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D E C I S I O N
of 28 June 2001

Case Number: W 0011/00 - 3.3.4

Application Number: PCT/US 97/12497

Publication Number: -

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Title of invention:
Antimicrobial agents, diagnostic reagents, and vaccines based on unique apicomplexan parasite components

Applicant:
ARCH DEVELOPMENT CORPORATION

Opponent:
-

Headword:
Apicomplexan parasites/ARCH DEVELOPMENT CORP.

Relevant legal provisions:
PCT Art. 17(3)(a)
PCT R. 40.1

Keyword:
-

Decisions cited:
G 0001/89

Catchword:
-

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Case Number: W 0011/00 - 3.3.4
International Application No. PCT/US 97/12497

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 28 June 2001

Applicant: ARCH DEVELOPMENT CORPORATION
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Subject of the Decision: **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 16 February 1998.**

Composition of the Board:

Chairman: U. Kinkeldey
Members: F. Davison-Brunel
B. Günzel

Summary of Facts and Submissions

I. International patent application PCT/US 97/12497 was filed on 18 July 1997 with 30 claims.

Claim 1 read as follows:

"The use of a component of a plant-like metabolic pathway in an Apicomplexan parasite, wherein the pathway does not involve the *pbs*A gene or PPi phosphofructokinase, is not encoded by the plastid genome, and is not generally operative in animals, to produce a composition that interferes with the growth or survival of the parasite."

Claims 2 to 13 were directed to further features of the use of claim 1. Claims 14 and 15 were directed to compositions capable of interfering with a component of a plant-like metabolic pathway of an Apicomplexan parasite, said component being selected from a group of specific nucleotide or amino acid sequences. Claims 16 and 17 were directed to a diagnostic reagent or an assay for identifying the presence of an Apicomplexan parasite in a subject or in a biological sample. Claims 18 to 25 were directed to vaccines for protecting an animal against infection by an Apicomplexan parasite. Claim 26 related to a method to identify a component of a plant-like pathway in an Apicomplexan parasite and claim 27, to an assay for a candidate inhibitor of a plant-like Apicomplexan metabolic pathway. Claims 28 and 29 related to an antibody and an antisense molecule to a component of a plant-like metabolic pathway in Apicomplexan, respectively. Claim 30 related to a method for developing a lead compound that interferes with the

growth and survival of an Apicomplexan parasite.

II. On 16 February 1998, the EPO acting as an International Searching Authority (ISA) sent to the applicant an invitation to pay 8 additional search fees pursuant to Article 17(3)(a) PCT and Rule 40.1 PCT.

III. The invitation stated that the application related to nine groups of inventions which were not linked by a single inventive concept.

The ISA observed that the use of components of a plant-like metabolic pathway to produce compositions which interfered with the growth or survival of an Apicomplexan parasite was already known from the prior art document WO 92/00734.

In the light of this prior art, the problem underlying the application could be defined as the provision of further uses of components of plant-like metabolic pathways in an Apicomplexan parasite to produce compositions that interfered with the growth or survival of the parasite.

The solutions proposed could be summarized as:

1- Claims 1,2,4-10,16-19,21,23,24,26-30 (all partially):
The use of a component of a plant-like metabolic pathway in an Apicomplexan parasite wherein the pathway does not involve the *pbs*A gene or PPi phosphofructokinase, is not encoded by the plastid genome, and is not generally operative in animals, to produce a composition that interferes with the growth or survival of the parasite; said use but limited to a

plant-like metabolic pathway, which is selected for synthesis of heme from glutamate and tRNA glu by the plant-like heme synthesis (5 carbon) pathway; a diagnostic reagent for identifying the presence of an Apicomplexan parasite in a subject; a vaccine for protecting an animal against infection by an Apicomplexan parasite, said vaccine comprising an Apicomplexan parasite in which a gene encoding a component of said pathway in the parasite is altered, a method to identify a component and an assay for a candicate inhibitor, of a plant-like pathway in an Apicomplexan parasite; an antibody to a component and an antisense molecule directed to a component of a plant-like metabolic pathway; a method for developing a lead component that interferes with the growth or survival of an Apicomplexan parasite, said method comprising: identifying a component of a plant-like metabolic pathway in an Apicomplexan; and developing an inhibitor to the component.

2- Claims 1,2,4-10,16-19,21,23,24,26-30 (all partially):
Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for synthesis of C4 acids by the breakdown of lipids into fatty acids and then acetyl CoA, and their use in the glyoxylate cycle.

3- Claims 1-10,16-19,21,23,24,26-30 (all partially), 11-15,20,22,25:
Idem as invention 1, but limited to: a plant-like metabolic pathway, which is selected for synthesis of chorismate from phosphoenolpyruvate and erythrose 4 phosphate by the shikimate pathway, synthesis of tetrahydrofolate from chorismate by the shikimate

pathway and synthesis from ubiquinone from chorismate by the shikimate pathway, synthesis of aromatic aminoacids from chorismate by the shikimate pathway, synthesis of menaquinone, enterobactin and vitamin K1 from the chorismate by the shikimate pathway, synthesis of auxin growth regulators from indolacetic acid derived from chorismate.

4- Claims 1,2,4-10,16-19,21,23,24,26-30 (all partially):
Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for electron transport through the alternative pathway with use of the alternative oxidase.

5- Claims 1-10,16-19,21,23,24,26-30 (all partially)
Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for the transport of proteins into or out of an organelle through the use of a transit peptide sequence.

6- Claims 1-10,16-19,21,23,24,26-30 (all partially):
Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for synthesis of the branched chain amino acids from pyruvate and alpha-ketobutyrate by the plant-like branched amino acid synthesis pathway; synthesis of essential amino acids, not synthesized by animals and including histidine, threonine, lysine and methionine by the use of plant-like amino acid synthases.

7- Claims 1-10,16-19,21,23,24,26-30 (all partially):
Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for synthesis of linoleneic and linoleic acid.

8- Claims 1-10,16-19,21,23,24,26-30 (all partially): Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for synthesis of amylose and amylopectin with starch synthases and branching enzymes, in their degradation.

9- Claims 1-10,16-19,21,23,24,26-30 (all partially): Idem as invention 1, but limited to a plant-like metabolic pathway, which is selected for synthesis of isoprenoids such as giberellins and abscidic acid by the mevalonic acid to giberellin pathway.

In view of the fact that the use of a component of a plant-like metabolic pathway to produce compositions which interfere with the growth or survival of an Apicomplexan parasite was already known in the art, due to the essential difference in the biological nature of the metabolic pathways and due to the fact that no other technical features could be distinguished which could be regarded as special technical features common to the solutions provided, there was no single inventive concept underlying the plurality of inventions and, therefore, lack of unity ensued.

III. On 30 March 1998, the applicant paid the additional fees under protest pursuant to Rule 40(2) PCT. The arguments submitted in favor of the protest insofar as they are relevant to the present decision were as follows:

WO 92/00374 described the use of p-acetamidobenzoic acid (PAcBA) which acted as an inhibitor of the plant-like enzyme DHPS, for the treatment or prevention of an infection by a Apicomplexan parasite. It did not teach that plant-like pathways existed in Apicomplexans.

The mere description of one inhibitor did not amount to a teaching of the general concept that plant-like pathways existed in such parasites, which provided multiple opportunities for drug development and therapeutic and preventive uses.

For these reasons, the finding of lack of unity by the ISA was not justified.

IV. On 22 July 1998, the Review Panel of the ISA confirmed the finding of lack of unity and invited the applicant to pay a protest fee.

V. On 24 August 1998, the applicant paid the protest fee and provided further arguments in reply to the decision of the review panel.

Reasons for the Decision

1. The protest is admissible.

2. In accordance with the decision G 1/89 of the Enlarged Board of Appeal (OJ EPO, 1991, 155),the ISA is empowered to raise an objection of lack of unity **a posteriori**, i.e. after having taken into account the prior art revealed by the search. In point 8.2 of the Reasons, the Enlarged Board of Appeal mentioned that the consideration by the ISA of the requirement of unity of invention should, of course, always be made with a view to giving the applicant fair treatment and that the charging of additional fees under Article 17(3)(a) PCT should be made only in clear cases. In particular, in view of the fact that such consideration under the PCT was made without the

applicant having had the opportunity to comment, the ISA should in border-line cases refrain from considering an application as not complying with the requirement of unity of invention on the ground of lack of novelty or inventive step.

3. Claim 1 of the present application is directed towards the use of a **component of a plant-like metabolic pathway** in an Apicomplexan parasite ... to produce a composition that interferes with the growth or survival of the parasite. In the light of the description (passage bridging pages 18 and 19, page 20 and Table 1) and of dependent claims 4 and 5, the Board understands that the "component of the plant-like metabolic pathway" is a compound which belongs to said pathway (enzymes, substrates, products etc...) whereas the "interfering principle" in the composition is a compound which does not belong to the pathway but interacts in a negative way with one or the other component of said pathway to prevent its successful completion.

4. The prior art document WO 92/00734 (passage bridging pages 1 and 2) teaches that metabolic pathways which are specific to pathogens (including Apicomplexan parasites) to the extent that they do not exist in the host cells of these pathogens are ideal targets for the development of anti-pathogenic agents since the host cells are not affected by the targeted action of said agents. It discloses on page 3 that a composition containing the interfering principle, p-acetamidobenzoic acid (PAcBA) exerts its anti-microbial effect by inhibiting the plant-like enzyme dihydropteroate synthase (DHPS) i.e. a component of a plant-like metabolic pathway which is naturally

synthesized by Plasmodium species but not by their host. Yet, it does not disclose the production of a composition containing PAcBA by using dihydropteroate synthase, since, according to the teachings on page 6, PAcBA was obtained from a chemical manufacturer.

5. Prima facie, document WO 92/00734 is not novelty destroying to the subject-matter of claim 1.

&. The Board notices that the ISA seems to have interpreted the claim as meaning that the component of the plant-like metabolic pathway and the interfering principle of the composition produced were the same molecule (see the invitation to pay additional fees; motivation of lack of unity). This interpretation, however, leads to the same conclusion with respect to novelty as reached in point 5 above. Indeed, the prior art document WO 92/00374 does not teach that the interfering principle PAcBA is a component of a plant-like metabolic pathway. What it teaches instead on page 9, lines 17 to 24 is that para-aminobenzoic acid (PABA), DHPS and tetrahydrofolate are components of a plant-like metabolic pathway and that DHPS is the target of PAcBA.

7. As the preliminary examination by the Board leads to the conclusion that novelty is not at stake, the request by the ISA for the payment of additional research fees on the ground of lack of novelty is not justified.

8. To reach a definite conclusion of lack of unity, it would be necessary to determine whether the claimed invention enjoys inventive step. Prima facie, the question of inventive step is not easy to answer

because it requires to evaluate whether or not the skilled person would have considered extending to other plant-like metabolic pathways the specific teaching in WO 92/00374 (concerning de novo folate synthesis as a target for treatment) as well as adapting said teaching for the production of a composition for medical use. The case is, thus, such as contemplated in the decision G 1/89 (see supra). It would be unfair to the applicant to decide against him on inventive step without hearing him on the matter. Hearing him could only have been done if the ISA had come to the same conclusion as the Board with respect to novelty and had expressed a negative view on inventive step. Consequently, it is not possible at that stage to decide that the application does not fulfil the requirement of unity of invention.

9. The request to pay 8 further search fees is not justified and these fees are to be reimbursed.

Order

For these reasons it is decided that:

Eight additional search fees shall be reimbursed.

The Registrar: The Chairwoman:

U. Bultmann U. Kinkeldey