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Datasheet for the decision of 28 June 2007

Case Number: T 1181/06 - 3.3.08

Application Number: 94928169.5

Publication Number: 0725778

IPC: C12N 15/52

Language of the proceedings: EN

Title of invention:
Recombinant production of novel polyketides

Patentees:
The Leland Stanford Junior University, et al

Opponent:
BIOTICA TECHNOLOGY LIMITED

Headword:
Polyketides/STANFORD

Relevant legal provisions:
EPC Art. 123(3)

Keyword:
"Main request: extension of protection (yes)"
"First auxiliary request: admissibility (no)"

Decisions cited:
-

Catchword:
-

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Case Number: T 1181/06 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 28 June 2007

Appellants I: (Patent proprietors)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 11 May 2006 concerning maintenance of the European Patent No. 0725778 in amended form.**

Composition of the Board:

Chairman: L. Galligani
Members: T. J. H. Mennessier
C. Rennie-Smith

Summary of Facts and Submissions

I. Both the patentees (appellants I) and the opponent (appellant II) lodged an appeal against the interlocutory decision of the opposition division dated 11 May 2006, whereby European patent No. 0 725 778, which had been granted on European application No. 94 928 169.5 published under the international publication No. WO 95/08548, was maintained in an amended form on the basis of the third auxiliary request filed on 12 April 2005. The main request, the first auxiliary request and the second auxiliary request then on file had been refused for non-compliance with the requirements of Article 123(2) EPC (main and first auxiliary requests) and lack of novelty (second auxiliary request).

Claim 1 as granted read as follows:

"1. Cells having introduced nucleic acid encoding a modular polyketide synthase (PKS) containing modules, each module comprising at least a PKS acyl transferase (AT) activity, a PKS ketoacyl carrier protein synthase (KS) activity, and a PKS acyl carrier protein (ACP) activity;

the introduced PKS module-encoding nucleotide sequences being operatively-linked to at least one control sequence, whereby said cells are capable of producing a functional modular PKS,
wherein at least one of the module-encoding nucleotide sequences for said functional modular PKS or one of said control is heterologous to the host cell."

II. The patent had been opposed on the grounds as set forth in Articles 100(a), (b) and (c) EPC that (i) the invention was neither new nor inventive (Articles 54 and 56 EPC), (ii) the invention was not sufficiently disclosed (Article 83 EPC) and (iii) the patent contained subject-matter which extended beyond the content of the application as filed (Article 123(2) EPC).

III. Appellants I filed a statement setting out the grounds of appeal in which they indicated that their claim requests were those considered by the opposition division in its decision plus a newly-filed auxiliary request, referred to as auxiliary request A.

IV. Together with its statement setting out the grounds of appeal appellant II filed 20 additional documents (D54 to D73).

V. The Board issued a communication under Article 11(1) of the Rules of Procedure of the Boards of Appeal expressing a provisional, non-binding opinion on some of the pending issues.

VI. Each of appellants I and appellant II replied to the other's statement of grounds of appeal. Appellants I filed a further auxiliary request (auxiliary IV) and requested that documents D54 to D73 not be admitted into the proceedings.

VII. Oral proceedings took place on 28 June 2007, at which appellants I filed a new main request and a new first auxiliary request to replace all the requests on file.

As none of documents D54 to D73 were relied on by appellant II, their admissibility was not discussed.

VIII. Claim 1 of the respective requests read as follows:

Main request:

"1. Host cells transformed with a recombinant vector comprising
(a) a modular polyketide synthase (PKS) gene cluster; and
(b) control elements that are operatively-linked to said gene cluster, whereby said cells are capable of producing a functional modular PKS from said gene cluster;
wherein said gene cluster or one of said control elements is heterologous to the host cells;
wherein at least one of said control elements is heterologous to said gene cluster; and
wherein the cells are actinomycetes and have been modified so as substantially to lack a PKS gene cluster normally present in the unmodified host cells".

First auxiliary request:

"1. Host cells transformed with a recombinant vector comprising
(a) **the complete 6-deoxyerythronolide B synthase (DEBS)** gene cluster; and
(b) control elements that are operatively-linked to said gene cluster, whereby said cells are capable of producing a functional **DEBS** from said gene cluster;
wherein said gene cluster or one of said control elements is heterologous to the host cells;

wherein at least one of said control elements is heterologous to said gene cluster; and
wherein the cells are actinomycetes and have been modified so as substantially to lack **the** PKS gene cluster normally present in the unmodified host cells".

(emphasis added by the Board to show the differences to claim 1 of the main request)

IX. The following documents are referred to in the present decision:

(D22) James Staunton and Barrie Wilkinson, Chem. Rev., Vol. 97, 1997, Pages 2611 to 2629

(D24) Yanina Volchegursky et al., Molecular Microbiology, Vol. 37, No. 4, 2000, Pages 752 to 762

X. The submissions made by appellants I, insofar as they are relevant to the present decision, may be summarised as follows:

Main request (Article 123(3) EPC)

Deletion in claim 1 of the minimal requirement that each module of the encoded polyketide synthase had to comprise at least a PKS acyl transferase (AT) activity, a PKS ketoacyl carrier protein synthase (KS) activity, and a PKS acyl carrier protein (ACP) activity was compensated by the requirement that the claimed cells had to be capable of producing a functional modular PKS.

First auxiliary request (Admissibility)

With claim 1 being directed to host cells transformed with a vector comprising the complete 6-deoxyerythronolide B synthase gene cluster, the first auxiliary request represented a direct response to the objection raised under Article 123(3) EPC against claim 1 of the main request. Therefore, it was admissible.

XI. The submissions made by appellant II, insofar as they are relevant to the present decision, may be summarised as follows:

Main request (Article 123(3) EPC)

There was no longer any requirement that each module of the encoded polyketide synthase had to comprise at least AT, KS and ACP activities. Therefore, the encoded synthase might possibly comprise only two of those activities. This was credible in view of document D22, which taught that the load module of the first DEBS polypeptide of erythromycin (eryAI) consisted of only two activities, namely AT and ACP (see scheme 6 on page 2616), and document D24 which taught that the loading module of the first DEBS polypeptide of megalomicin (megAI) also lacks a KS domain (see right-hand column on page 754).

First auxiliary request (Admissibility)

Admitting the first auxiliary request filed in an attempt to overcome the objection of extension of the protection conferred raised against claim 1 of the main request would be a waste of time, as that objection was only one of numerous objections to be considered.

XII. Appellants I (patentees) requested that the decision under appeal be set aside and that the patent be maintained on the basis of either the main request or the first auxiliary request filed during the oral proceedings.

XIII. Appellant II (opponent) requested that the decision under appeal be set aside and the patent be revoked.

Reasons for the Decision

Main request (Article 123(3) EPC)

1. Claim 1 of the main request differs from claim 1 as granted in that the minimal requirement to be complied with by each module of the encoded modular polyketide synthase, namely the requirement that each module has to comprise at least a PKS acyl transferase (AT) activity, a PKS ketoacyl carrier protein synthase (KS) activity, and a PKS acyl carrier protein (ACP) activity, has been eliminated. This amendment was made in response to an Article 123(2) EPC objection against the formulation of that minimal requirement in the claim as granted.

2. As a result claim 1 of the main request encompasses embodiments in which at least one module may comprise only one or two of the three enzymatic activities which were all "mandatory" according to claim 1 as granted. Thus, claim 1 has been amended in such a way as to extend the protection conferred and consequently does

not comply with the requirement as set out in Article 123(3) EPC.

3. The argument made by appellants I that the elimination of the minimal requirement is compensated by the feature that the cells should be capable of producing a functional modular PKS is not accepted as this latter feature was already present in claim 1 as granted and, as such, may have no impact on the situation created by the amendment.

4. Thus, the main request cannot form a basis for the maintenance of the patent.

First auxiliary request (Admissibility)

5. Claim 1 of the first auxiliary request differs from claim 1 of the main request in that it has been specified that (i) the recombinant vector comprises the complete 6-deoxyerythronolide B synthase (DEBS) gene cluster (cf. "a polyketide synthase gene cluster" in the main request) and (ii) that the cells lack "**the**" PKS gene cluster (cf. "a PKS gene cluster" in the main request).

6. At first glance, it appears that, as shown below, the amended wording of claim 1 generates **additional** objections in particular in respect of the clarity requirement of Article 84 EPC and the prohibition of added matter in Article 123(2) EPC.

6.1 It is not clear whether the feature "to lack the PKS gene cluster" should relate to the 6-deoxyerythronolide

B synthase gene cluster, i.e. whether the host cells specifically lack the DEBS gene cluster.

6.2 The application as filed describes in Example 5 (see pages 56 to 58 of the international application together with from page 29, line 30 to page 31, line 5) the specific vector pCK7, which carries the *eryA* genes from *Saccharopolyspora erythraea* encoding the three polypeptides of the 6-deoxyerythronolide B synthase and placed under the control of actinorhodin (*act*) promoters, and subsequently moved into *Streptomyces coelicolor* CH999, a strain which has been genetically engineered to remove the native *act* gene cluster (see page 42, lines 14 to 19 in the international application). Thus, what is described in Example 5 is a host cell/vector system consisting of a vector comprising the **complete 6-deoxyerythronolide B synthase gene cluster** and a cell which has been modified so as to lack its endogenous **actinorhodin gene cluster**. This specific cell/vector system is only one of the numerous embodiments encompassed by claim 1, which therefore appears to contain an unjustified form of generalisation.

7. Using its discretion, the Board regards it as inappropriate to admit at such a late stage of the proceedings a request which would be subject to additional objections and, thus, decides not to admit the first auxiliary request into the present proceedings.

8. Therefore, in the absence of any other allowable request, the patent should be revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar The Chairman

A. Wolinski L. Galligani