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Datasheet for the decision of 17 March 2017

Case Number: T 2369/12 - 3.3.04

Application Number: 07797730.4

Publication Number: 2029166

IPC: A61K39/02

Language of the proceedings: EN

Title of invention:
Vaccination of Young Animals against Lawsonia Intracellularis Infections

Applicant:
Boehringer Ingelheim Vetmedica, Inc.

Headword:
Lawsonia intracellularis vaccination of young pigs/BOEHRINGER INGELHEIM

Relevant legal provisions:
EPC Art. 83
RPBA Art. 12(4), 13(1)

Keyword:
Sufficiency of disclosure - (no)

Decisions cited:

Catchword:

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Case Number: T 2369/12 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 17 March 2017

Appellant: (Applicant)	Boehringer Ingelheim Vetmedica, Inc. 2621 North Belt Highway St. Joseph MO 64506-2002 (US)
Representative:	Simon, Elke Anna Maria Boehringer Ingelheim GmbH Binger Strasse 173 55216 Ingelheim am Rhein (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 4 June 2012 refusing European patent application No. 07797730.4 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	A. Chakravarty
	P. de Heij

Summary of Facts and Submissions

I. Appeal was filed by the applicant against the decision of the examining division to refuse European patent application EP 07797730, with the title "*Vaccination of Young Animals against Lawsonia Intracellularis Infections*".

II. The examining division considered a main and four auxiliary requests. It used its discretion according to Rule 137(3) EPC not to admit the main and auxiliary requests 1 and 2 into the proceedings. The subject-matter of claims 1 and 8 of auxiliary request 3 was held to lack novelty, while that of claims 1 to 14 of auxiliary request 4 was found to be obvious (Article 56 EPC). In addition claims 1 and 8 of auxiliary request 4 were held to relate to an invention that was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC).

III. With the statement of grounds of appeal the appellant filed a main request and two auxiliary requests and submitted a document (Exhibit A) with the title "*Efficacy of Enterisol® Ileitis administered to Lawsonia-positive pigs 1 to 6 days of age*".

IV. The board issued a communication pursuant to Article 15(1) RPBA, setting out its preliminary appreciation of substantive and legal matters concerning the appeal.

V. The appellant responded to the board's communication by letter and by the filing of a new main and auxiliary requests I to IV, replacing all previous requests.

VI. Claim 1 of the main request reads:

"1. The use of an *L. intracellularis* antigen for the preparation of a medicament for the vaccination of a mammal having maternally derived *anti-L. intracellularis* antibodies, wherein said mammal is to be vaccinated with an effective dose of said attenuated *L. intracellularis* bacteria at day 1 to 9 of age by oral drench".

Claim 1 of auxiliary request I reads:

"1. The use of attenuated *L. intracellularis* bacteria for the preparation of a medicament for the vaccination of a mammal against *L. intracellularis* infections having maternally derived *anti-L. intracellularis* antibodies, wherein said mammal is to be vaccinated with an effective dose of said attenuated *L. intracellularis* bacteria at day 1 to 9 of age by oral drench, and, wherein said mammal is a pig".

VII. Oral proceedings before the board were held on 17 March 2017. At the end of these proceedings the Chairwoman announced the decision of the board.

VIII. The appellant's arguments relevant to the decision can be summarised as follows:

Main request

Admission into the proceedings - Articles 12(4) and 13(1) RPBA

The main request and auxiliary requests I to IV were filed to expedite the prosecution of the case. The amendments made to the claims of the main request and

auxiliary requests I to IV aimed to address the issues raised by the board in the communication according to Article 15(1) RPBA and should therefore be admitted into the proceedings.

Auxiliary request I - Claim 1

Disclosure of the invention - Article 83 EPC

The claimed subject-matter was the use of attenuated *L. intracellularis* bacteria for the preparation of a medicament for the vaccination of 1 to 9 day old pigs having maternally derived *anti-L. intracellularis* antibodies against *L. intracellularis* infections. The medicament was to be administered by oral drench.

The invention was disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. Example 1 demonstrated, *in vitro*, that colostrum and milk from sows and gilts contained antibodies specific for *L. intracellularis*. Example 2 showed that *L. intracellularis* specific antibodies were not effective in inactivating *L. intracellularis* during gastrointestinal passage. This taught the skilled person that a live *L. intracellularis* vaccine would not be negatively affected by the maternal immunity status of the pig.

The question of whether or not pigs as young as 1 to 9 days old could mount an effective immune response after vaccination with attenuated *L. intracellularis* bacteria was answered by Example 3, which demonstrated that the *L. intracellularis* vaccine was efficacious when administered to 1 day old, maternal antibody negative piglets.

It was established case law of the Boards of Appeal that the requirements for sufficient disclosure of the invention were met when at least the suitability of the product for the claimed treatment (claimed therapeutic application) was disclosed in the application. In contrast, it was not necessary for the results of clinical trials to be provided. Rather, it was sufficient that the patent application provided information making it plausible that the claimed compound had a direct effect or activity. Furthermore, once said suitability was available, then post-published evidence must be taken into account.

From Examples 2 and 3 the skilled person could conclude that it was plausible that the *L. intracellularis* vaccine would be efficacious when administered to young piglets that were anti-*L. intracellularis* antibody positive.

This conclusion was further supported by the data of Example 4 which demonstrated that vaccination with the *L. intracellularis* vaccine in the face of maternal immunity in pigs at 3 weeks of age was effective. Thus, Example 4 confirmed that there was no interference between the anti-*L. intracellularis* antibodies and the *L. intracellularis* vaccine.

In addition to the positive evidence in the application, there was no evidence on file that there were serious doubts substantiated by verifiable facts that the application lacked sufficient disclosure. Indeed, the post-published data contained in "Exhibit A", filed with the statement of grounds of appeal, showed that the vaccine as claimed, provided protection when administered to piglets (at 1 week of age) in the

face of maternal immunity (i.e. in a piglet having anti-*L. intracellularis* antibodies).

The study showed that vaccinated piglets from sows with anti-*Lawsonia* antibodies (group 1) had improved overall lesion scores when compared to a challenge control (group 5) and had improved clinical symptoms compared to several groups.

Thus, in view of the experimental data provided by the patent application and by Exhibit A, it was plausible that vaccination with the *L. intracellularis* vaccine in the face of maternal immunity in young pigs would be effective.

IX. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or on one of the auxiliary requests.

Reasons for the Decision

Admission into the proceedings - Articles 12(4) and 13(1) RPBA

Main request

1. By virtue of Article 12(4) RPBA, the board has the discretionary power to hold inadmissible facts, evidence or requests which were filed with the statement of grounds of appeal if they "*could have been presented [...] in the first instance proceedings*".

1.1 The main request was filed as auxiliary request I with the statement of grounds of appeal. Claim 1 relates to the use of an *L. intracellularis* antigen to treat a mammal having maternally derived *anti-L. intra-*

cellularis antibodies wherein the mammal to be treated is 1 to 9 days old. None of the requests considered by the examining division related to this combination of features. The board therefore has to either give a first ruling on this issue or to remit the case to the examining division (cf. Case Law of the Boards of Appeal of the EPO, 8th edition 2016, IV.E.4.3).

1.2 The board exercises its power under Article 12(4) RPBA and does not admit the main request into the appeal proceedings.

Auxiliary requests I to IV

2. The board admitted auxiliary requests I to IV into the proceedings (Article 13(1) RPBA).

Auxiliary request I - Claim 1

Disclosure of the invention - Article 83 EPC

3. Article 83 EPC requires that the European patent application discloses the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. In the case of a therapeutic use, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application (see Case Law of the Boards of Appeal of the European Patent Office, 8th edition, II.C.6.2).

4. For the therapeutic use of claim 1, the application must disclose the suitability of the attenuated *L. intracellularis* bacteria for the vaccination (i.e. for inducing immunity) of 1 to 9 day old pigs against

L. intracellularis infections, when administered by oral drench.

5. The appellant argued that the application disclosed the suitability of attenuated *L. intracellularis* bacteria for the vaccination of 1 to 9 day old pigs against *L. intracellularis* infections. In particular, Examples 2 and 3, taken alone, demonstrated the suitability of attenuated *L. intracellularis* bacteria for the vaccination of 1 to 9 day old pigs against *L. intracellularis* infections.

6. The board does not consider these arguments as persuasive in the face of the evidence of Exhibit A, submitted by the appellant with the statement of grounds of appeal (see points 7 to 8.5, below). The results contained in the application were either from *in vitro* or tissue culture assays (Examples 1 and 2) or, if they were generated through animal studies, relate to maternal antibody-negative piglets or piglets of 3 weeks of age (Examples 3 and 4, respectively). On the other hand, the evidence in Exhibit A derives from a clinical study representing an embodiment of the claimed subject-matter, i.e. it provides direct evidence of the suitability of attenuated *L. intracellularis* for the purpose claimed and is therefore given more weight than the results contained in the application.

7. The Exhibit provides the results of a study "*conducted to evaluate Enterisol® Ileitis vaccine efficacy in suckling piglets derived from Lawsonia intracellularis exposed (group A) and negative sows (group B) and to determine if there was any maternal interference with vaccine efficacy against a virulent, pure culture L. intracellularis challenge*" (see Exhibit A, page 1).

8. Piglets in groups A and B were further divided into subgroups 1 to 6 (see Tables 1 and 2 of the Exhibit). Piglets in subgroups 1 and 4 were vaccinated with a single dose of attenuated modified live *L. intracellularis* (*Enterisol® Ileitis*) at 1 week of age. Piglets in groups 2, 3, 5 and 6 received a placebo. At 6 to 7 weeks of age, piglet groups 1, 2, 4 and 5 received a virulent, pure culture of *L. intracellularis* challenge, while groups 3 and 6 did not.

8.1 All piglet groups were humanely euthanised and evaluated for macroscopic (gross) and *Lawsonia*-specific microscopic lesion development at 3 weeks post challenge administration (9 to 10 weeks of age; *supra*).

8.2 Table 2 provides a summary of average gross lesion scores for the small and large intestines, with group 1 being the trial group (piglets from *L. intracellularis* exposed sows, vaccinated) and group 2 being the control group (piglets from *L. intracellularis* exposed sows, unvaccinated). It can be seen from the table that the trial group has significantly larger intestinal lesions than the control group.

8.3 Table 3 provides a summary of average microscopic lesion scores for the small, large and whole intestines, with group 1 being the trial (vaccinated) group and group 2 being the control (unvaccinated) group. Here too, the trial group has significantly larger intestinal lesions than the control group.

8.4 The appellant argued that, although Tables 2 and 3 of the study report showed that group 1 piglets (from *Lawsonia* positive sows, vaccinated and challenged) had greater gross average lesion scores than the

unvaccinated challenge control (group 2), the data in Table 4 confirmed that the same group, had better daily clinical scores than the unvaccinated control group.

8.5 Table 4 does indeed show that group 1 piglets had fewer clinical symptoms of infection than those in the challenge control (group 2). However, given the significance of intestinal lesions as a symptom of infection and of the fact that two out of three measures of infection were significantly worsened in piglets from sows exposed to *L. intracellularis* bacteria in comparison to the non-vaccinated piglets from the same sows, the board must conclude that Exhibit A as a whole raises serious doubts as to the suitability of attenuated *L. intracellularis* bacteria for the vaccination of 1 to 9 day old pigs against *L. intracellularis* infections when administered by oral drench, which cannot be overcome by the results in the application, given their indirect nature (see point 6 above).

9. In view of the above, the board holds that the application does not disclose the invention of claim 1 in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Auxiliary requests II to IV

10. Claim 1 of all of these requests relates, at least in an embodiment, to the same subject-matter as claim 1 of auxiliary request I. Thus, the conclusion reached for claim 1 of auxiliary request I on the disclosure of the invention applies equally.

11. In view of the above considerations, none of the pending claim requests relates to an invention for which the application meets the requirements Article 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated