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Datasheet for the decision of 19 October 2021

Case Number: T 1131/18 - 3.3.07

Application Number: 12813324.6

Publication Number: 2793866

IPC: A61K9/20, A61K31/4184, A61K31/501, A61K47/12

Language of the proceedings: EN

Title of invention:
NEW COMBINATION

Patent Proprietor:
Elanco Tiergesundheit AG

Opponent:
Boehringer Ingelheim Vetmedica GmbH

Headword:
Combination of Pimobendan and Benazepril/ ELANCO

Relevant legal provisions:
EPC R. 103(1)(a)
RPBA Art. 12(4)
RPBA 2020 Art. 13(2)
EPC Art. 123(2), 83, 84, 54, 56

Keyword:

Violation of procedure (No) - Reimbursement of the appeal fees (No)
Admission of documents (Yes)
Admission of the main request (Yes)
Main request - Extension beyond the original content (No)
Main request - Sufficiency of disclosure (Yes)
Main request - Clarity (Yes)
Main request - Novelty (Yes)
Main request - Inventive step (Yes)

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Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1131/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 19 October 2021

Appellant: (Opponent)	Boehringer Ingelheim Vetmedica GmbH Binger Strasse 173 55216 Ingelheim am Rhein (DE)
Representative:	Banse & Steglich Patentanwälte PartmbB Patentanwaltskanzlei Herzog-Heinrich-Straße 23 80336 München (DE)
Respondent: (Patent Proprietor)	Elanco Tiergesundheit AG Mattenstr. 24A 4058 Basel (CH)
Representative:	Potter Clarkson The Belgrave Centre Talbot Street Nottingham NG1 5GG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 8 March 2018 concerning maintenance of the European Patent No. 2793866 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	D. Boulois
	K. Kerber-Zubrzycka

Summary of Facts and Submissions

I. European patent No. 2 793 866 was granted on the basis of a set of 13 claims.

Independent claim 1 as granted read as follows:

"1. A fixed dose combination comprising benazepril hydrochloride and pimobendan in a ratio of 2 : 1, in form of a bilayer tablet,
wherein the benazepril layer comprises 2.5, 5 or 10 mg benazepril hydrochloride which are contained in the form of pellets, and
wherein the pimobendan layer comprises 1.25, 2.5 or 5 mg pimobendan."

II. An opposition was filed under the grounds that the subject-matter of the granted patent lacked novelty and inventive step, was not sufficiently disclosed, and extended beyond the content of the application as filed.

III. The present appeal lies from the decision of the opposition division that the patent in amended form met the requirements of the EPC. The decision was based on 2 sets of claims filed as main request with letter of 30 January 2017 and as auxiliary request 1 during the oral proceedings of 15 December 2017.

The subject-matter of independent claim 1 of auxiliary request 1 was the same as claim 1 as granted. This request differed in the subject-matter of dependent claims 3 and 4.

IV. The documents cited during the opposition proceedings included *inter alia* the following:

D5: O'Grady M. et al., J. Vet. Intern. Ned., 2008, 22, 897-904
D8: WO 2011/111066
D9: US 6,162,802
D10: Divya A. et al., J. Appl. Pharm. Sci., 2011, 01(08), 43-47
D11: Deshpande R. et al., IJPSR, 2011, 2(10), 2534-2544
D12: Lotensin Tablet. NDA Approved 2/2/07, 1-18
D13: Vetmdin, Freedom of information summary, 04/2007, NADA, 141-144
D14: EP 1 490 037
D15: WO 2006/085208
D18: Benazepril hydrochloride, European Pharmacopoeia 7.0, 1454-1456
D19: GB 2 394 660
D20: WO 03/075842
D21: Gana M. et al., J. Pharm. Biomed. Anal., 2002, 27, 107-116
D25: Declaration of Dr. Martin Folger
D28: Declaration of Mateja Sikovec
D29: Stability testing of pimobedan and benazepril fixed combination
D30: Declaration of Dr. Stefan Haas
D31: Salsa T. et al., Drug Dev. Ind. Pharm., 1997, 23(9), 929-938

V. According to the decision under appeal, the main request did not meet the requirements of Article 123(2) EPC.

Auxiliary request 1 met the requirements of Article 123(2) EPC. The subject-matter of auxiliary request 1 was sufficiently disclosed and was novel over D8.

As regards inventive step, the opposition division considered D5 as a better closest prior art than D8, which was the choice of the opponent. The difference between the claimed subject-matter and D5 was the fixed dose combination in form of a bilayer tablet and benazepril HCl being comprised in the form of pellets. The technical effect was a more convenient administration and better compliance in dogs. The problem was the provision of a stable solid dosage form comprised a fixed dose combination comprising pimobendane and benazepril HCl for the treatment of congestive heart failure in dogs showing improved compliance. The claimed solution was inventive.

As regards the assessment of inventive step starting from D8 as the closest prior art, the opposition division identified four differences between the claimed subject-matter of claim 1 of auxiliary request 1 and the disclosure of D8. The opposition division could not follow the opponent's arguments that there was no evidence of an improved stability and that no effect was shown for the whole breadth of claim 1. The opposition division considered that D8 did not disclose a combination of benazepril and pimobedan, nor their incompatibility. The skilled person would not have considered a combination of D8 with D9 or D15.

VI. The opponent (hereinafter the appellant) filed an appeal against said decision. With the statement setting out the grounds of appeal the appellant submitted the following items of evidence:

D32: Lachmann et al., "The Theory and Practice of Industrial Pharmacy", 3rd ed., 1086, pages 330-331

D33: Voigt, Bornschein, "Lehrbuch der pharmazeutischen Technologie», 1973, pages 131, 132, 158, 159, 228, 229
D34: Parikh, "Handbook of Pharmaceutical Granulation Technology", 1997, pages 7-23
D35: Serno et al., "Granulieren», 2. Auflage 2017, pages 10-37
D36: Request for correction of written decision and minutes filed by the appellant onJuly 13, 2018.

Additionally, the appellant requested reimbursement of the appeal fee in light of a substantial procedural violation committed by the opposition division.

VII. With a letter dated 13 November 2018, the patent proprietor (hereinafter the respondent) filed a main request and auxiliary requests 1 to 10. The main request corresponded to auxiliary request 1 maintained by the opposition division.

VIII. With a letter dated 1 February 2019, the appellant requested that auxiliary requests 1-10 and documents D28-D31 not be admitted into the proceedings.

IX. A communication from the Board, dated 6 December 2019, was sent to the parties. In it the Board expressed its preliminary opinion that *inter alia* the opposition division did not make any violation of procedure and that a reimbursement of the appeal fees did not appear to be justified, that the main request appeared to be sufficiently disclosed, novel and inventive over D5, which had to be considered as the closest state of the art, rather than D8.

X. With a letter dated 16 January 2020, the respondent filed a new main request and auxiliary requests 1-13.

Claim 1 of the main request was similar to claim 1 of auxiliary request 1 as maintained by the opposition division with the modification of the feature "in a ratio of 2 : 1" to "in a ratio of 2:1" (i.e. the spaces have been removed in the ratio "2 : 1").

The main request also differed from auxiliary request 1 as maintained by the opposition in the modification of the feature "a butyl methacrylate-2-dimethylaminoethyl)methacrylte-methylmethacrylate copolymer (1:2:1)" in dependent claim 3 to "a butyl methacrylate-2-**(**dimethylaminoethyl)methacrylte-**methyl-methacrylate** copolymer (1:2:1)" (modification shown in bold and underlined).

XI. Oral proceedings took place on 19 October 2021.

XII. The arguments of the appellant may be summarised as follows:

Reimbursement of the appeal fee

At first, the Opposition Division ignored relevant facts and arguments submitted by the opponent orally and in writing. Secondly, the decision was based on grounds which the opponent could not expect and on which the opponent was not heard.

Admission of D28-D31 into the appeal proceedings

All these documents should have been filed earlier. D29 related in particular to example 6 of the patent which was not reproducible.

Admission of the main request into the appeal proceedings

This request was filed after the Board had issued summons for oral proceedings and had claims 1 and 3 modified; it should not be admitted under Article 13(1) RPBA 2020. According to Rule 80 EPC, such an amendment of a dependent claim was not acceptable. Moreover there was nor clear copy of the request, which amounted to a lack of clarity under Article 84 EPC.

Main request - Amendments

The original application had been used as a reservoir for creating arbitrary new embodiments in all claims. All claims 1 to 13 of the opposed patent related to feature combinations which were not disclosed directly and unambiguously in the application as originally filed.

Main request - Sufficiency of disclosure

There was a lack of enablement over the entire claim breadth, since neither the general description nor the working examples disclosed the essential steps and parameters of the production process. Thus, the patent did not enable the skilled person to obtain a stable bilayer tablet without undue burden.

The working examples could not provide evidence of any increase of stability of a composition according to claim 1 of the opposed patent. Even if one acknowledged that examples 2 and 3 demonstrated improved stability regarding impurity C compared to example 1, this would have resulted in lack of enablement over the entire claim breadth. Claim 1 of the opposed patent did not

relate to masked, coated pellets or layers in which pellets were embedded in protective matrices, as they were in these examples.

There were undefined terms in the claims, such as "bilayer tablet", “pellets”, “in the form of a granulate”, in claim 6. Claim 5 related to "excipients of the benazepril layer having a particle size from 200 to 400 µm". Also in view of the description, it was not clear how certain "excipients" should have a particle size, let alone in the claimed range, especially when present in a layer of a tablet.

Main request - Clarity

Claim 3 lacked clarity under Art. 84 EPC, since it was not clear how benazepril pellets should have been coated with benazepril.

Main request - Novelty

The subject matter of claim 1 was not novel in view of document D8, which related to a composition including an inhibitor of phosphodiesterase-3 activity, such as pimobendan, and an inhibitor of angiotensin receptor activity, such as ACE inhibitor benazepril (claims 1, 2, 5, 6). D8 also disclosed explicitly to provide the composition as a bilayer tablet (page 25, line 37).

Main request - Inventive step

During oral proceedings, the appellant considered D5 to be the closest prior art. The distinguishing features between the claimed subject-matter and D5 were the bilayer tablet, the presence of pellets and the exact doses of the active agents. No technical effect could

be attributed to the use of pellets and thus this feature could not be taken into account for assessing inventive step. Furthermore, there was no evidence in the opposed patent that a bilayer tablet is better than any other dosage form, in which benazepril and pimobendan are spatially separated; D25 also showed that it was not possible to repeat the examples. The problem was the provision of an alternative dosage form. The skilled person had a strong incentive to provide both active ingredients in a combination product for convenient and regular administration. He was aware of the stability and incompatibility problems of benazepril and pimobendan. He was also aware of numerous advantages of bilayer tablets as described in D10/D11/D32, and that it was easy to prepare them as noted in D33. Therefore, the mere aggregation of features of claim 1 of the opposed patent was obvious in view of document D5 and common general knowledge, as evidenced by D10, D11, D32, D33, or other documents such as D8, D9, D14 or D15. The fixed dose combination of claim 1 of the opposed patent was therefore not based on an inventive step in view of these documents.

In the written proceedings, the appellant also considered D8 as closest prior art. In view of this document, the problem was providing an alternative composition. The solution was obvious at least when taking into account D14, D10, D11, D32 or D33.

XIII. The arguments of the respondent may be summarised as follows

Reimbursement of the appeal fee

There was no violation of procedure that would justify a reimbursement of the appeal fees. The opposition division addressed all points in a normal way.

Admission of D28-D31 into the proceedings

All documents were filed before the Rule 116 EPC limit date in the opposition proceedings and there was no reason not to admit them.

Admission of the main request into the appeal proceedings and amendments

The main request comprised only minor amendments and did not contravene Rule 80 EPC. The amendments intrduced in the main request had a basis in the original application.

Main request- Sufficiency of disclosure

It appeared that the underlying question being asked was whether the problem of stability had been credibly solved across the breadth of the claim. Since claim 1 of the opposed patent did contain no requirement for stability, this was a question relevant to inventive step. Moreover, all terms used in the claims were clear and known to the skilled person.

Main request - Novelty

There was no clear and unambiguous disclosure of the subject matter of claim 1 in D8.

Main request - Inventive step

D8 could not represent the closest prior art, in view of its disclosure which was very remote from the claimed subject-matter.

D5 was the closest prior art. The claimed subject-matter differed in the fact it was a single product, a bilayer tablet containing pellets, and the dose was different. The effect was the provision of a stable combination of the two drugs with a good compliance. The problem had been solved in view of examples 3 and 6 of the patent. The solution was not obvious over the prior art. D5 did not mention any instability when both drugs were combined, and there was no guidance in D5 or any other cited documents for a combination product.

With regard to the argument that the problem was not solved, the burden of proof was on the appellant. It could have reproduced the examples . It was not possible to argue that the manufacture of bilayer tablets were obvious and at the same time not be able to repeat the examples of the patent.

XIV. Requests

The appellant requested that the decision under appeal be set aside and the patent be revoked. Additionally, the appellant requested the reimbursement of the appeal fee in light of a substantial procedural violation committed by the Opposition Division, and that the main

request, auxiliary requests 1-13 filed with letter of 16 January 2020 and documents D28-D31 not be admitted into the proceedings.

The respondent (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained according to the main request filed on 16 January 2020 or alternatively, in accordance with one of auxiliary requests 1-13 filed at the same date.

Reasons for the Decision

1. Reimbursement of the appeal fee

1.1 According to the appellant, the opposition division violated the right to be heard of the opponent in the written proceedings and the oral proceedings, since the opposition division ignored relevant facts and arguments submitted by the opponent and the decision was based on grounds which the opponent could not expect and on which the opponent was not heard.

1.2 The detailed points raised by the appellant are the following.

The preliminary non binding opinion of the opposition division was premature, since said opinion annexed to the summons to oral proceedings was transmitted three weeks after the reply of the patent-proprietor to the notice of opposition.

Furthermore, the appellant considered that its right to be heard was not respected for following reasons:

(a) Relevant facts (D25) and arguments were not taken in account at all by the opposition division. The opposition division did not comment all the submissions regarding the working examples, knowledge of the skilled person in the field of pharmaceutics, common general knowledge and declaration D25.

(b) The opposition division had based the written decision on grounds on which the opponent had not been heard. The four-steps approach regarding inventive step of the decision of the opposition division had never been communicated to the opponent. The opposition division did not give the opponent a fair chance to have the patent revoked for lack of inventive step in the written and oral proceedings.

(c) Further, the four-step approach and the further grounds provided by the opposition division severely violated established case law of the Boards of appeal (cf. T 234/03, T 37/82 or T 939/92).

1.3 The Board cannot follow the appellant on any of the raised points.

With regard to the transmission of the summons and the preliminary opinion three weeks after the reply of the patent-proprietor to the notice of opposition, the Board considers this delay to be reasonable, and it is not understood how this timing could amount to a violation of the right to be heard. The preliminary opinion of the opposition appears furthermore to be complete and to address all the points raised by the opponent in its notice of opposition and by the patent proprietor in its response. Furthermore, the opposition division even issued a second communication in response

to a further letter of the opponent contesting the first preliminary opinion.

With regard to relevant facts and arguments not taken in account, the opposition division appears to have provided a response to all points raised by the opponent in its decision. In particular, documents D10, D11, D14, D15 and D9, which were presented as indicative for the general knowledge, were discussed in the decision of the opposition division. As regards D25, this document is a statement of Dr Folger, employed by the opponent which relies on other documents, such as D14, D18, D19, D20, D21, D22 and D23, and provides common general knowledge in relationship with the instability of benazepril, the solubility problem of pimobedan, and the incompatibility of benazepril and pimobedan. All these specific points, namely the instability of benazepril, the solubility problem of pimobedan, and the incompatibility of benazepril and pimobedan, appear to have been explicitly addressed in the decision of the opposition division. Hence, all relevant facts and arguments appear to have been taken in account by the opposition division in its decision. In the Board's view, this point appears to be rather a criticism of the judgment of the opposition division on the obviousness of the claimed solution. Even on the assumption that there had been an error of judgment, this is not a matter which can be taken into account when assessing whether or not a substantial procedural violation occurred.

With regard to points (b) and (c), the Board notes that inventive step was assessed through the following steps in the decision of the opposition division:

(i) Point 10.1, Choice of the closest prior art

(ii) Point 10.2, Distinguishing features
(iii) Point 10.3, Technical effect derivable from the distinguishing feature
(iv) Point, 10.4, Objective problem to be solved
(v) Point 10.5, Obviousness of the solution.

Accordingly, inventive step was correctly assessed through the problem-solution approach by the opposition division, and said problem-solution was subdivided in the necessary relevant steps. The objection raised by the appellant appears therefore unfounded.

More specifically, with regard to the choice of the closest prior art, this point was discussed during the oral proceedings, and the choice was justified by the opposition division in point 10.1 of its decision. The opposition division also explained in its decision why D8, D15 or D9 were not relevant in the assessment of inventive step. The fact that the opposition division disagreed with the opponent in the choice of the closest prior art cannot constitute a violation of procedure.

The same applies to the teaching of document D14, which was also discussed in the decision of the opposition division under the point 10.5 of obviousness, as it had been by the opponent in its notice of opposition.

Finally, the Board notes that the opposition division devoted specifically point 2 of its decision to the right to be heard which was questioned by the opponent several times in the opposition proceeding, in the written proceedings as well as during oral proceedings. The respect of the right to be heard was directly confirmed by the appellant in its statement of grounds of appeal which clearly stated that "during the oral proceedings, the opposition division initially

indicated that the opponent's right to be heard would be granted in full. Unquestionably, the opponent was then given sufficient time to present his facts and arguments. The opponent had sufficient time to explain in detail all facts and arguments, which were basically those as summarized above in section VI".

1.4 Consequently, the objections raised by the appellant appear to represent a criticism of the decision of the opposition division. They neither substantiate a violation of the right to be heard nor a fundamental deficiency in the decision of the opposition division. Consequently, there is no substantial procedural violation which would justify a reimbursement of the appeal fee under Rule 103(1)(a) EPC.

2. Admission of D28-D31 into the appeal proceedings

Documents D28-D31 have been filed by the patent proprietor during the opposition proceedings, in response to the successive filing of documents D19-D24 and D25-D27 by the opponent. Said documents D28-D31 were filed before the final date of submissions mentioned in Rule 116 EPC, and their admission in the opposition proceedings was contested by the opponent already during the opposition proceedings.

Even if it appears that the opposition division did not take any decision with regards to the admission of D28-D31 into the opposition procedure, the Board does not see any reason to not admit them in the appeal procedure, in view of their date of submission (Article 12(4) RPBA 2007).

3. Admission of the main request into the appeal proceedings

The main request corresponded to auxiliary request 1 maintained by the opposition division with minor modifications in independent claim 1 and in dependent claim 3.

Hence, in claim 1 the feature "in a ratio of 2 : 1" was modified by the suppression of the empty spaces to "in a ratio of 2:1".

In claim 3, the feature "a butyl methacrylate-2-dimethylaminoethyl)methacrylate-methylmethacrylate copolymer (1:2:1)" was modified by the addition of a bracket (shown in bold and underlined) to "a butyl methacrylate-2-**(**dimethylaminoethyl)methacrylate**-**methyl-methacrylate copolymer (1:2:1)" (modification shown in bold and underlined).

The Board considers that the changes in claims 1 and 3 were only typographical or editorial changes that do not result in any amendment of the subject-matter claimed. They have no incidence on the subject-matter claimed and do not introduce any unclarity, as argued by the appellant. Consequently, the main request is admitted into the appeal proceedings (Article 13(2) 2020 and Rule 80 EPC).

4. Main request - Amendments

4.1 According to the appellant, claim 1 should be based on the features of original claims 1 and 5 and page 2, fourth paragraph of the description. However, it was not clear from the original claims and description that such a composition was an embodiment of the invention,

and claim 1 was an artificially created new embodiment. All claims 1-13 related to feature combinations, in particular the combination of claims 1,3 and 7, which were not disclosed directly and unambiguously in the application as filed.

4.2 The subject-matter of claim 1 of the main request finds a basis on page 2, fourth paragraph of the original description. The feature requiring the benazepril hydrochloride to be contained in the form of pellets finds a basis in original claim 5 referring back to claim 1 that defines a combination of benazepril hydrochloride and pimobendan in form of a bilayer tablet. The Board also concurs with the conclusion of the opposition division (see point 3.1) that the subject-matter of claim 1 can be directly and unambiguously derived from the combination of the embodiments found in paragraphs 1, 4 and 5 on page 11 of the original application.

The definition of the protective layer in dependent claim 3 originate from page 5, 2nd paragraph of the original description which mentions Eudragit® EPO as preferred coating material; the subject-matter of this claim can therefore not be see as being singled out from the original application. The precise chemical name of said polymer is given on page 17 and has been taken as such in claim 3.

The presence of succinic acid as claimed in dependent claim 7 is found on page 7, line 6 and page 9, line 13 of the description; in both passages it is the only acid cited. Said succinic acid is also present in all examples of the original application which is a clear pointer that it is a preferred embodiment.

Claim 1, 3, and 7 are based therefore on combinations of preferred embodiments which are disclosed in the application as filed.

The subject-matter of claim 2 finds also a direct basis in the last paragraph of page 9 or on page 6, 5th and 6th paragraph of the original description.

The subject-matter of dependent claims 4 and 5 can be found in the original description on page 6 , 3rd and 6th paragraph, and constitute also preferred embodiments with regard to the carrier particle size and the benazepril layer size. This subject-matter does therefore not constitute a selection among different possibilities.

The subject-matter of claims 6, 10, 11 12 and 13 finds a direct basis in the respective original claims 6, 10, 11, 12 and 9.

The subject-matter of claims 8 and 9 are also preferred embodiments disclosed on page 10, 4th paragraph of the original application.

4.3 Consequently, the features of all claims can be derived directly and unambiguously from the original application. The main request meets therefore the requirements of Article 123(2) EPC.

5. Main request - Clarity

According to the appellant, claim 3 of the main request lacks clarity, since it is not clear "how benazepril pellets shall be coated with benazepril".

The Board notes that the claims of the main request are substantially identical to the granted claims, and are thus not open for a re-examination pursuant Article 84 EPC (cf. G 3/14).

6. Main request - Sufficiency of disclosure

6.1 According to the appellant, the problem underlying the invention could not be solved over the entire claim breadth. Moreover, some terms, such as "bilayer tablet", "pellets", "excipients" and "granulate" were so undefined that the skilled person would not be able to determine what was the subject of the claims.

6.2 The objections raised by the appellant are of no relevance for the assessment of sufficiency of disclosure. The subject-matter of claim 1 is rather simple and relates to a bilayer tablet with two different active ingredients in the different layers. Said claim is not limited by any particular technical effect such as the stability, and the resolution of the problem underlying the invention is therefore an irrelevant question for the assessment of sufficiency of disclosure. The points raised by the appellant relate to the assessment of inventive step or to the clarity of the claims, and do not fall under the ground of sufficiency of disclosure.

As regards the clarity of the terms "bilayer tablet", "pellets", "excipients" and "granulate", these terms are furthermore known and very common in the pharmaceutical field.

6.3 The claimed invention is therefore sufficiently disclosed.

7. Main request - Novelty

Document D8 was cited as relevant for the novelty.

A combination of benazepril and pimobedan is not disclosed directly and unambiguously in D8, since both molecules are mentioned in lists of possible drugs; pimobedan is indeed envisaged as possible inhibitor of phosphodiesterase 3 among other possibilities from a list (see D8 paragraph [0030]) and benazepril is envisaged as inhibitor of angiotensin in a second list (see inter alia paragraph [0032]). The subject-matter of claim 1 is therefore novel over D8 already in view of this differentiating feature.

The main request meets the requirements of Article 54 EPC.

8. Main request - Inventive step

8.1 The invention relates to a combination of benazepril with pimobendan. Its object is to provide a fixed dose combination form for the treatment of congestive heart failure in dogs, which would be convenient to use, improve veterinarian and pet owner compliance and treatment outcomes.

8.2 The opposition division considered document D5 to be the closest prior art. The appellant maintained in its written proceedings that the closest prior art should be document D8 and mentioned also D9 and D15, while during oral proceedings before the Board the appellant assessed inventive starting from D5.

8.2.1 D5 discloses the oral and separate administration of pimobendan (0.25 mg/kg *per os*), benazepril HCl (0.5 mg/

kg *per os*) and furosemide (*per os* as required) in dogs for the treatment of congestive heart failure. The dose ratio between pimobendan and benazepril is 1:2 (see Materials and Methods). This document does neither disclose bilayer tablets, nor the precise claimed dosages, nor the presence of pellets. D5 does also not mention a possible interaction between pimobendan and benazepril.

8.2.2 D9 and D15 relate to dosage forms of amlodipine and benazepril such as bilayer tablets (see example 3) for the treatment of cardiovascular diseases. These documents do not relate to pimobendan or to an association of pimobendan and benazepril.

8.2.3 D8 relates to the treatment of conditions associated with hyperglycemia or hypertriglyceridemia by an association between a) an inhibitor of phosphodiesterase 3 and b) an inhibitor of angiotensin receptor activity. It concerns therefore a technical subject different and remote from the subject-matter of the main request. Pimobendan is envisaged as possible inhibitor of phosphodiesterase 3 among other possibilities from a list (see D8 [0030]) and benazepril is envisaged as inhibitor of angiotensin (see inter alia [0032]). The possibility of using a hydrochloric salt is disclosed in a list on page 13, as well as a bilayer tablet among another list of possible formulations (see pages 23-29). There is no disclosure of any specific amounts, and multiple possible doses are given on page 30. The examples of D8 show a specific combination of cilostazol and telmisartan.

Consequently, the disclosure of D8 is technically remote from the claimed subject-matter and does not relate to the same technical problem or even the

general purpose of the claimed invention. No common technical features appear to exist between the claimed subject-matter and the disclosure of D8, apart from the isolated citations of benazepril and pimobendan. Hence, the Board concurs with the opposition division that D8 cannot constitute a starting point for assessing inventive step.

8.2.4 Consequently, the Board does not see any reason to deviate from the decision of the opposition division as regards the choice of the closest prior art, which is document D5.

8.3 The problem as defined by the opposition division in its decision is the provision of a stable solid dosage form comprising a fixed dose combination comprising pimobendane and benazepril HCl for the treatment of congestive heart failure in dogs showing improved compliance.

The appellant defined the problem to be solved as the provision of an alternative composition comprising benazepril and pimobedan.

The respondent defined the problem as the provision of a stable solid dosage form comprising a fixed dose combination comprising pimobendan and benazepril HCl.

8.4 As a solution to any of these problems, claim 1 of the main request proposes a bilayer tablet comprising benazepril hydrochloride and pimobendan in a weight ratio of 2 : 1, in form of a bilayer tablet, wherein the benazepril layer comprises 2.5, 5 or 10 mg benazepril hydrochloride which are contained in the form of pellets, and wherein the pimobendan layer comprises 1.25, 2.5 or 5 mg pimobendan.

8.5 The respondent relied on the content of the patent, in particular the examples, for the assessment of the credibility of the alleged technical effect with regard to stability.

On the other side, according to the appellant, it was neither shown, nor rendered credible that a composition as claimed would solve stability over the entire breadth. Moreover, according to the appellant, the examples of the contested patent relate to a composition different from claim 1, did not provide any comparison with the prior art, and said examples are not reproducible and verifiable.

8.5.1 The description in paragraphs [0019]-[0022] and [0033] describes the preparation of the benazepril pellets and the pimobedan granulates used in the examples, as well as the preparation of the tablets in paragraph [0049]-[0051], by conventional preparation methods. Example 2 shows also the detailed preparation of a bilayer tablet as claimed. The argument of the appellant that the examples were not reproducible and verifiable is therefore unfounded.

8.5.2 Examples 1 and 2 of the patent show a comparison between a monolayer tablet comprising pimobedan and pellets of benazepril and a bilayer tablet comprising respectively pimobedan and pellets of benazepril in each separate layer, with a weight ratio of pimobedan:benazepril of 1:4 (5 mg and 20 mg) ; said comparison is performed to show the difference of stability when pimobedan and benazepril are in contact in a tablet or are separated in different layers.

As shown by the examples, the presence of pimobedan and pellets of benazepril in the same monolayer tablet results in a greater level of the benazepril hydrolytic degradation product "Impurity C" in comparison to the situation in which the two ingredients are in separated layers. These results, even if the weight ratio in said examples is different than the weight ratio as claimed, show that the separation of the drugs in different layers stabilizes the composition. Indeed the appellant did not provide any valid argument to support the position that an effect of stabilisation would not be present if pimobedan and benazepril were combined in a 2:1 ratio. The comparative example 1 is furthermore closer from the claimed invention, than the disclosure of D5, which shows the separate oral administration of the two drugs. The fact that it is not a direct comparison with the closest prior art, as argued by the appellant, is therefore irrelevant.

Further stability studies were shown in example 3, which has similar composition as Example 2, only that 5% benazepril pellets were used instead of 20% benazepril pellets, which means that benazepril has a lower concentration in the bilayer tablet, and that the weight ratio between the drugs appears to be less than the claimed ratio of 2:1. Example 3 confirms the results of examples 1 and 2 in Table 3 and shows also a decrease of the level of "Impurity C" for this composition.

Moreover, the experimental results of examples 1, 2 and 3 show that the stability is reached for a large palette of weight ratios of pimobendan and benazepril, which invalidates the appellant's argument that it was not shown or rendered credible that a composition as claimed would solve the problem of stability over the

entire breadth of the claims. In this regard the Board observes that no evidence was submitted by the appellant to support its position.

8.5.3 The Board agrees with the opposition division (see point 10.3 of the decision) that the combination of two active agents in one single dosage form enables a more convenient administration and better compliance in dogs.

8.5.4 Accordingly, the technical problem is as it was defined by the opposition division or the respondent, i.e. the provision of a stable solid dosage form comprising a fixed dose combination comprising pimobendane and benazepril HCl for the treatment of congestive heart failure in dogs showing improved compliance.

8.6 It remains to determine whether the claimed solution was obvious.

8.6.1 There is no suggestion or guidance in D5 to prepare a combined medication comprising pimobedan and benazepril. There is furthermore no mention in D5 of a possible instability when both drugs are combined together and the skilled person would not have any reason to prepare a combined dosage form separating both drugs, even less with pellets of benazepril.

8.6.2 Documents D12, D13, D14 and D18 were cited by the appellant to show that the claimed solution was obvious. In the written proceedings, the appellant also cited documents D8, D10, D11 and D25.

Moreover, the appellant cited documents D18-D21 to demonstrate that it was known that benazepril is susceptible to hydrolysis, which is also acknowledged

by the contested patent in paragraph [0008]. The problem of the claimed invention is however not the stabilization of a composition comprising benazepril as such, but the provision of a stable dosage form combining benazepril and pimobedan, and none of the cited documents show specifically the instability of benazepril in presence of a compound having an amino group, even less with pimobendan (cf. paragraph [0007] of the patent).

None of the documents cited by the appellant shows furthermore the preparation of a bilayer tablet with benazepril, or a tablet combining pellets of benazepril with another active compound. Hence, none of the cited documents D8, D10, D11, D12, D13, D14 and D18 and D25 is considered to be relevant for the assessment of obviousness of the claimed solution.

As discussed above under point 8.2.2, D8 does not show any bilayer tablet or combination of pimobedan and benazepril, it does not mention any stability problem and is too remote to be relevant.

D10 and D11 are about bilayer tablets in general and do not relate specifically to pimobendan and benazepril.

D12 relates to the Lotensin® tablet comprising benazepril alone, and is irrelevant to the claimed invention.

D13 relates to chewable tablets of pimobendan.

D14 discloses the preparation of tablets comprising taste-masked pellets of benazepril, which are further compressed into tablets. This document does not mention the association with another drug, or the preparation

of a bilayer tablet with another drug and relates to a different technical problem.

D18 is a monography of Benazepril Hydrochloride from the European Pharmacopoeia which gives general information about the drug, such as its hygroscopic properties or that it should be protected from light.

D25 is a declaration of a technical expert which mentions the instability of benazepril by referring to documents D14, D18, D19 and D20, the solubility problem of pimobendan by referring to D22 and D23, and the possible incompatibility of both drugs. On the basis the disclosure in these documents, the technical expert concludes that the skilled person had a strong incentive to separate both active agents in a combination product. As argued by the respondent (page 13 of the statement setting out the grounds of appeal) it is doubtful whether the technical expert who has provided declaration D25 could be compared to the notional skilled person. In any case, for the reasons explained above, the Board does not agree with the conclusions in D25. Indeed, there is no document teaching that there may be problems of stability due to the interaction between the two active ingredients. Furthermore, it is not explained in D25 why the skilled person would formulate benazepril in form of pellets.

8.7 Consequently, the claimed solution is not obvious and the main request meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of the main request filed by letter dated 16 January 2020.

3. The request to reimburse the appeal fee is rejected.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated