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Patenting of Gene Sequences

The view of the EPO

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Current Challenges in Intellectual Property Rights and Biotechnology



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Product-of-nature doctrine (modernized by the EU-Directive)



"One may not obtain a patent on something that is indistinguishable from a product of nature"



EU-Directive 98/44/EC on the legal protection of biotechnological inventions.



Implemented into **Rule 23(b)-(e)** of the EPC for further interpretation of the provisions of the EPC on the protection of biotechnological inventions.



Rule 23b-e

Rule 23(e)(1): [...] the simple discovery of [...] a sequence or partial sequence of a gene cannot constitute patentable inventions.

Rule 23e (2) EPC: 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 this element is identical to that of a natural element."

Rule 23c(a) EPC: Biological material which is isolated from its natural environment or produced by means of a technical process shall be patentable even if it previously occurred in nature.





Patentability of Gene Sequences

ARTEFACTS

"man-made products"

NATURALLY OCCURRING COMPOUNDS

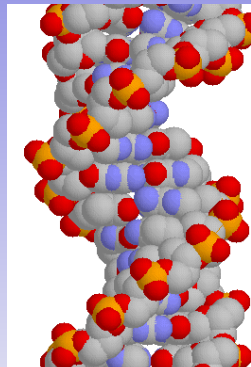
"products of nature"

dyes
flavours
antibiotics
etc...

DNA/protein
sequences

whole organisms

cells



Rule 23e(2) EPC



Patenting of biological sequences

Specific Requirements

- Isolated or technically produced
Rule 23c (a)
- Technical effect is to be revealed
Guidelines C-IV, 2.3
- Specify Structure and Function
Guidelines C-IV, 4.6
- Function specific and credible
T 1329/04 (GDF-9)
- Industrial application must be disclosed in the application
Rule 23c (3), T 0870/04 (BDP1)





Clarity (Art.84 EPC)

- Art 84 EPC: [The claims] shall be **clear** and **concise...**
- Rule 29(1): The claims shall define the matter for which protection is sought in terms of **technical features**
 - ⇒ A sequence should be clearly and unambiguously defined by reference to the corresponding **SEQ ID NO**





Clarity (Art.84 EPC)

- Without further restriction, functional equivalents, analogues, variations, derivatives, fragments etc. are generally not considered to meet the requirements of Art. 84 EPC.
- The terms “homology” and “similarity” are considered to be ambiguous and to have no generally accepted technical meaning → instead indicate **identity** and (where appropriate) length over which identity is calculated.
- If **hybridizing sequences** are claimed, indicate:
 - exact hybridization conditions
 - length of hybridizing fragment



Decisions of the Boards of Appeal

T 1329/04 (GDF-9)



Article 56 EPC

Inventive step



"An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. [...]"





Decisions of the Boards of Appeal

T 1329/04 (GDF-9)



- GDF-9 was cloned as an alleged member of a known gene family based on the occurrence of sequence motives.
- Highest identity with further family members: 34%
- Only 6 cystein residues, instead of 7
- Ovary-specific expression pattern
- No proven function, mere speculation





Decisions of the Boards of Appeal

T 1329/04 (GDF-9)



- **The definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve.**
- **Therefore, even if supplementary post-published evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve.**





Decisions of the Boards of Appeal

T 0870/04 (BDP1)



Article 57 EPC

Industrial application



"An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry."

Rule 27 (1)(f) EPC

"The description shall indicate explicitly, [...] the way in which the invention is capable of exploitation in industry."





Decisions of the Boards of Appeal

T 0870/04 (BDP1)



- BDP1, a cytoplasmic tyrosine phosphatase, was cloned as a member of a known gene family based on occurrence of conserved sequence motives.
- Epithelial- and tumour-specific expression pattern
- BDP1 is involved in signal transduction and plays a potential role in the development of cancer
- No proven function



Decisions of the Boards of Appeal

T 0870/04 (BDP1)



- Merely because a substance could be produced in some ways does not necessarily mean that the requirements of Article 57 EPC are fulfilled.
- A vague and speculative indication of possible objectives that might or might not be achievable by carrying out further research with the tool as described is not sufficient for fulfilment of the requirement of industrial applicability. The purpose of granting a patent is not to reserve an unexplored field of research for an applicant.
- In cases where a substance, naturally occurring in the human body, is identified, and possibly also structurally characterised, but either its function is not known or it is complex and incompletely understood, then industrial applicability cannot be acknowledged. Even though research results may be a scientific achievement of considerable merit, they are not necessarily an invention which can be applied industrially.





Credibility of Assigned Functions



The more **specific** an alleged function is, the more **evidence** is usually needed to render it **credible**.

In case of **substantiated** doubts the **burden of proof** lies with the Applicant (Guidelines for Exam. in the EPO, C-II, 4.9).

Literature or experimental data may be provided during the examination procedure to **confirm a technical effect already indicated** in the application as filed (Guidelines for Exam. in the EPO, C-IV, 9.10).

So-called “**wish**” or “**laundry lists**” of functions are not credible and are not considered to disclose a function or technical effect.





EP0630405 (revoked in Opposition)



Claimed:

Novel putative G-protein coupled receptor V28

Disclosed:

Precise sequence; predicted function based on structural elements; methods for the verification of said function; no results of said methods

Opposition on the ground of non-compliance with the requirements of : **Art. 52, 56, 57 and 83 (EPC)**





EP0630405 (revoked in Opposition)



Inventive Step (Art 56 EPC)

Closest prior art:

Review of 74 Members of 7TM receptor family

Problem to be solved as stated by the OD:

„Provision of a sequence encoding an additional 7TM protein which is predicted to be a receptor“

⇒ The disclosure of the primary structure of an additional 7TM which is arrived at using well established methods disclosed in the prior art is not inventive.





EP0630405 (revoked in Opposition)



Sufficiency of Disclosure (Art 83 EPC):

The disclosure of the amino acid sequence of V28 protein and the prediction of a function as a receptor in combination with the method disclosed for the identification of the respective ligand is not sufficient to disclose a receptor protein with SEQ ID NO: 28.

⇒ The disclosure of a **predicted function** of a protein in combination with a **method of verification** of this function is **not necessarily adequate** to sufficiently disclose the function of the protein!





EP0630405 (revoked in Opposition) Industrial applicability (Art 57 EPC)



A list, in the description, of **speculative functions** of a protein is **not** in itself a **reliable basis** for acknowledging industrial applicability.

With respect to recital 23 of EU Directive 98/44/EC:
The requirement of an “indication of function” is to be interpreted to be a requirement for indications which are **more than speculative**.





T 0111/100



Claimed:

cDNA encoding a mammalian monokine induced by γ -interferon (MIG) being at least 90% identical to a DNA molecule having a sequence according to SEQ ID NO:4 (human cytokine)

Closest prior art:

Document (D1) describes isolation of a cDNA encoding a mouse cytokine (**m119**) induced by γ -interferon from a macrophage cell line and identifies it as member of the platelet factor 4 (PF4) family of cytokines; points out that m119 does **not** represent the **homologue** of any of the then **known human members** of the PF4 family; emphasizes potential therapeutic value **“because of the wide involvement of macrophages in processes relevant to human health and disease”**





T 0111/100



Problem to be solved:

Provision of further cytokines

Solution:

Provision of cytokines having at least 90% identity to the human cytokine (SEQ ID NO:4)

Obvious because of

- **incentive** to look for the human homologue in D1
- isolation of human cytokine DNA by **straightforward methods** using m119 cDNA as probe
approach of “reasonable expectation of success does not apply here”!

Note: the specific sequence of a DNA molecule **as such** does not justify acknowledgement of an inventive step, only if the specific sequence imparts some unexpected properties to the molecule





Conclusions

If genes have been isolated or technically produced, they are patentable, provided that:

- ✓ The application assigns a specific and credible function
- ✓ They are neither known nor obvious
- ✓ They are clearly and unambiguously defined by technical features
- ✓ The application sufficiently discloses how they can be obtained





Thank you!

