim as originally submitted:

25. Transformed host organism characterised in that it contains a nucleic acid fragment according to one of claims 18 to 20.

Claim as acceptable:

25. Transformed *non-human* host organism characterised in that it contains a nucleic acid fragment according to one of claims 18 to 20.

Claims 18 to 20: Nucleic acid fragment

Patentability of genes

Clarity, support Transgenic plant patents



Claim as originally submitted:

33. Transformed plants, characterised in that it is derived from the cultivation and/or crossing of the plants according to claims 31 or 32.

Claim as acceptable:

33. Transformed plant, characterised in that it is derived from the cultivation and/or crossing of the plants according to claims 31 or 32 *and that it contains a nucleic acid fragment according to one of the claims 18 to 20.*

Claim 31: transformed plant cell

Claim 32: transformed plant

Patentability of genes

Clarity, support Transgenic plant patents



Claims as originally submitted:

34. Seeds of transformed plants according to one of claims 31 to 33.

Claims as acceptable:

34. Seeds of transformed plants according to one of claims 31 to 33 *containing a nucleic acid fragment according to one of claims 18 to 20.*

Claim 31: transformed plant cell

Claims 32, 33: transformed plant

Patentability of genes

Clarity, support Transgenic plant patents



Claim as originally submitted:

16. Peas harvested from the plant of claim 15.

Claim as acceptable :

16. Peas (*characterised in that it is derived from the plant of claim 15) comprising a DNA molecule of any one of claims 1 to 4 and/or a vector of any of claims 5 to 7.*

Claim 15: transgenic plant

Patentability of genes

Clarity, support Transgenic plant patents



Claim as originally submitted:

21. A process of producing highly wrinkled mature seed of a *Pisum sativum* variety that contains the *bsg* gene within its genome, the process comprising the steps of: crossing a *Pisum sativum* variety or line that contains the *bsg* gene within its genome with a *Pisum sativum* variety or line that does not contain the *bsg* gene within its genome; collecting mature seeds; planting the collected mature seeds; growing the mature seeds into *Pisum sativum* plants; allowing the *Pisum sativum* plants to self-pollinate; collecting mature seeds; selecting highly wrinkled mature seeds that do not contain organized starch grains, growing the mature seeds into *Pisum sativum* plants, selecting plants with desirable phenotypic traits; allowing the plants to self-pollinate until a uniform line is produced; allowing the *Pisum sativum* line to self-pollinate; and collecting the mature seeds.

Patentability of genes

Clarity, support Transgenic plant patents



Claim as acceptable*:

21. A method for producing of a *Pisum sativum* plant comprising a DNA molecule according to any of claims 1 to 4 and/or a vector of any one of claims 5 to 7 within its genome, said method comprising crossing a plant according to claims 15 to 17 with another *Pisum sativum* plant and collecting, selecting and planting the seeds resulting from said crossing.

Method for producing of plant was disclosed in the application.

*According to Article 6 plant varieties are not patentable. Plants are patentable, if the technical feasibility of the invention is not confined to a particular plant variety.

Patentability of genes



Conclusions The most important considerations

- The human intervention (isolation) ensures the patentability
- For genes absolute product protection is allowed
- For patenting of genes the structural features are required
- In the description the industrial applicability (special function) has to be disclosed
- The disclosed function should be real (supported) not speculative
- Homologs, variants, mutants are patentable only when are characterised by structural and functional features
- DNA showing a high homology with known DNA without unexpected effect is not patentable
- The same origin of the DNAs does not assure the unity of the application



Thank you for your attention !