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D E C I S I O N
of 12 May 2005

Case Number: W 0037/04 - 3.3.8

Application Number: PCT/DK03/00337

Publication Number: WO 03/100045

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Language of the proceedings: EN

Title of invention:
Plant thymidine Kinases and their use

Applicant:
Knecht, Wolfgang et al

Opponent:
-

Headword:
Thymidine kinases/KNECHT

Relevant legal provisions:
PCT Art. 34(3)(a)
PCT R. 13, 66, 68.2, 68.3(c)
EPC Art. 154(3)

Keyword:
"Invitation to pay additional fees sufficiently reasoned (no)"

Decisions cited:
W 0003/93, W 0006/99, W 0013/99, W 0001/00, W 0005/01,
W 0015/01, W 0018/01, W 0001/02, W 0010/02, W 0003/03,
W 0026/03

Catchword:
-



Case Number: W 0037/04 - 3.3.8

International Application No. PCT/DK03/00337

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 12 May 2005

Applicant: Knecht, Wolfgang et al.

Representative: Norgaard, Jens Viktor
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Decision under appeal: Protest according to Rule 68.3(c) of the Patent Cooperation Treaty made by the applicants against the invitation of the European Patent Office (International Preliminary Examining Authority) to restrict the claims or pay additional fees dated 30 April 2004.

Composition of the Board:

Chairman: L. Galligani
Members: P. Julià
B. Günzel

Summary of Facts and Submissions

I. International patent application PCT/DK03/00337 was filed on 21 May 2003 with 46 claims, of which claim 1 read as follows:

- "1. *An isolated polynucleotide encoding a plant thymidine kinase enzyme derived from a plant, said isolated polynucleotide being selected from the group consisting of:*
- i) an isolated polynucleotide encoding thymidine kinase enzyme derived from pine (*Pinus taeda*), rice (*Oryza sativa*) or tomato (*Lycopersicum esculentum*),*
 - ii) an isolated polynucleotide encoding a thymidine kinase enzyme derived from a plant, which thymidine kinase enzyme, when compared to human Herpes simplex virus type 1 thymidine kinase (HSV1-TK) and upon transduction into a eukaryotic cell, decreases at least four (4) fold the IC₅₀ of at least one nucleoside analogue,*
 - iii) an isolated polynucleotide encoding a thymidine kinase enzyme derived from a plant, which thymidine kinase enzyme is capable of phosphorylating at least one nucleoside analogue monophosphate at a higher degree than thymidine monophosphate,*
 - iv) an isolated polynucleotide encoding a thymidine kinase enzyme derived from a plant, which thymidine kinase enzyme has a ratio of $[k_{cat}/K_m (\text{Thd})] / [k_{cat}/K_m (\text{at least nucleoside analogue})]$ of less than two (2),*

- v) *an isolated polynucleotide encoding a thymidine kinase enzyme derived from a plant, which thymidine kinase enzyme, when expressed and compared to human Herpes simplex virus type 1 thymidine kinase (HSV1-TK), has a decreased ratio of $[k_{cat}/K_m (Thd)] / [k_{cat}/K_m (at\ at\ least\ one\ nucleoside\ analogue)]$ of at least five (5) fold, wherein analogue is any nucleoside analogue, and*
- vi) *an isolated mutated and/or truncated polynucleotide encoding a thymidine kinase enzyme variant derived from a plant, which thymidine kinase enzyme variant, when compared to human Herpes simplex virus type 1 thymidine kinase (HSV1-TK) and upon transduction into a eukaryotic cell, decreases at least four (4) fold the IC_{50} of at least one nucleoside analogue."*

Further independent claims 7, 24, 26-27, 29-32, 36 and 43-46 related to, respectively, isolated plant thymidine kinase enzymes encoded by the polynucleotide of any of the claims 1-6 or having the properties as defined in claim 1 (claim 7), vector constructs (claim 24), packaging cell lines (claim 26) and host cells (claim 27), pharmaceutical compositions (claims 29-31), a method of sensitising a cell to a pro-drug (claim 32), a method of inhibiting a pathogenic agent in a warm-blooded animal (claim 36), use for phosphorylation of a nucleoside or a nucleoside analog and a method therefor (claims 43 and 44), a method of controlling or modifying growth of a plant (claim 45) and articles containing a nucleoside

analogue and the thymidine kinase of claims 7-23 for administration in cancer therapy (claim 46).

II. On 30 April 2004 the European Patent Office, acting as an International Preliminary Examining Authority (IPEA), issued an "Invitation to restrict or to pay additional fees" (PCT Rule 66), Form PCT/IPEA/405 (January 2004). It considered that the international application did not comply with the requirements of unity of invention (Rule 13 PCT) and invited the applicant to restrict the claims or to pay three additional fees. The applicant was inter alia also informed that, according to Rule 68.3(c) PCT the payment of any additional fee may be made under protest.

III. The invitation stated that the application lacked unity as required by Article 34(3)(a) PCT and Rule 13 PCT and it related to four groups of inventions identified as:

Group 1: thymidine kinase from pine and related subject-matter (claims 1, 3-7, 9-14, 23-46, all partially, and claim 17)

Group 2: thymidine kinase from tomato and related subject-matter (claims 1, 3-7, 9-14, 23-46, all partially, and claims 15 and 18)

Group 3: thymidine kinase from rice and related subject-matter (claims 1, 3-7, 9-14, 23-46, all partially, and claim 19)

Group 4: thymidine kinase from *A. thaliana* and related subject-matter (claims 10-14, 23-46, all partially, and claims 2, 8, 16 and 20-22)

IV. The IPEA reasoned that the common concept (technical relationship) linking these groups of inventions together was plant thymidine kinases. However, this concept was not regarded as the "special technical feature" required by Rule 13.2 PCT because it was neither novel nor inventive, since plant thymidine kinases were already known from the prior art (e.g. document D11, database Medline AN AF066050, cited in document D8, H. Ullah et al., Plant Physiology, Vol. 119, 1999, pages 1567-1568, and corresponding to the mRNA for thymidine kinase from rice). Thus, the common concept was not novel and consequently there was a lack of unity.

V. With letter dated 27 May 2004 the applicant paid all three additional examination fees under protest and set out reasons for disagreeing with the findings of the IPEA. In particular, it was stated that:

a) Rule 66 PCT provided no legal basis for an invitation to restrict or to pay additional fees.

b) it was contrary to the principles of the PCT law, as indicated in the PCT Examination Guidelines (PCT Gazette Special Issue No. 07/1998, VI-5.13) and the established practice of the EPO confirmed by the EPO Boards of Appeal in decision W 6/99 (OJ EPO, 2001, 196), to deny the applicant an opportunity to counter - by argument or by amendment - the unity objection without the need to pay additional fees. Lack of unity a posteriori during international preliminary examination had always to be raised in a first written opinion and not in an invitation to pay further fees.

c) A posteriori lack of unity should be raised only in clear-cut cases. Document D8 did not deprive the invention of novelty since, as commented in the application as filed and also acknowledged in the International Search Report, it only disclosed a partial sequence insufficient for expression of the whole protein and it was completely silent about any possible use of rice thymidine kinase. Unity of the invention was given because no experimental work towards characterization, properties, use or biological function of plant thymidine kinases was accomplished prior to the priority date of the present invention. Therefore, the provision of plant thymidine kinases in isolated and bioactive form, with entirely unexpected and unforeseeable properties, represented a novel contribution to the art.

d) Since the International Searching Authority (ISA) had considered it straightforward for a search to be conducted covering all the claimed subject-matter without the need for payment of any additional fee, no additional or little effort was necessary for carrying out a complete international preliminary examination and thus, there was no need for the payment of additional examination fees.

VI. The PCT first written opinion was issued on 28 July 2004 based on claims 1 to 46 as originally filed and, under Section IV ("Lack of unity of invention"), the reasoning was identical to the one present in the communication inviting the applicant to restrict the claims or to pay additional fees (cf. section IV *supra*).

VII. With a notification dated 6 August 2004, the Review Panel within the meaning of Rule 68.3(c) PCT examined the arguments of the applicant for supporting unity of invention and confirmed the opinion of the IPEA with regard to lack of unity. The applicant was invited to pay within one month the protest fee under Rule 68.3(e) PCT for the examination of the protest. The review panel basically stated that:

- a) it was not on the review panel to decide or comment on the formal content of form PCT/IPEA/405,
- b) Decision W 6/99 (*supra*) did not modify the procedure of the EPO acting as IPEA when issuing an invitation to restrict or pay additional fees; this procedure derived from long established practice at the EPO which was enshrined in Rule 68.2 PCT, which did not require any official communication between the examiner and the applicant prior to the dispatch of said invitation. Other decisions of the Boards of Appeal (W 18/01 of 23 January 2002) did not comment on this point.
- c) Documents D8 and D11 (cf. section IV *supra*) disclosed a gene for rice thymidine kinase. Thus, the concept of a plant thymidine kinase was already disclosed in the prior art and it could not be considered as a "special technical feature" linking the identified groups of inventions.
- d) According to Rule 68.2 PCT it was the option of the IPEA to decide to issue an invitation to pay additional fees, independently of the findings by the ISA.

VIII. The protest fee was paid on 3 September 2004. This was accompanied by further comments on the reasons given by the review panel, namely: a) Rule 66 PCT referred to in the invitation to restrict or to pay additional fees did not provide a legal basis for this invitation, b) contrary to the principles of the PCT law, the applicant was denied an opportunity to counter the unity objection without the need to pay additional fees, c) an objection of lack of unity a posteriori was to be raised only in clear-cut cases, which was not the present case since document D8 did not deprive the invention of novelty and the provision of plant thymidine kinases in isolated form with unexpected properties represented an important contribution to the art, and d) no additional effort was necessary for carrying out a complete international preliminary examination and thus, the invitation to pay for additional examination fees was unjustified.

Reasons for the Decision

1. The protest is admissible.
2. Pursuant to Article 154(3) EPC the Boards of Appeal of the EPO are responsible for deciding on a protest made by an applicant against the payment of an additional fee charged by the EPO under the provisions of Article 34(3)(a) PCT.
3. The applicant's protest, as stated in its letter of 3 September 2004, is based on four points: a) the invitation to pay further fees wrongly referred to Rule 66 PCT and was thus without legal basis, b) the

invitation did not comply with the legal principles of the PCT as laid down in the PCT Examination Guidelines and the established practice of the EPO which required an objection of lack of unity to be raised first in a written opinion, c) the invitation was not substantiated, and d) the additional effort did not justify the payment of further examination fees (cf. Sections V and VIII *supra*).

a) Lack of indication of legal basis in the invitation to pay further fees

4. Under the main heading of the "Invitation to restrict or to pay additional fees" issued by the IPEA with Form PCT/IPEA/405 (January 2004), reference is indeed - only - made to Rule 66 PCT. Rule 66 PCT deals with the generalities of the procedure before the IPEA and, in particular, with the first written opinion of the IPEA and with applicant's right to submit arguments and, where appropriate, amendments. The procedure before the IPEA in cases of lack of unity of invention is laid down in Rule 68 PCT. Thus, the correct provisions of the PCT to be cited under the heading "Invitation to restrict or to pay additional fees" before the IPEA are Article 34(3)(a) and Rule 68.2 and 68.3 PCT, as it appears in the original Form PCT/IPEA/405, drawn up under Section 102 of the Administrative Instructions under the PCT (as in force from 1 July 1998). The Board has no information as to why the IPEA has used a different version of Form PCT/IPEA/405 to the original one. According to Section 102(a) Administrative Instructions, the use of Form PCT/IPEA/405 is mandatory and only slight variations in layout are permitted for specific reasons (see Section 102(b) and (c)). It is

clear, however, that the citation of a different legal basis in the PCT for the action to be undertaken via the use of the form is not simply a question of layout. Therefore Form PCT/IPEA/405 should be corrected without delay unless this has already been done.

5. That, thus, an incorrect provision is cited under the heading of the form used by the IPEA does, however, not ipso facto mean that the invitation as such, taken as a whole, would lack sufficient identification of the legal basis for the objections raised. The text of the communication explicitly refers to Rules 13.1, 13.2 and 13.3 PCT for the requirements of unity of invention (cf. point 1 of the text), to Rule 68.3(c) for the payment of additional fees under protest (cf. point 2 of the text) and to Article 34(3)(a) PCT in the Annex to the invitation (Sheet 1, July 1992). Thus, the legal basis for the invitation to restrict or to pay additional fees was indeed clearly indicated in the text of the invitation. Equally, with regard to the number and the format of the form used as well as the remaining text of the invitation there could be no doubt that what was issued was not a first written opinion but an invitation to restrict or to pay under Article 34(3)(a), Rule 68.2 PCT. This was evidently also the applicant's understanding of the communication, as he has criticised the action taken as being contrary to the legal principles of the PCT.

b) The invitation was contrary to the legal principles of the PCT and the established practice of the EPO

6. The applicant has argued that an objection of lack of unity a posteriori during the international preliminary

examination (IPE) had always to be raised in a first written opinion and not in an invitation to restrict the claims or to pay further fees. In the applicant's view, it is contrary to the PCT, as indicated in the PCT International Preliminary Examination Guidelines (IPE-G1) and the established practice of the EPO, confirmed by the Boards of Appeal in decision W 6/99 (*supra*), to deny the applicant the opportunity to counter the objection of lack of unity of invention - by argument or by amendment - without the need to pay additional fees.

7. Decision W 6/99 (*supra*, Keyword and point 4 of the reasons) cited by the applicant has held that under the PCT IPE-G1 binding on the EPO, an invitation pursuant to Rule 68.2 PCT may not be issued until the applicant's reply to the examiner's first written opinion has failed to overcome the IPEA's "a posteriori" lack-of-unity objection. In that decision the Board took the view that Chapter VI-5.13 PCT IPE-G1 prescribed the order for the two actions of the IPEA as being first the examiner's opinion and then the invitation pursuant to Rule 68.2 PCT. The decision was confirmed in unpublished decision W 13/99 of 10 August 2000.
8. It is noted, however, that the approach taken in these decisions does not appear to have been generally endorsed by the Boards of Appeal in protest cases concerning international preliminary examination. On the contrary, the apparent practice of the EPO acting as IPEA to issue the invitation to restrict or pay before or simultaneously with the first written opinion was not objected to in other unpublished decisions (see

e.g. W 1/00 of 8 August 2000, W 5/01 of 27 June 2001, W 15/01 of 31 July 2001, W 18/01 of 23 January 2002, W 1/02 of 20 August 2002, W 10/02 of 9 December 2002, which were all given after decision W 6/99 (7 April 2000), see also the doubts expressed in decision W 3/03 of 30 September 2003, point 9 of the reasons).

9. The reasoning given by the Board in decision W 6/99 that Chapter VI-5.13 of the PCT IPE-G1 was meant to give the applicant an opportunity to submit arguments or amendments in response to the objection substantiated in the examiner's first opinion before being forced to decide on potentially far-reaching consequences of the alleged lack of unity, certainly carries weight. Nevertheless, this Board has doubts as to whether, when considered in their context, the cited passage can be read to mean that in IPE a first written opinion raising an "a posteriori" lack of unity objection would necessarily have to precede an invitation under Rule 68.2 PCT. The cited statements from the PCT IPE-G1 are made under the heading "First written opinion". By contrast, under the preceding heading "First stage of international preliminary examination" and "General" it is stated (Chapter VI-5.3) that in addition to matters which require a written opinion, there may be a lack of unity of invention which the examiner will generally deal with before the first written opinion is issued to the applicant or, if appropriate, concurrently therewith. There is no indication in this passage that this should only apply to "a priori" non-unity objections. The same holds good for the following passages explaining, under the heading "Lack of compliance with the requirement of unity of invention" the procedure to be followed in

cases of a finding of lack of unity by the IPEA. Therefore, the Board has doubts whether it could clearly be said that issuing an invitation to restrict or to pay additional fees before the first written opinion in "a posteriori" non-unity cases constitutes a violation of the PCT IPE-G1.

10. In the present case this issue may remain undecided because the reimbursement of the fees paid is justified for the following reasons.

c) Substantiation of the invitation

11. In accordance with Article 34(3)(a) PCT if the IPEA considers that the international application does not comply with the requirements of unity it may choose to invite the applicant to restrict the claims or to pay additional fees. Rule 68.2 PCT requires this invitation to specify "*the reasons for which the international application is not considered as complying with the requirement of unity of invention*".
12. According to the established case law, a logical chain of reasoning containing the basic considerations behind the finding of lack of unity is required to enable the applicant and the appeal body to examine whether the invitation to pay additional fees was justified. The specification of these reasons in the invitation is thus an essential requirement and an invitation is not legally effective unless reasons are given to substantiate lack of unity (cf. "Case Law of the Boards of Appeal of the European Patent Office", 4th edition 2001, IX.C.2 to 2.1, pages 576 to 579 and IX.D.1 to 1.2, pages 582 to 584).

13. In the present case, the invitation to pay additional fees identified four groups of inventions and referred to document D11 (cited in document D8) as anticipating the common concept (plant thymidine kinase) linking these inventions (cf. sections III and IV *supra*). There was, however, no reference to the technical problem underlying the application nor to the subject-matter for which these documents were considered to be novelty destroying and the reasons therefor.

Document D8 only discloses a list of entries into an electronic register - the Electronic Plant Gene Register (not peer-reviewed for any technical merit) - with a cross-reference to document D11. This latter document is referred to in the present application as disclosing a partial nucleotide sequence of a gene from rice which, based only on homology comparison, is proposed to encode a (putative) thymidine kinase. The disclosed partial nucleotide sequence is said, however, in the present application not to be sufficient for the expression of an active thymidine kinase enzyme (cf. page 2, lines 2 to 3 of the published application). Notwithstanding the available information, the IPEA failed to identify the technical problem underlying the present application and to give any reasons in the invitation to pay for additional fees why these disclosures were considered to be technically relevant for solving the identified technical problem and the specific subject-matter considered to be anticipated thereby.

The IPEA also failed to indicate whether any considerations were given to other possible common technical relationship between the identified different groups of inventions (presence of common structural features, enzymatic activity, specific use, etc.) and there was no reasoning explaining why the IPEA considered that, once one of these specified groups of inventions was anticipated by the prior art, there was no other possible technical connection or common link between the remaining multiple groups of inventions. This would have required in turn to address the technical problems underlying these different groups of inventions.

14. The purpose of the protest procedure under Rule 68.3(c) PCT is to enable the justification for the invitation to pay for additional fees to be submitted to substantive review. The only issue to be examined by the board therefore is whether, considering the reasons given by the IPEA and the submissions made by the applicant in support of the protest, retaining additional examination fees was justified. The board cannot investigate *ex-officio* whether an objection of lack of unity would have been justified for reasons other than those given in the invitation to pay for additional fees issued by the IPEA. To the extent that the reasons given for charging additional fees are insufficient or wrong, the protest is justified and the fees have to be reimbursed, irrespective of whether or not, as a result, the finding of non-unity could be regarded as justified as to substance (cf. *inter alia* W 3/93, OJ EPO 1994, 931, Headnote III and point 4 of the reasons; W 26/03 of 27 October 2004, point 6 of the reasons).

15. It follows therefrom that, in the light of the deficiencies found in the present case (cf. point 13 *supra*), the additional fees paid under protest are to be reimbursed without considering the question of unity in substance. Moreover, the protest fee must also be refunded.
16. In view of the conclusion arrived at in the preceding paragraph, the board is not called upon to assess whether or not the additional effort justified the payment of further examination fees (cf. sections V, VIII and point 3 *supra*).

Order

For these reasons it is decided that:

1. Three additional examination fees are reimbursed.
2. The protest fee is reimbursed.

The Registrar:

The Chairman:

G. Rauh

L. Galligani