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D E C I S I O N
of 30 March 1999

Case Number: T 0977/93 - 3.3.4

Application Number: 84902632.3

Publication Number: 0145783

IPC: A61K 39/12

Language of the proceedings: EN

Title of invention:
Canine coronavirus vaccine

Patentee:
American Home Products Corporation

Opponent:
Rhone Merieux

Headword:
Canine coronavirus vaccine/AMERICAN HOME PRODUCTS CO.

Relevant legal provisions:
EPC Art. 123(2), (3), 54, 56

Keyword:
"Availability of the intrinsic and extrinsic features of a vaccine (no)"
"Inventive step (yes)"

Decisions cited:
G 0001/92, G 0002/88

Headnote:
A product made available to the public is not reproducible

within the meaning of decision G 0001/92 (point 4.1) and thus does not belong to the state of the art if the skilled person is not in a position to establish identity of the reproduced product with the commercially available product because the intrinsic and extrinsic features of the product are not accessible and there is a high probability of variation upon reproduction. (See points 11.1 to 11.3 and 12 of the "Reasons")

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Case Number: T 0977/93 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 30 March 1999

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 14 September 1993 revoking European patent No. 0 145 783 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: R. E. Gramaglia
C. Holtz

Summary of Facts and Submissions

I. European patent No. 0 145 783 (application No. 84 902 632.3) was granted on the basis of 28 claims. The patent relates to an inactivated canine coronavirus vaccine.

II. Notices of opposition were filed by two opponents (opponent I and opponent II). Revocation of the patent in its entirety was requested on the grounds of lack of novelty and inventive step (Articles 54, 56 and 100(a) EPC). In particular opponent II argued that two vaccines (Duramune C® and Coronavac®) falling within the ambit of claim 1 of the patent in suit had been made available to the public before the earliest priority date of the patent by way of either an offer for sale or sale.

III. The Opposition Division revoked the patent. The decision was based on the claims as granted. Claim 1 as granted for all the contracting states except AT read as follows:

"1. A vaccine composition comprising the avirulent antigenic product produced by either
(a) attenuating live canine coronavirus by passages through cells of feline origin such that when administered to a dog by injection the attenuated live virus selectively infects the intestinal epithelium, or
(b) inactivating feline or canine cell propagated canine coronavirus,
the avirulent antigenic product being present in an amount effective to protect a dog from infection by virulent canine coronavirus;

and a non-toxic pharmaceutically acceptable carrier."

Dependent claims 2 to 10 were directed to specific embodiments of the vaccine of claim 1. Claims 11 to 28 related to processes for making canine coronavirus vaccines (claims 11 to 16), for propagating the canine coronavirus (claims 17 to 24) and for evaluating the effectiveness of the vaccine (claims 25 to 28). Claims 1 to 28 for AT were formulated as corresponding process or method claims.

IV. The Opposition Division considered that Coronavac® fell within the scope of claim 1 and had been made publicly available because the purchaser of this vaccine, Mr Fazzi, was in a position to elucidate the intrinsic and extrinsic features of this vaccine and to reproduce it. Therefore the subject-matter of claim 1 of the patent was anticipated by the offer for sale of Coronavac®.

V. In view of the negative finding on the issue of novelty, the Opposition Division did not evaluate the other ground for opposition, namely the lack of inventive step (Article 56 EPC).

VI. The appellant (patentee) lodged an appeal against this decision, paid the fee and filed a statement of Grounds of Appeal. The respondents (opponents) filed counter-arguments.

VII. In a letter dated 10 March 1998, Opponent I withdrew the opposition.

VIII. With the submission of 3 November 1998, the Appellant filed a new main request, auxiliary request 1 and

auxiliary request 2.

IX. Oral proceedings were held on 30 March 1999, during which the Appellant filed a sole main request replacing any preceding requests.

Claim 1 of the main request for all the contracting states except AT reads as follows (the addition vis-à-vis the granted claim 1 is shown in bold):

"1. A vaccine composition comprising the avirulent antigenic product produced by either
(a) attenuating live canine coronavirus by **at least eight passages at a low virus to cell ratio of about 1:1000 to 1:10000, as measured by the $TCID_{50}$ method**, through cells of feline origin such that when administered to a dog by injection the attenuated live virus selectively infects the intestinal epithelium, or
(b) inactivating feline or canine cell propagated canine coronavirus,
the avirulent antigenic product being present in an amount effective to protect a dog **by parenteral administration** from infection by virulent canine coronavirus;
and a non-toxic pharmaceutically acceptable carrier."

Claims 2 to 28 were identical to claims 2 to 28 as granted, except for the introduction into claim 11 of a reference to claim 1 and of the wording "an inactivated" between the words: "A process of making" and "canine coronavirus" and of a reference to claim 1(a) in claim 17.

X. The following documents are cited in the present

decision:

(3) US-A-3,704,203

(7) Horzinek M. C. et al., Infection and Immunity, Vol. 37, No. 3, pages 1148-1155 (1982)

(8) Woods R. D., Veterinary Microbiology, Vol. 7, pages 427-435 (1982)

(10) Appel M. et al., Canine Practice-Medicine, Vol. 7, pages 25-29 and 32-35 (1980)

(15) Pollock R. et al., Veterinary Clinics of North America: Small Animal Practice, Vol. 13, No. 3, pages 551-566 (August 1983).

(21) Vaccines Inc., Outline of production, Canine corona virus vaccine, Modified live virus, Cell line origin US. Veterinary licence No. 227 (22 July 1981)

(25) Declaration of Dr R. Wichmann before the US District Court of California dated 24 April 1991

(26) Declaration of Dr C. J. York before the US District Court of California dated 19 April 1991

(27) Deposition of Dr C. J. York before the US District Court of California dated 6 February 1991

(46) Schultz R. H. et al., Can. Vet. J., Vol. 31, pages 617-620 (1990)

(47) Declaration of Dr Acree before the USPTO dated 20 September 1984

(49) Letter from Prof. L. Carmichael to Dr G. Chappuis dated 27 May 1994

(62) Proceedings of the "Canine Virus Disease Seminar" held by Fort Dodge Laboratories on 7 April 1983

(63) Horst Glathe, Virusimpfstoffe, Akademie Verlag GmbH, Berlin, pages 32, 41 and 65 (1991)

(64) Declaration of Prof. L. Carmichael dated 28 October 1998

(66) Encyclopaedia of Virology, Vol. 1, Academic Press, pages 255-260 (1994)

XI. In support of this request, the appellant submitted in writing and at the oral proceedings the following arguments:

Novelty

- Duramune C® was covered by confidentiality agreements between the patentee and Vaccine Inc. and thus it could not have been publicly available.

- The claimed CCV vaccine was characterised by the following three features:

  (1) the vaccine contained CCV attenuated by at least eight passages through feline cells at

a low virus to cell ratio of about 1:1000 to 1:10000, as measured by the $TCID_{50}$ method;

(2) upon parenteral injection, the attenuated virus selectively infected the intestinal epithelium and

(3) the vaccine protected dogs from infection by CCV.

- No evidence had been provided by the respondents that the composition Coronavac® fell within the scope of claim 1 of the patent in suit. It had not been demonstrated that Coronavac® possessed the three features (1), (2) and (3) above.

- The prior use of an attenuated CCV vaccine according to claim 1 of the patent in suit had not been proved.

- Even by assuming that the skilled person actually had Coronavac® and Duramune C® in his/her hands before the priority date of the patent in suit, this would not have been tantamount to having had access to the intrinsic and extrinsic features thereof. The three features (1), (2) and (3) above could not have been derived. In order for these features to have been publicly available, the skilled person had to be in a position to analyse the product and to reproduce it without undue burden (decision G 1/92, OJ EPO 1993, 277). However, it was not possible to establish how the virus had been attenuated and how many passages it had undergone (feature (1)). Features (2) and (3)

were also concealed from the skilled person because the immune response to CCV was poorly understood and no challenge model existed. Further, it was not possible to reproduce the virus because no "master seed virus" ("working stock") was available. Reproduction of an attenuated CCV vaccine by further propagation of Coronavac® was impossible because only limited passages could be made to prevent undesirable mutations (documents (63) and (66)).

Inventive step

- The closest prior art was represented by document (10). It was stated in this document that a vaccine for protection against CCV was not available and that parenteral inoculation of attenuated CCV provided only limited protection. Later document (15) confirmed this. The problem solved by the patent in suit was to provide the means for arriving at a CCV vaccine.

- Document (62) merely reported that a CCV vaccine administered parenterally elicited 95% intestinal protection. It did not specify whether the vaccine was a live attenuated vaccine or inactivated one. Further, "intestinal protection" did not imply the feature "selectively infects the intestinal epithelium".

- Neither the availability to the public before the priority date of the patent in suit of Duramune C® and Coronavac®, nor document (62) or (10) or the combination thereof provided any guideline for

arriving at the claimed vaccine.

- The attenuated transmissible gastroenteritis virus (TGEV) of document (3) was not akin to dogs' coronaviridae but was only serologically cross-reactive with CCV and did not protect dogs from CCV (document (10), page 28, r-h column). Documents (3), (7) and (8) did not teach the features recited in claim 1.

- The scientific community did not expect an inactivated CCV vaccine to confer protection, let alone if parenterally administered, because there was the conviction that only attenuated live CCV vaccine administered orally could have elicited a sufficient immunological response.

- The influence of the inactivation procedure on the epitopes required for conferring protection was unpredictable.

XII. The respondents essentially submitted the following arguments in writing and at the oral proceedings:

Novelty

- Two vaccines (Duramune C® and Coronavac®) falling within the ambit of claim 1 of the patent in suit had been made available to the public before the earliest priority date of the patent by way of an offer for sale or actual sale. Coronavac® was made from the CCV strain CCV(K-378)-51 attenuated through feline cells (see documents (25), (26) (27) and (49)). Duramune C® was made from the CCV

strain TN-449 attenuated through 12 passages in feline cells (see document (21)).

- The prior use of these vaccines satisfied the requirements of decision G 1/92 (supra) of analysability and reproducibility. A prior use of a product encompassed all written and oral information which unambiguously accompanied this use. The skilled person was aware that these vaccines were made from attenuated CCV and that they had to be injected parenterally. By following these instructions all the extrinsic and intrinsic features had necessarily to be present ("doctrine of inherency"). Further, since Coronavac® and Duramune C® were protective and since protection was linked to infection of the intestinal epithelium, Coronavac® and Duramune C® implicitly had to exhibit features (2) and (3), also inherent to all CCV strains (see document (47), points 6 and 9).

- Feature (2) had also been disclosed by Dr Acree at the "Canine Virus Disease Seminar" held on 7 April 1983 (see document (62)), ie before the earliest priority date of the patent in suit.

- The very act constituting the novelty-destroying event was the prior use itself, not the fact of analysing the product.

- As to the reproducibility, it was current practice in the USA for small firms to make vaccines from commercially available vaccine vials. It was therefore possible to reproduce the claimed

vaccine by departing from a single vial of eg Coronavac® used as a master seed stock and subjecting it to a limited series of passages in canine cells.

Inventive step

- The closest prior art was represented by document (62) and by Coronavac® and Duramune C® available on the market. On the one hand, pages 9 and 10 of document (62) informed the public that live attenuated CCV conferred protection on the intestinal tract upon parenteral injection. On the other hand, two vaccines based on attenuated CCV for parenteral administration were already on the market. It was therefore obvious to attenuate CCV and to check whether it infected the intestinal tract as shown in document (62) and to arrive with a high probability of success at the claimed vaccine.

- Document (3) disclosed the manufacture of an attenuated TGEV live vaccine which conferred protection upon parenteral administration. TGEV was immunologically very similar to CCV (see documents (7) and (8)). Therefore, there was a very high probability of success that attenuating CCV would have led to the claimed vaccine.

- As to the vaccine comprising inactivated CCV, document (3) showed that a TGEV inactivated vaccine also conferred protection upon parenteral administration. This showed that the inactivation process preserved the epitopes rather than

destroyed them.

XIII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request as filed in the oral proceedings.

The respondent (opponent II) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible

Article 123(2) and (3) EPC

2. The passage in claim 1 "at least eight passages at a low virus to cell ratio of about 1:1000 to 1:10000, as measured by the $TCID_{50}$ method" finds a basis on page 7, lines 10 to 15, of the application as filed. The wording in claim 1 "by parenteral administration" finds a basis on page 5, line 19, of the application as filed. These added features are restrictive in nature. The amendments in claims 11 and 17 (see section IX above) merely make it clear that the canine coronavirus vaccine has to be inactivated (see claim 1b) and that the claimed method relates to a vaccine according to claim 1a respectively. Consequently, the requirements of Article 123(2) and (3) are fulfilled.

Prior use

3. According to decision G 1/92, point 1.4 (supra), an essential purpose of a technical teaching is to enable the person skilled in the art to manufacture or use a given product by applying such teaching. Where such teaching results from a product put on the market, the person skilled in the art will have to rely on his general technical knowledge to gather all the information enabling him to prepare the said product. Where it is possible for the skilled person to discover the composition or the internal structure of the product and to reproduce it, then both the product and its composition or internal structure become part of the state of the art. The rationale emerging from this decision is that the properties of a product are considered **not** to have been made available to the public within the meaning of Article 54(2) EPC if the skilled person had no means of establishing the composition or the internal structure of the product and was not able to reproduce it, in spite of the product's being in the public's hands before the priority date of the patent.

4. The respondents have provided a great many documents to substantiate the prior use of the invention by the public availability of Duramune C® and Coronavac®. The board will deal first with the question of whether or not the prior use argued by the respondents satisfies the requirements of analysability and reproducibility prescribed by decision G 1/92 (supra). If it transpires that the prior use does not satisfy these requirements, then the task of establishing whether Duramune C® and Coronavac® were actually in the hands of a member of the

public before the priority date of the patent in suit and fell within the scope of claim 1 at issue, becomes superfluous.

5. It should be established whether or not the skilled person having Coronavac® or Duramune C® in his/her hands could have derived therefrom any of the three features (1) to (3) indicated in claim 1 at issue (see paragraph IX supra), namely that:

(1) the vaccine contained CCV attenuated by at least eight passages through feline cells at a low virus to cell ratio of about 1:1000 to 1:10000, as measured by the $TCID_{50}$ method (claim 1a), that

(2) the attenuated virus when administered to a dog by injection selectively infected the intestinal epithelium (claim 1a), and that

(3) upon parenteral administration, the avirulent antigenic product protected dogs from infection by virulent CCV (claim 1a and 1b).

6. As regards feature (1), it is common general knowledge that attenuation of a virus is performed in living material (eg animal cells) in order to induce specific genetic changes (mutations, deletions, etc.) reducing virulence of the virus while maintaining its immunogenicity. By each additional passage through the host cell, further genetic modifications occur influencing immunogenicity and/or infectivity of the virus. These changes depend upon the host cell in which attenuation is performed and on the conditions (inter alia the number of passages and the virus/cell ratio)

applied. As to the possibility by a skilled person in possession of Coronavac® or Duramune C® before the priority date of the patent in suit to determine the conditions and the host cell in which the virus was attenuated, the board is convinced by the statement in paragraph 6 of document (64) that achieving this task was impossible. One major obstacle was obviously represented by the impossibility of correlating the genetic modifications to the number of passages, to the nature of the host cell or to the virus/cell ratio.

7. As for feature (2), namely the selective infection of the dog's intestinal epithelium upon parenteral administration of the claimed attenuated vaccine, the board agrees with the respondents that this feature is inherent (cf "the doctrine of inherency") in the interaction of the attenuated live CCV vaccine with the dog. Yet, this does not mean that the board is exempted from evaluating whether this feature was a "hidden" one or was accessible to the skilled person before the priority date of the patent in suit. This follows from the rationale emerging from decision G 2/88, OJ EPO 1990, 93, see point 10.1), which states: "Under Article 54(2) EPC the question to be decided is what has been "made available" to the public: the question is not what may have been "inherent" in what was made available (by a prior written description, or in what has previously been used (prior use), for example)".

8. The board notes that a prerequisite for feature (2) to have become accessible to the skilled person is that the exact mechanism through which Coronavac® or Duramune C® conferred protection on dogs had to be known to him/her. However, before the priority date of the

patent in suit, nothing was even known about the immunity mechanism to the CCV and later document (15), published in August 1993, taken as an expert's opinion, shows this (see page 558, last full paragraph: "Still less is known about immunity to canine coronavirus"). What was known before the priority date was that **virulent** CCV infected the dog's intestine via the oral route (see document (10), page 26, under the heading "Route of infection") but that parenteral administration of the virus did not result in intestinal infection (ibid., page 28, l-h column). This did not mean to the skilled person that an **attenuated** CCV had to behave in the same way. Especially where the attenuated virus was administered via the parenteral route, there was no certainty that this characteristic would remain active. Therefore it is the board's view that there was no means available by which this feature could have been established.

9. The respondents argue that feature (2) and a method for testing it had been revealed during Dr Acree's conference (see document (62), page 24/51, section IV.5.a, and page 25/51, section E.1). However, the board observes that document (62) merely reports that an **undefined** CCV vaccine administered parenterally elicits 95% intestinal protection. The document does not specify whether the vaccine is Coronavac® or Duramune C® or whether it is a live attenuated vaccine, an inactivated one or something else. Furthermore, "intestinal protection" is not necessarily linked to feature (2), namely "selectively infects the intestinal epithelium" since intestinal protection may be due to local antibodies and not to infection by the virus. It is also true that document (62) (see page 9/51,

section 3) discloses a technique based on "fluorescent antibody staining of intestinal material". However, this technique is cited in the context of the diagnosis of canine coronavirus (see heading on page 9/51), not in the context of evaluating "intestinal protection" of the undefined CCV vaccine referred to therein. Thus, in conclusion, even assuming that combining document (62) with the prior use of Coronavac® or Duramune C® were permissible in a novelty issue, feature (2) remained concealed from the skilled person before the priority date of the patent in suit.

10. As regards feature (3), namely that the avirulent antigenic product emerging either from the live canine coronavirus attenuated according to claim 1a or from inactivated feline or canine cell propagated canine coronavirus (claim 1b) protected dogs by parenteral administration from infection by CCV, the board observes that before the priority date of the patent in suit diagnosis of CCV infection based only on the clinical signs was impossible. In fact, later document (15) (published August 1983) taken as an expert's opinion confirms this on page 551 under the heading "Clinical Diagnosis". Document (62) also states on page 9/51 (point 2) that "a diagnosis of CCV gastroenteritis based on the symptoms can be misleading". Thus, field efficacy trials did not correlate with and thus could not be predictive of immunoprotection. This lack of correlation also applied to serological studies since humoral antibodies did not imply protection (see document (10), page 28, l-h column, under "Immunity"). Thus, in order to overcome this obstacle, the skilled person had to turn to a reliable experimental challenge model for evaluating

whether a given vaccine actually conferred protection. However, this experimental challenge model was not available to the skilled person before the priority date of the patent in suit. It was also kept secret during Dr Acree's conference (see document 61, page 25/61, section E.1: "The specific procedure used to evaluate the efficacy of a vaccine cannot be discussed"). This experimental challenge model was based on the finding of claim 25 of the patent in suit which consists in examining intestinal tract samples of the vaccinated dog and control dog both challenged with the CCV to determine the degree of replication of the challenge virus. Consequently, since the skilled person could not reliably evaluate before the priority date of the patent in suit whether or not feature (3) was shared by a given CCV vaccine, it must be concluded that feature (3) was also concealed from the skilled person.

Reproducibility

11.1 The respondents argue that availability of one of the prior use vaccines was possible by reproduction of the vaccine by departing from a single vial of eg Coronavac® used as a master seed stock and subjecting it to a limited series of passages in canine cells. However, in the board's view, two important reasons exist against the respondents' line of argument.

11.2 Firstly, point 1.4 of decision G 1/92 (see point 3 supra) states that an essential purpose of a technical teaching is to enable the person skilled in the art to manufacture or use a given product by applying such teaching. Thus, as a corollary, the manufacture or use

of a given product requires that one has to understand the composition or the internal structure of the product. Hence reproducibility of a product requires that one has to understand before and after reproduction **what** one has in one's hands, otherwise "blindfold" reproduction will lead to something uncontrollable. But in the particular situation at issue, the skilled person did not and could not know whether features (1) to (3) above were present in the vaccine commercially available or in a reproduced vaccine (see points 6 to 10 supra). Therefore it was impossible to establish the identity of the reproduced vaccine with the starting vaccine.

11.3 Secondly, the probability of a genetic change in the virus' genome upon propagation in a living host cell was very high. Any virus when propagated may undergo genetic changes susceptible to alter eg the tissue tropism, the virulence, the attenuations markers or the thermal stability. This is in line with document (46), according to which, when propagating a live virus vaccine, only a limited number of passages have to be made to prevent undesirable mutations (see page 618, l-h column, second paragraph). But later documents show that single-stranded RNA viruses such as CCV are particularly predisposed to said mutations (see document (66), paragraph bridging pages 257 and 258 and document (63), bottom of page 65). As already pointed out under point 6 supra, these genetic alterations depend upon the host cell in which propagation is performed and on the conditions (inter alia the number of passages and the virus/cell ratio) applied.

12. Before the priority date of the patent in suit, the two

facts mentioned above (ie, the lack of understanding of the composition or the internal structure of the product by the skilled person **and** the high probability of a genetic change in the virus' genome upon propagation in a living host cell) thus combined to induce an uncontrollable situation, if one attempted to expand a commercially available CCV vaccine vial. For instance, since it was not possible to understand the true nature of the vial's content, other than that it was "a modified live CCV vaccine modified by special tissue procedures" (see page 72 of document (25), ie the leaflet accompanying the vial), there was also a lack of guidance as to the measures to be taken to propagate the CCV and the probability was high that the virus would have reverted to the virulent stage (see patent in suit, page 5, lines 25 to 29) if the skilled person did that. In conclusion, while it is not in dispute that it was possible to amplify the CCV virus by departing from a single vial of, for example, Coronavac® used as a "master seed stock" and subjecting it to a limited series of passages, the board cannot accept that this amplified CCV virus be qualified as the "claimed vaccine", in the absence of means to make sure that it is. Thus, there is a close connection between the requirements stated in decision G 1/92 (supra) that a product belonging to the public domain can be made and used and its analysability.

13. Thus, even presuming that Duramune C® and Coronavac® were in the hands of the public before the priority date of the patent in suit, features (1) to (3) referred to in the claim would **not** have been made available to the public within the meaning of Article 54(2) EPC since the skilled person had no means

of establishing these features and was also not able to monitor reproduction so as to ensure that features of the "master feed stock" were maintained. The subject-matter of the claims at issue is therefore not affected by the mere existence in the public domain of Duramune C® and/or Coronavac®.

The board is also not in a position to identify further prior art disclosing the claimed subject-matter. It must be concluded that the claims of the sole request satisfy the requirements of Article 54 EPC.

Inventive step

Closest prior art

14. The respondents maintain that the closest prior art is represented by Dr Acree's oral disclosure (document (62)) and by Coronavac®'s and Duramune C®'s being available on the market, while the appellant views document (10) supplemented by later document (15), taken as an expert's opinion, as the closest prior art. Yet post-published document (15) cannot be taken into consideration for evaluating the inventive step. The board will also disregard in this context the vaccines Coronavac® and/or Duramune C® since, as stated above, the latter failed to reveal any intrinsic or extrinsic feature of the vaccine to the skilled person, and therefore it was not possible to produce and use them.

Document (10) is considered by the board as the closest prior art since it is concerned with CCV enteritis in dogs and immunity to CCV. It states that in previous experiments including parenteral administration of CCV

preparations, whether attenuated or not, no full protection could be obtained and that a vaccine for protection against CCV was not available. It also states that local immunity in the intestine is essential for protection against CCV infection.

Document (62) reports that an undefined CCV vaccine administered parenterally elicits 95% intestinal protection, without specifying whether the vaccine is a live attenuated vaccine, an inactivated one or something else, and without teaching how the said vaccine is arrived at. Thus, in conclusion, this document does not provide any further technical teaching in comparison with document (10) but merely confirms what was already known from document (10), namely that local immunity at the intestinal level is essential for protection against CCV infection.

Problem to be solved and its solution

15. Departing from document (10), the technical problem to be solved by the patent in suit can be seen in the provision of effective protection for dogs from CCV infection and means for arriving at an effective vaccine. The board is satisfied that said problem has been solved by the vaccines according to claims 1 to 10, the process according to claims 11 to 16 and the methods according to claims 17 to 28, in view of the immunisation results referred to in eg Examples 5 and 15.

16. It has to be established whether or not the solution to the above problem followed in an obvious manner from document (10). In the board's opinion document (10)

provided no guidelines for arriving at the claimed vaccines other than the teaching that an effective vaccine had to confer local immunity at the intestinal level. Moreover, the statement made in document (10) (see page 28, r-h column), according to which parenteral administration of CCV preparations, whether or not attenuated, did not achieve full protection, would have discouraged the skilled person from embarking upon the development of a vaccine to be administered parenterally. Rather, the skilled person would have thought of developing an oral vaccine because it is stated on page 28, l-h column of document (10), that "dogs infected orally become immune".

17. As regards the inactivated CCV vaccine (claim 1b), not only did no prior art document suggest making an inactivated CCV vaccine, but, in the board's judgment, nor did the scientific community expect an inactivated CCV vaccine, let alone a parenterally administered one, to confer intestinal protection since there was a conviction within that community that only attenuated live CCV vaccine administered orally could have elicited a sufficient immunological response (see point 16 supra). Further, the influence of the inactivation procedure on the epitopes required for conferring protection was unpredictable.

18. The board also observes that arriving at the claimed vaccines was not straightforward because the important blockage emphasised in point 9 supra (an experimental challenge model was not available to the skilled person before the priority date of the patent in suit) had to be overcome. No prior art document pointed to the method for evaluating the effectiveness of a CCV

vaccine according to claim 25 of the patent in suit which consisted of examining intestinal tract samples of the vaccinated dog and control dog both challenged with the CCV to determine the degree of replication of the challenge virus. Nor was the further technical information for arriving at the claimed vaccines suggested by any prior art document, namely that attenuation of the CCV had to be made according to independent method claim 23 at issue, ie by passaging CCV between 8 to 60 times in feline cells at a very low virus to cell ratio (between 1:1000 to 10000).

19. The respondents' argument based on document (62) and the availability on the market of the two vaccines Coronavac® and/or Duramune C® is also not convincing. This is because, on the one hand, document (62) did not specify whether the vaccine was a live attenuated vaccine, an inactivated one or something else, and more importantly it did not teach how the said vaccine was arrived at, and on the other hand, Coronavac® and/or Duramune C®, even if they were available to the public, would have been of no help (see points 9 to 10 supra).

20. The respondents further argued that there was a very high expectation of success that attenuating CCV would have led to an effective vaccine in view of document (3), which disclosed the manufacture of an attenuated TGEV live vaccine and an inactivated vaccine both conferring protection when administered parenterally. Yet the board observes that TGEV is not akin to dogs' coronaviridae but only serologically cross-reactive with CCV and the virus does not protect dogs from CCV infection (document (10), page 28, r-h column). In the light of the fact that the even closer prior art

relating to CCV (documents 10 and 62) did not provide any hint that protection upon parenteral administration of an attenuated CCV vaccine would be envisaged, the board does not consider the results obtained with TGEV to be transferable to CCV. In any case, document (3) does not teach or suggest the features indicated in claim 1.

21. In view of the above findings, the board concludes that the subject-matter of claim 1 and dependent claims 2 to 22 satisfy the requirements of Article 56 EPC. This conclusion also extends to the subject-matter of independent claims 23 and 25 because, as already discussed in point 18 supra, these claims are directed to a CCV attenuation method and a method for evaluating the effectiveness of a CCV vaccine respectively, not suggested by any prior art document on file. These are thus non-obvious means of arriving at the claimed vaccines, and also to claims 24 and 26 to 28 dependent thereupon.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of the main request as filed in the oral proceedings.

The Registrar: The Chairwoman:

U. Bultmann U. M. Kinkeldey