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Datasheet for the decision of 8 February 2016

Case Number: T 1403/14 - 3.3.04

Application Number: 07827554.2

Publication Number: 2073839

IPC: A61K39/12

Language of the proceedings: EN

Title of invention:
A vaccine for Chikungunya virus infection

Applicant:
Bharat Biotech International Limited

Headword:
Chikungunya virus vaccine/BHARAT BIOTECH

Relevant legal provisions:
EPC Art. 56, 111(1)

Keyword:
Appeal decision -
remittal to the department of first instance (yes)

Decisions cited:
G 0010/93

Catchword:
-

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Case Number: T 1403/14 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 February 2016

Appellant: (Applicant)	Bharat Biotech International Limited Genome Valley Turkapally Shameerpet Hyderabad 500 078 (IN)
Representative:	Kütterer, Sandra Dr. Meyer- Dulheuer & Partners LLP Franklinstrasse 46-48 60486 Frankfurt am Main (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 6 February 2014 refusing European patent application No. 07827554.2 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	L. Bühler

Summary of Facts and Submissions

I. The applicant ("appellant") has lodged an appeal against the decision of the examining division refusing European patent application No. 07827554.2, which was published as international patent application WO 2008/026225 and has the title "*A vaccine for Chikungunya virus infection*".

II. In the annex to the summons to oral proceedings the examining division took position with regard to the claim request (claims 1 to 17) filed with a letter dated 13 April 2013 then pending before them. Claim 1 of this request read:

"1. A vaccine formulation for the prophylaxis and treatment of Chikungunya virus infection in mammals wherein the Chikungunya virus antigen is an isolate of the genotype CHK/03/06, whose structural polyprotein sequence is as given in SEQ ID 4 and is applicable to any genotype or genetic variants of the Chikungunya virus."

The examining division observed that the problem to be solved by the claimed subject-matter was the provision of a vaccine formulation based on the Indian Ocean outbreak isolate CHK/03/06. However, the claimed solution was "*obvious in light of D2 when combined with D8. D8 teaches that the identification an Indian Ocean outbreak Chikungunya virus isolates and the structural characterization thereof. The molecular data about these isolates are regarded as valuable tools to combat Chikungunya virus infections (see page 1068). Furthermore, the passages in the right-hand column on page 1067 of D8 clearly teach the advantages of virus isolates obtained from infected patients and of*

lowering the number of in-vitro passages of virus isolates." and concluded that the subject-matter of the claims of the main request lacked an inventive step.

III. During the oral proceedings before the examining division, on 12 December 2013, the applicant filed a new main request (claims 1 to 9) and argued that beta-propiolactone (BPL) inactivation of Chikungunya virus as compared to formalin was faster and thus less damaging for the structure of the virus. When requested to indicate in the application as filed where this alleged advantage was shown, the applicant referred to example 14 of the application as filed (see minutes of the oral proceedings points 11, 13 and 17).

IV. In the impugned decision the examining division held that the subject-matter of claims 1 to 8 of the main request lacked an inventive step (Article 56 EPC), *inter alia* because experimental data demonstrating the alleged advantages were lacking. Moreover, the examining division decided that the main request lacked unity of invention (Article 82 EPC) in respect of the subject-matter of claims 1 to 8 on the one hand and of claim 9 on the other hand. An auxiliary request 1, also filed during the oral proceedings, was not admitted into the proceedings pursuant to Rule 137(3) EPC.

V. With the statement of grounds of appeal, the appellant submitted a new main request, *i.e.* consisting of claims 1 to 8 which are identical to the same claims of the main request considered by the examining division in the decision under appeal, a new document called "Additional Technical Information" and arguments in favour of inventive step of the claimed subject-matter by reference to this technical information and to a post-published document (Kumar et al. (2012), Vaccine,

Vol. 30, No. 43, pages 6142-6149; hereinafter "Kumar *et al*.").

Independent claims 1, 4 and 8 of the main request read:

"1. A vaccine for the prophylaxis and treatment of Chikungunya virus infection in mammals comprising a purified and inactivated Chikungunya virus wherein the purified Chikungunya virus is inactivated by beta-propiolactone (BPL) either before or after purification of the virus, wherein BPL is used at a concentration ranging from 0.001 % to 0.4 %(v/v), preferably from 0.01 % to 0.1 %(v/v).

4. A pharmaceutical composition comprising a purified and inactivated Chikungunya virus as defined in any of claims 1 - 3 in an effective amount for use as a vaccine in a pharmacologically acceptable carrier with or without an adjuvant and a stabilizing agent.

8. A method of preparing a vaccine formulation for the prophylaxis and treatment of Chikungunya virus infection in mammals comprising a purified Chikungunya virus which is inactivated by beta-propiolactone (BPL) either before or after purification of the virus, wherein BPL is used at a concentration ranging from 0.001 % to 0.4 % (v/v), preferably from 0.01 % to 0.1 % (v/v)."

VI. The board issued a communication pursuant to Article 17(2) RPBA and Rule 100(2) EPC and expressed its preliminary opinion that the objection as to lack of unity (Article 82 EPC) appeared no longer to apply to the claims of the new main request. The board was further of the preliminary opinion that the newly filed document "Additional Technical Information" and the

reference by the appellant to the publication of Kumar *et al.* (*supra*), a document which the board introduced into the proceedings by annexing a copy of the document to the communication, constituted a serious attempt to prove that the problem underlying the claimed invention was to obtain an improvement over the closest prior art rather than an alternative. The board therefore expressed the opinion that in the light of the new evidence the reasons for the refusal under Article 56 EPC appeared no longer valid and that at the same time the case before the board had substantially changed as compared to the case as it stood before the examining division. The board accordingly informed the appellant that it intended to remit the case to the examining division for further prosecution. The appellant was therefore requested to indicate whether it agreed with remittal as indicated by the board.

VII. Subsequently, the appellant informed the board that it agreed "*with the intention of the board to remit the case to the Examining Division pursuant to Article 111(1) EPC for further prosecution, since the factual framework regarding the contested decision has changed due to the newly filed additional technical information.*"

VIII. The appellant's arguments can be summarised as follows:

Unity of invention (Article 82 EPC)

In the new main request former claim 9 had been deleted. The objection as to lack of unity of invention (Article 82 EPC) therefore did no longer apply.

Inventive step (Article 56 EPC)

The document "Additional Technical Information", which comprised additional experimental data on immunogenicity testing, serum micro neutralization tests, ELISA measurements and hemagglutination-inhibition tests, showed positive effects of the BPL inactivation for the Chikungunya virus. This newly submitted technical information supported the appellant's argument submitted before the examining division that inactivation of Chikungunya virus by BPL had several advantages in comparison to inactivation using formalin.

BPL was a better inactivating agent for Chikungunya virus than formalin, non-ionic detergents, ascorbate, hydrogen peroxide and glutaraldehyde under the conditions studied. *In vitro* and *in vivo* studies showed that BPL inactivated the virus completely at the tested concentrations and produced a high titer of neutralizing antibodies in vaccinated animals at the various doses studied. Comparative studies of serum neutralisation tests of BPL inactivated vaccine and formalin inactivated vaccine showed that the BPL-inactivated Chikungunya virus vaccine elicited a far higher antibody titer after administration of the second dose than formalin-inactivated vaccine. This was in line with recent publications which showed that BPL-inactivated virus induced a four-fold higher neutralizing antibody titer over formalin inactivated virus (see Kumar *et al.*).

The positive effects of BPL inactivation were neither known nor expected to the skilled person. Therefore, the use of BPL for inactivation of Chikungunya virus

was not obvious and the subject-matter of the claims of the main request involved an inventive step.

Reasons for the Decision

1. The appeal is admissible.

Unity of invention (Article 82 EPC)

2. In the decision under appeal, the examining division considered that, *a priori*, the subject-matter of claim 9 of the main request pending before them (see section III above) was not linked with the subject-matter of claims 1 to 8 of the same request by a common inventive concept as required by Article 82 EPC and Rule 44 EPC.

3. The new main request no longer comprises former claim 9 and the examining division, in the impugned decision, did not object to the unity of invention in relation to the subject-matter of claims 1 to 8 as such.

4. The board is therefore satisfied that the requirements of Article 82 EPC are fulfilled.

Inventive step (Article 56 EPC)

5. In the decision under appeal the examining division held *inter alia* that that the application lacked experimental data which supported the appellant's arguments alleging that the inactivation of Chikungunya virus by beta-propiolactone (BPL) provided advantages over inactivation by other means, in particular formalin. Therefore the problem to be solved was to be formulated as the provision of an alternative Chikungunya virus formulation. The examining division

further held that it was also not derivable from the application that the claimed virus formulation which was obtained by BPL-inactivation was associated with a previously unknown or unexpected effect. Accordingly, the examining division held that the use of BPL was an arbitrary and random choice from the possibilities known to the skilled person for obtaining inactivated virus formulations. The subject-matter of claims 1 to 8 therefore lacked an inventive step.

6. It can be taken from the history of the file that the claims of the main request as subject of the decision under appeal (see section V) and the claims of the previous main request (see section II) which was pending before the examining division at the time when it formulated the annex to the summons of oral proceedings, differed substantially.

7. It is furthermore apparent from a comparison of the arguments against inventive step as formulated by the examining division in the annex to the summons to oral proceedings (see section II) and those formulated in the decision under appeal (see point 5 above), that the examining division considerably changed the substantiation of its finding of lack of inventive step. The latter was based mainly on the fact that no evidence was available evidencing advantageous or unexpected effects. This reason had also been conveyed to the applicant during the oral proceedings (see section III above).

8. With the statement of grounds of appeal the appellant has filed new evidence in the form of the newly filed document "Additional Technical Information" and has referred to a post-published document Kumar *et al.*, which the board has introduced into the proceedings

(see section VI above). It was submitted that the document disclosed comparative test results of immunogenicity tests, serum micro neutralisation tests for the estimation of neutralising antibody titers, indirect ELISA measurements for estimating the antibody titer as well as hemagglutination-inhibition tests of Chikungunya virus vaccines resulting from of BPL and formalin inactivation. Furthermore, Kumar *et al. (supra)* had the title "Evaluation of recombinant E2 protein-based and whole-virus inactivated candidate vaccines against Chikungunya virus" and disclosed likewise comparative data of Chikungunya virus vaccines either inactivated by BPL or formalin.

9. The board is satisfied that the submission of the document "Additional Technical Information" and the reference by the appellant to the publication of Kumar et al. (*supra*), overcome the reason for refusing the application in relation to the requirement of inventive step, a reason which the appellant had only been confronted with at the oral proceedings, namely that data were lacking in the application for the appellant's contention that the problem underlying the claimed invention was to obtain an improvement over the closest prior art rather than an alternative. This means by the same token that the case to be considered by the board has substantially changed as compared to the case as it stood before the examining division.

10. Since proceedings before the boards of appeal in *ex parte* cases are primarily concerned with reviewing the contested decision, the board, taking into account that in the present case there has been a significant change in the factual framework with respect to the contested decision, has decided, in accordance with the request of the appellant, to remit the case to the examining

division pursuant to Article 111(1) EPC for further prosecution (see decision G 10/93, OJ EPO 1995, 172, point 5 of the Reasons).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution on the basis of claims 1 to 8 of the main request filed with the statement of grounds of appeal dated 10 June 2014.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated