Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 7 October 2016

Case Number: T 2536/11 - 3.3.01

Application Number: 00935420.0

Publication Number: 1296672

IPC: A61K31/22, A61K31/366, A61K31/404, A61K47/02

Language of the proceedings: EN

Title of invention:
STABLE PHARMACEUTICAL PRODUCT AND FORMULATION

Patent Proprietor:
LEK Pharmaceuticals d.d.

Opponents:
reuteler & cie SA
Teva Pharmaceutical Industries Ltd.
Saetre, Ellen

Headword:
HMG-CoA reductase inhibitor/LEK

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 123(2), 123(3)
RPBA Art. 13

Keyword:
Main request, auxiliary request 1 - admitted (no)
Auxiliary requests 2 to 4 - sufficiency of disclosure (no)
Auxiliary requests 5 to 7 - admitted (no)
Auxiliary request 8 - allowable

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern
Boards of Appeal
Chambres de recours

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 2536/11 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 7 October 2016

Appellant 1: (Patent Proprietor)	LEK Pharmaceuticals d.d. Verovskova 57 1526 Ljubljana (SI)
Representative:	TBK Bavariaring 4-6 80336 München (DE)
Appellant 2: (Opponent 3)	Saetre, Ellen Kiellands Gate 14 1767 Halden (NO)
Representative:	Alt, Michael Bird & Bird LLP Maximiliansplatz 22 80333 München (DE)
Respondent 1: (Opponent 1)	reuteler & cie SA Chemin de la Vuarpillière 29 1260 Nyon (CH)
Respondent 2: (Opponent 2)	Teva Pharmaceutical Industries Ltd. 5 Basel Street P.O. Box 3190 49131 Petah Tiqva (IL)
Representative:	D Young & Co LLP 120 Holborn London EC1N 2DY (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on**

11 October 2011 concerning maintenance of the European Patent No. 1296672 in amended form.

Composition of the Board:

Chairman	A. Lindner
Members:	M. Pregetter
	M. Blasi

Summary of Facts and Submissions

I. European patent No. 1 296 672 is based on European patent application No. 00935420.0, filed as international application published as WO2001/093859.

II. The following documents, cited during the opposition and appeal proceedings, are referred to below:

(1) Physician's Desk Reference, "PDR", 1995, Ed. 49, pages 732 to 735

(2) Package insert of Pravachol® (Pravastatin Sodium tablets), Bristol-Myers Squibb, Princeton, NJ. Apr. 1997

(3) WO 99/06035

(4) EP-A-0 547 000

(6) EP-A-0 336 298

(17) US 5 225 202

(18) Material safety data sheet for lithium hydroxide Sigma Chemical Co.

III. The present appeal lies from the interlocutory decision of the opposition division that the patent as amended according to auxiliary request 3 complied with the EPC.

The opposition division decided that the subject-matter of the patent as granted contained added subject-matter (Article 123(2) EPC). Subject-matter claimed in auxiliary request 1 was not held to be novel in view of document (17). The subject-matter of auxiliary

request 2 was sufficiently disclosed but the subject-matter of claim 1 lacked inventive step starting from document (4) as closest prior art in combination with any of documents (1) to (3). The claims of auxiliary request 3, filed during oral proceedings on 15 September 2011, were held to comply with Article 123(2) and (3) and Articles 83 and 84 EPC. Inventive step of the claimed subject-matter was acknowledged starting either from document (4) or from document (1).

IV. The proprietor (appellant 1) and the opponent 3 (appellant 2) both appealed against the decision of the opposition division.

V. With its statement of grounds of appeal, appellant 1 upheld the main request and filed auxiliary requests 1-7, which were identical to those filed during opposition proceedings.

VI. With its statement of grounds of appeal, appellant 2 raised objections with respect to auxiliary request 3 under Articles 123(2), 83, 84, 54 and 56 EPC.

VII. By letters dated 28 June 2012 and 4 July 2012 respectively, appellants 1 and 2 submitted further arguments and documents.

VIII. In its letter dated 7 September 2016, appellant 1 filed auxiliary requests 1 to 13.

IX. By letter dated 7 September 2016, appellant 2 provided further arguments and filed another document. In its letter dated 14 September 2016, appellant 2 objected to the admission of auxiliary requests 5 to 13 into the proceedings.

X. Oral proceedings were held before the board on 7 October 2016 in the absence of opponents 1 and 2 (respondents 1 and 2). Both had informed the board that they would not attend the oral proceedings.

After discussion on the construction of claim 1 of the patent as granted (main request) and on sufficiency of disclosure, appellant 1 filed a new main request and a new first auxiliary request and withdrew the main request (patent as granted) and the first auxiliary request of 7 September 2016.

XI. The following claims are relevant for the present decision:

The patent was **granted** with twenty-one claims, claims 1, 17, 18 and 20 being independent claims. Claims 1 and 17 read as follows:

"1. A process of stabilizing a HMG-CoA reductase inhibitor selected from the group consisting of pravastatin, atorvastatin, fluvastatin, cerivastatin and pharmaceutically acceptable salts thereof in air comprising the steps of combining:
a) said HMG-CoA reductase inhibitor with
b) a substance capable of binding and/or neutralizing carbon dioxide, wherein the components a) and b) are contained in separate elements of a package or a pharmaceutical administration material."

"17. Use of a substance capable of binding and/or neutralizing carbon dioxide in a pharmaceutical packaging or an administration material which contains one or more formulations of a HMG-CoA reductase inhibitor selected from the group consisting of pravastatin, atorvastatin, fluvastatin, cerivastatin

and pharmaceutically acceptable salts thereof, wherein said substance is contained in an element of a package or a pharmaceutical administration material separate from the HMG-CoA reductase inhibitor and said substance is defined as in claims 9 to 14."

The new **main request** corresponds to the claims of the patent as granted, with the introduction of the following passage into claims 1 and 17:

"wherein the affinity of said substance towards carbon dioxide by means of binding, neutralizing and/or reacting is higher than the respective affinity of the HMG-CoA reductase inhibitor in order to provide protective effect",

and the deletion of claims 18-21.

The new **first auxiliary request** corresponds to the claims of the patent as granted, with the introduction of the following passage into claims 1 and 17:

"wherein the affinity of said substance towards carbon dioxide by means of binding, neutralizing and/or reacting is much higher than the respective affinity of the HMG-CoA reductase inhibitor in order to provide a significant protective effect",

and the deletion of claims 18-21.

Auxiliary request 2 corresponds to the patent as granted, with the deletion of claims 20 and 21 and of the words "or a pharmaceutical administration material" from independent claims 1 and 17 and the words "or an administration material" from independent claims 17 and 18.

Auxiliary request 3 comprises independent claims 1, 17 and 18. Claim 1 reads as follows:

"A process of stabilizing a HMG—CoA reductase inhibitor selected from the group consisting of pravastatin, atorvastatin, fluvastatin, cerivastatin and pharmaceutically acceptable salts thereof against the negative effect of carbon dioxide from the air comprising the steps of combining: a) said HMG—CoA reductase inhibitor with b) a substance capable of binding and/or neutralizing carbon dioxide, wherein the components a) and b) are contained in separate elements of a package."

Claim 1 of **auxiliary request 4** reads as follows:

"Use of a substance capable of binding and/or neutralizing carbon dioxide in a pharmaceutical packaging or an administration material which contains one or more formulations of a HMG—CoA reductase inhibitor selected from the group consisting of pravastatin, atorvastatin, fluvastatin, cerivastatin and pharmaceutically acceptable salts thereof, wherein said substance is contained in an element of a package or a pharmaceutical administration material separate from the HMG—CoA reductase inhibitor and said substance is selected from the group of compounds which are effective for adsorbing, absorbing and/or neutralizing carbon dioxide and/or reacting with carbon dioxide for stabilizing the HMG—CoA reductase inhibitor."

Claim 1 of **auxiliary request 8** corresponds to claim 1 of auxiliary request 4, except that the definitions of the substance capable of binding and/or neutralising carbon dioxide have been changed from functional to

chemical ones. It reads as follows:

"Use of a substance capable of binding and/or neutralizing carbon dioxide in a pharmaceutical packaging which contains one or more formulations of a HMG—CoA reductase inhibitor selected from the group consisting of pravastatin, atorvastatin, fluvastatin, cerivastatin and pharmaceutically acceptable salts thereof, wherein said substance is contained in an element of a package separate from the HMG—CoA reductase inhibitor and said substance is selected from the group consisting of alkali metal hydroxides, alkali metal carbonates, alkali metal hydrogen carbonates and alkali metal superoxides, activated carbon, zeolites, activated aluminium oxide and Fuller's earth for stabilizing the HMG—CoA reductase inhibitor."

XII. Appellant 1's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

The new main request and the new auxiliary request had been filed at this late stage in view of the discussion during oral proceedings before the board that seemed to lead to a different outcome than in opposition proceedings. In view of this new situation the filing of amended claims was justified. There had been no need to file these amendments during the opposition proceedings or at an earlier stage of the appeal proceedings. The inclusion of the passage from the description was no surprise to the opponent, since the issue had already been discussed at length during opposition proceedings. The newly included passage was based on page 13, lines 23 to 28 of the application as originally filed. This passage mirrored the content of page 13, lines 23 to 28 and represented said content as

understood by the person skilled in the art.

For auxiliary request 1 the exact wording of said passage had been introduced. A person skilled in the art was aware of the meaning of "much higher", which was to be read as "significant", and of "significant protective effect", which relied on terms well known in statistics. Any method of measurement for the parameters now included would produce the same results. Methods for determining said parameters were known to the skilled person.

Concerning auxiliary request 2, it was stated that the substance capable of binding and/or neutralising carbon dioxide removed the carbon dioxide from the atmosphere. Due to this removal there was no carbon dioxide left that could degrade the HMG-CoA reductase inhibitor, thus leading to stabilisation. No absolute stabilisation was required; the time frame of stabilisation depended on the form of the HMG-CoA reductase inhibitor (bulk, surface-volume considerations) and the required length of the stabilisations (short-term during various stages of the production process of the medicament, longer during storage/transport of the medicament). The person skilled in the art was aware of which substances to choose and could find guidance in the description of the patent in suit.

Claim 1 of auxiliary request 3 further specified the type of stabilisation, i.e. against the negative effect of carbon dioxide from the air. The complete claim had to be assessed and the required effect had to be achieved. The achievement of the effect, which could be measured as described in the examples of the patent in suit, determined the substances to be selected. Given

the guidance of the examples it was very easy for the person skilled in the art to select appropriate substances. Further suitable substances were mentioned in other passages of the description. There was thus no undue burden for the person skilled in the art when selecting an appropriate substance.

Claim 1 of auxiliary request 4 was a use claim with the effect of stabilisation as a technical feature. There was no need to define the extent to which the HMG-CoA reductase inhibitor was to be stabilised. The person skilled in the art, guided by the disclosure of the patent application, knew how to achieve the effect. The functional feature "effective for adsorbing, absorbing and/or neutralizing carbon dioxide and/or reacting with carbon dioxide" gave a clear indication.

Auxiliary requests 5 to 13 should be admitted into the proceedings. The set of auxiliary requests presented a consistent line of defence. The features were narrowed down step by step and some of the requests included were almost identical to requests presented in the first-instance proceedings. The amendments made in the auxiliary requests addressed various arguments by the opponent or included specific embodiments. Due to unforeseeable events at the proprietor's these requests could not have been filed earlier. Not admitting auxiliary requests should be the exception; requests should be admitted as long as there was no abuse. The situation was similar as in case T 1635/09 in which the number of auxiliary requests was higher and all of them were admitted.

On the question of novelty, appellant 1 submitted that the subject-matter of auxiliary request 8 was novel over the disclosure of document (17). Document (17)

disclosed neither a separate packaging nor the purpose of stabilising an HMG-CoA reductase inhibitor by a compound capable of binding and/or neutralising carbon dioxide. Carbon dioxide is present in the air, as opposed to the acidic environment of the stomach, which was the issue in document (17). The sodium hydroxide in the enteric coating of document (17) played a role in release processes. There was no involvement of the sodium hydroxide in a stabilisation that corresponded to the subject-matter of claim 1 of auxiliary request 8.

With respect to the issue of inventive step, appellant 1 argued that document (4), like document (6), concerned protection against low pH conditions. Such protection did not correspond to protection against carbon dioxide from the air. This was reflected on page 2 of document (4), lines 40 to 43, where various destabilising conditions were listed, but where, however, the exclusion of carbon dioxide from the air was not mentioned. Document (4) did not recognise the need for protection against carbon dioxide from the air, i.e. from the gaseous phase. Document (4) provided a stabilisation in view of pH-related problems. PH-related destabilisation could be overcome only by means that were present in the same composition as the drug. The wording of claim 1 of auxiliary request 8 reflected stabilisation in view of harmful influences from the gaseous phase by defining the properties of the substances acting as the stabiliser due to being "capable of binding and/or neutralizing carbon dioxide" and by defining the separation of the sensitive drug and the substance acting as stabiliser. The stabilisation was due to the properties of the listed substances in view of carbon dioxide. Documents (1) and (2) could not lead to the subject-matter of claim 1 of

auxiliary request 8, since they dealt exclusively with desiccants, i.e. stabilisation in view of moisture. The combination of documents (4) and either (1) or (2) was the result of hind sight.

XIII. Appellant 2's arguments, insofar as they are relevant to the present decision, may be summarised as follows: The new main request and new auxiliary request 1 should not be admitted into the proceedings. They had been filed at a very late stage in the appeal proceedings, had not formed part of the first-instance proceedings, and included subject-matter from the description. These were no minor amendments and made an additional prior art search necessary. Furthermore, claim 1 of the new main request introduced subject-matter going beyond the disclosure as originally filed by omitting the terms "much" and "significant". Claim 1 of new auxiliary request 1 was not clear in view of the terms "affinity" and "significant protective effect". No method was defined for measuring the affinity.

Concerning sufficiency of disclosure for auxiliary requests 2 to 4, appellant 2 provided the following arguments: A person skilled in the art did not know whether a certain substance bound carbon dioxide or not. This lack of knowledge was aggravated by certain passages in the description of the patent in suit, cf. page 5, lines 53 to 56, where the required affinity was described as being preferably much higher than the respective affinity of the HMG-CoA reductase inhibitor. In view of the wording of claims 1 of auxiliary requests 2 to 4, the binding of said substance to carbon dioxide could be weaker than the binding to the HMG-CoA reductase inhibitor. Appellant 2 stressed that no guidance could be obtained from the examples, since the examples did not show a stabilisation effect after

70 hours. The inclusion of a further functional definition of the substance capable of binding and/or neutralising carbon dioxide by specifying that said substance was selected from the group of compounds which were effective for adsorbing, absorbing and/or neutralising carbon dioxide and/or reacting with carbon dioxide did not change appellant 2's arguments.

Auxiliary requests 5 to 13 should not be admitted into the proceedings, since they had been filed only one month before the oral proceedings. The claim sets of auxiliary requests 5 to 13 contained numerous amendments leading to a very complicated situation for appellant 2 shortly before the oral proceedings. The auxiliary requests were not converging, and no consistent line of defence as required by decision T 1685/07 existed.

Claim 1 of auxiliary request 8 was not new in view of the disclosure of document (17). Example 2 of document (17) disclosed pellets comprising pravastatin in their core. The core was coated twice, wherein the sub-coating acted as a separating layer and the outer enteric coating comprised sodium hydroxide, an alkali hydroxide capable of binding and/or neutralising carbon dioxide. Document (17) disclosed the use of enteric coatings to protect a medicament which was unstable in an acidic environment, such as the stomach, against degradation (column 2, lines 4 to 8 and 35 to 48). The activity of the sodium hydroxide lay in counteracting the acidity of the stomach. Example 2 was thus novelty-destroying for the subject-matter of claim 1 of auxiliary request 8.

In its assessment of inventive step of claim 1 of auxiliary request 8, appellant 2 relied on documents

(1), (2), (4) and (18). The closest prior art was document (4). It concerned the same technical problem as the patent in suit. The solution to the stability issues of the HMG-CoA reductase inhibitors was the addition of a basifying agent. The stability problem of document (4) was due to pH-related destabilisation (page 2, lines 40 and 41). Document (4), on page 3, lines 12 to 15, described the intimate contact of the drug substance and the alkaline medium. This description was given under the heading "preferably", thus implying that a separation of the drug and the alkaline substance was not excluded. The difference between claim 1 of auxiliary request 8 and the closest prior art lay in the explicit separation of the HMG-CoA reductase inhibitor and the stabilising agent in the form of a basifying substance. No technical effect could be linked to this difference. The objective technical problem was thus the provision of an alternative pharmaceutical formulation. Separation of the drug and the agent responsible for the stabilisation was obvious. In documents (1) and (2) a stabilising agent in the form of a desiccant was kept separate from an HMG-CoA reductase inhibitor. It was well known that the lowering of pH in pharmaceutical formulations was due to the carbon dioxide in the air. Also, it was common knowledge that substances such as sodium hydroxide, potassium hydroxide and lithium hydroxide (cf. document (18)) were not healthy. It was obvious to keep these substances separate from the composition to be ingested by the patient.

XIV. Appellant 1 requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the claims of the main or, alternatively, of the first auxiliary request, both filed during oral proceedings before the board, or, as

a further alternative, on the basis of one of the sets of claims filed as auxiliary requests 2 to 13 together with the letter of 7 September 2016.

Appellant 2 requested that the decision under appeal be set aside and that the patent be revoked. It further requested that the main request and the first auxiliary request, as filed during the oral proceedings before the board, and auxiliary requests 5 to 13 not be admitted into the proceedings.

Respondents 1 and 2 did not make any requests in the appeal proceedings.

XV. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeals are admissible.

Oral proceedings were held and the proceedings were continued in the absence of the duly summoned respondents 1 and 2 in accordance with Article 15(3) RPBA and Rule 115(2) EPC.

2. *Admission of the claim requests*

2.1 According to the Rules of Procedure of the Boards of Appeal (RPBA), appeal proceedings in inter partes cases are based on the statement(s) of grounds of appeal and the reply/replies of the other party/parties, subject to further conditions (Article 12(1),(4) RPBA). The admission of subsequent submissions (requests, facts or evidence) representing an amendment to a party's case

is at the discretion of the boards (Article 114(2) EPC and Article 13 RPBA). This discretion has to be exercised appropriately, requiring the boards to consider all relevant factors, taking into account the specific circumstances of the case. Examples of criteria to be taken into consideration by the boards when exercising their discretion include the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy (cf. Article 13(1) RPBA). These criteria are not exhaustive, and the boards have also considered aspects such as the reasons for the new submission or the extent of the amendments.

2.2 *Main request and auxiliary request 1*

The main request and auxiliary request 1 were filed at a very advanced stage of the appeal proceedings, namely at the oral proceedings before the board, after the discussion of claim language and issues of sufficiency of disclosure of the previous main request. The board does not consider that a new situation had arisen during the oral proceedings before it which might justify the filing of these requests. That a board, on the basis of arguments presented by a party, might take a different view than the department whose decision is appealed, can as such not be a surprising event as it is one of the two possibilities. In fact, both appellants submitted, by referring to the circumstance that the issue had already been discussed during the opposition proceedings, that the respective other party should not have been surprised and, hence, should have been prepared. As the patent proprietor is the party that is solely responsible for determining the text of the patent (cf. Article 113(2) EPC), it is, however, his obligation to submit amendments or possible fall-

back positions. For reasons of procedural economy and fairness to the other party this must be done at the earliest possible stage.

Furthermore, a passage from paragraph [0032] of the description of the patent in suit has now been incorporated, partially in claims 1 and 17 of the main request and completely in claims 1 and 17 of auxiliary request 1. This incorporation of a passage stemming from the description raises *prima facie* issues under Articles 123(2) and 84 EPC:

For the main request, the last sentence of paragraph [0032] of the description of the patent in suit has only been partially incorporated into the independent claims. The precise and exact meaning of the omitted terms, "much" and "significant", would have to be established in order to examine the requirement of Article 123(2) EPC. Since no straightforward conclusion as to the meaning of said terms presents itself, the board sees *prima facie* issues under Article 123(2) EPC.

Auxiliary request 1 comprises the complete incorporation of the last sentence of paragraph [0032] of the description. The meaning of some of the terms now included, for example "affinity" and "significant protective effect", immediately raises new clarity issues. In this context the board also notes the absence of a definition of the method of measuring for both the "affinity" and the "protective effect" in claim 1 of auxiliary request 1.

In view of *prima facie* issues concerning Articles 123(2) and 84 EPC, the extremely late state of the proceedings and the need for procedural economy,

the board did not admit these requests into the proceedings (Article 13(1) and (3) RBPA).

2.3 Auxiliary requests 2 to 4

The claims of auxiliary requests 2 to 4 filed together with the letter of 7 September 2016 corresponded to the claims of auxiliary requests 2 to 4 of appellant 1's statement of grounds of appeal. Consideration of these requests was neither contested by appellant 2 nor did the board see a reason to hold them inadmissible pursuant to Article 12(4) RPBA.

2.4 Auxiliary request 5 to 7

Auxiliary requests 5 to 7 were filed for the first time on 7 September 2016, after the parties were summoned to attend oral proceedings before the board, almost five years after the filing of the proprietor's appeal in December 2011 and more than four years after receiving appellant 2's letter of 4 July 2012 dealing with the auxiliary requests then on file. No new aspects arose after these stages of the written phase of the appeal proceedings. Therefore, the filing of auxiliary requests 5 to 7 cannot be seen as a timely or appropriate reaction to developments during the appeal proceedings. The admission of new requests at such a late state of the proceedings is only in keeping with the principle of procedural economy if the requests are not prima facie unsuitable to overcome the doubts as to the allowability of the claims. That is not the case here, as the objections concerning insufficiency in connection with auxiliary requests 2 to 4 (see point 3 below) would equally apply to each claim 1 of auxiliary requests 5 to 7.

The question of whether or not a consistent line of defence was pursued by appellant 1 by filing auxiliary requests 5 to 13 was therefore not relevant under the present circumstances. Nor was the decision cited by appellant 1 relevant because, in the underlying case, the substantial number of auxiliary requests had already been submitted with the statement of grounds of appeal.

In view of the above, the board decided not to admit auxiliary requests 5 to 7 into the appeal proceedings (Article 13(1),(3) RPBA).

2.5 Auxiliary request 8

The subject-matter of the claims of auxiliary request 8 is closely related to those of the auxiliary request filed on 5 September 2011 as auxiliary request 4, renumbered as auxiliary request 6 on 15 September 2011 during oral proceedings before the opposition division and relied upon in the grounds of appeal filed on 20 February 2012. Present auxiliary request 8 differs from this request, first filed on 5 September 2011, in the deletion of the terms "administration material" in claim 1. The deletion of one alternative, i.e. the alternative of having any of the ingredients contained in an "administration material", raises no complex new questions. Thus the board decided to admit auxiliary request 8 into the appeal proceedings (Article 13(1), (3) RPBA).

3. Auxiliary requests 2 to 4 - Sufficiency of disclosure

3.1 Auxiliary request 2

Claim 1 of auxiliary request 2 defines a process of

stabilising an HMG-CoA reductase inhibitor. The process requires a step of combining the HMG-CoA reductase inhibitor with "a substance capable of binding and/or neutralizing carbon dioxide". The process of claim 1 will only lead to a "stabilising" if the "substance capable of binding and/or neutralizing carbon dioxide" has a higher binding capability for carbon dioxide than the respective affinity of the HMG-CoA reductase inhibitor to carbon dioxide. Otherwise, the HMG-CoA reductase inhibitor will be involved in degradation processes while the substance capable of binding and/or neutralising carbon dioxide is inactive. This was acknowledged by appellant 1 in its letter dated 28 June 2012: "For the skilled person, it is evident from the overall teaching of the opposed patent that the substance capable of binding and/or neutralizing carbon dioxide stabilizes the HMG-CoA reductase inhibitor. Since this substance either neutralizes or binds carbon dioxide, it has to have a higher affinity to carbon dioxide compared to the affinity of the HMG-CoA reductase inhibitor to carbon dioxide. This is evident for the skilled person in view of the general common knowledge. If this prerequisite does not apply, the carbon dioxide would react with the HMG-CoA reductase inhibitor and not react with the substance capable of binding and neutralizing carbon dioxide so that as a result, this substance would not show any stabilising effect. Therefore, not every compound which binds carbon dioxide, e.g. in only traces is such a substance in the sense of the claimed invention because it would simply not function as a stabilizer" (appellant 1's letter of 28 June 2012, page 5, second paragraph).

Claim 1 of auxiliary request 2 does not indicate a strength of binding or degree of affinity towards

carbon dioxide for its substances "capable of binding and/or neutralizing carbon dioxide". When following the argumentation given above it becomes clear that substances which have a lesser affinity to carbon dioxide than the HMG-CoA reductase inhibitor will not provide a protective, stabilising effect. Such substances are however included by the definition given in present claim 1. These compounds do not make it possible to achieve the aim of the process of claim 1. Since claim 1 of auxiliary request 2 includes the combination of HMG-CoA reductase inhibitor with substances that, although capable of binding and neutralising carbon dioxide to an unspecified lesser degree, will not lead to a stabilisation of the HMG-CoA reductase inhibitor, it encompasses subject-matter that will not allow the process of stabilisation to happen.

Appellant 1 has further argued that a person skilled in the art was aware of which substances to choose and that guidance was given in the description of the patent in suit. The board cannot follow this argumentation. The appellant has provided no evidence that it was generally known which substances had a higher affinity to HMG-CoA reductase inhibitors than to carbon dioxide from the air. The description of the patent in suit simply provides a list limited to a few specific classes of compounds as suitable substances of binding and/or neutralizing carbon dioxide in the sense of the patent in suit. Also no general test for determining which substances are capable of binding and/or neutralizing carbon dioxide (from the air) in the sense of the patent in suit is disclosed. The person skilled in the art was thus not aware which substances to generally choose.

Since the claimed process does not take place over the

whole scope of claim 1 of auxiliary request 2, the process of said claim is insufficiently disclosed (Article 83 EPC).

3.2 Auxiliary request 3

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 2 only in that the stabilising is further defined as being "against the negative effect of carbon dioxide from the air". The effects due to carbon dioxide have already been considered in the discussion of auxiliary request 2. The same argumentation as for auxiliary request 2 applies to claim 1 of auxiliary request 3.

The subject-matter of claim 1 of auxiliary request 3 is insufficiently disclosed (Article 83 EPC).

3.3 Auxiliary request 4

Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 2 by a change of category and by the further definition of the substance capable of binding and/or neutralising carbon dioxide as being "selected from the group of compounds which are effective for adsorbing, absorbing and/or neutralizing carbon dioxide and/or reacting with carbon dioxide."

The functional technical feature of the use claim, namely that the use of claim 1 of auxiliary request 4 is "for stabilizing the HMG-CoA reductase inhibitor" has already been discussed for auxiliary requests 2 and 3. The same argumentation as provided for auxiliary requests 2 and 3 also applies to claim 1 of auxiliary request 4.

The further definition of the substance capable of binding and/or neutralising carbon dioxide clarifies the mechanisms underlying said binding and/or neutralising capacity. The mechanism does not however change the extent of the effect (i.e. the magnitude of stabilising) due to any strength of binding or degree of neutralising. The incorporation of the mechanism does not overcome the lack of definition concerning the substance capable of binding and/or neutralising carbon dioxide. Consequently, the argumentation set out above for auxiliary requests 2 and 3 still applies.

The subject-matter of claim 1 of auxiliary request 4 is insufficiently disclosed (Article 83 EPC).

4. Auxiliary request 8

4.1 Amendments - Article 123(2) and (3) EPC

Claim 1 of auxiliary request 8 is based on page 1, lines 4 to 14 of the description as originally filed, describing the purpose of the invention as the provision of a new concept of stabilising an HMG-CoA reductase inhibitor. Page 5, lines 8 to 12 of the description as originally filed discloses the means for this purpose as being a combination of an HMG-CoA reductase inhibitor and a substance capable of binding and/or neutralising carbon dioxide. This is also reflected on page 7, lines 1 to 4. The carbon dioxide binding and/or neutralising substance is to be separated from the element or compartment containing the HMG-CoA reductase inhibitor (page 7, lines 25 to 31, claims 19 or 20 of the application as filed). Lists of substances that are capable of binding and/or neutralising carbon dioxide are defined in claims 11 and 14 as originally filed. The HMG-CoA reductase

inhibitors now claimed are defined in claim 17 as originally filed, which has been completely incorporated into claim 1 of auxiliary request 8. All the technical features of claim 1 of auxiliary request 8 are disclosed in the application as originally filed. The dependent claims also have a basis in the original disclosure.

Claim 1 of auxiliary request 8 has been limited with regard to the claims of the patent in suit as granted.

The subject-matter of claim 1 thus fulfils the requirements of Article 123(2) and (3) EPC. This has not been contested by appellant 2.

4.2 *Claim language - sufficiency of disclosure (Articles 83 and 84 EPC)*

Claim 1 of auxiliary request 8 concerns the use of a substance for stabilising certain HMG-CoA reductase inhibitors. The stabilisation is not further defined or restricted. The substance for stabilising is selected from the group consisting of alkali metal hydroxides, alkali metal carbonates, alkali metal hydrogen carbonates and alkali metal superoxides, activated carbon, zeolites, activated aluminium oxide and Fuller's earth. The substance is contained in an element of a package separate from the HMG-CoA reductase inhibitor. Claim 1 thus defines the use of certain substances for any type of stabilisation of certain chemical compounds.

Appellant 2 no longer raised objections based on Articles 84 or 83 EPC.

The board is also satisfied that the wording of the

claims of auxiliary request 8 is clear and concise. Due to the incorporation of a list of specific classes of compounds for the substances capable of binding and/or neutralising carbon dioxide, the objections concerning sufficiency of disclosure raised in connection with higher-ranking requests have been overcome.

4.3 *Novelty (Articles 52(1) and 54 EPC)*

Appellant 2 argued that the disclosure of document (17) was novelty destroying for the subject-matter of claim 1 of auxiliary request 8.

Document (17) discusses the protection of a medicament which may degrade in a low pH environment by an enteric coating (column 2, lines 35 to 48). The medicament which may degrade in a low pH environment is for example pravastatin (example 2). Pravastatin is an HMG-CoA reductase inhibitor listed in claim 1 of auxiliary request 8. According to document (17) the medicament is contained in the core of pellets, beadlets or tablets with an enteric coating. The enteric coating provided in example 2 of document (17) comprises sodium hydroxide. Sodium hydroxide is an alkali metal hydroxide listed as one of the substances for stabilising the HMG-CoA reductase inhibitor in claim 1 of auxiliary request 8.

As explained above, sodium hydroxide is contained in the enteric coating. Said enteric coating comprises as main components hydroxypropylmethyl cellulose phthalate, triethylcitrate and talc. There seems to be no doubt that the sodium hydroxide is included in the enteric coating for a certain purpose, i.e for achieving a certain function. What remains to be

determined is whether a specific functionality is attributed to the sodium hydroxide in document (17) and whether this functionality can be directly linked to the stabilisation of the HMG-CoA reductase inhibitor. Claim 1 of document (17) defines that the hydroxypropylmethyl cellulose phthalate in the enteric coating is to be totally or at least about 80% neutralised. In example 2, sodium hydroxide is the only possible neutralising agent. The functionality of the sodium hydroxide in the enteric coating of example 2 is thus to neutralise the hydroxypropylmethyl cellulose phthalate. The effects of this neutralising on the stability of the pravastatin in the core of the pellet are not discussed in document (17). There is thus no explicit disclosure of a stabilising activity of the sodium hydroxide on an HMG-CoA reductase inhibitor.

Appellant 2 has argued that the sodium hydroxide of the enteric coating will counteract the effects due to the acidic environment of the stomach and thus contributes to the stabilising effect. Appellant 1 has asserted that the sodium hydroxide of the enteric coating will influence the release properties of the pharmaceutical composition of document (17). It questions whether it is clear that the sodium hydroxide contributes to the stabilisation.

Document (17) itself neither links the neutralising agent to the acidic environment of the stomach nor discusses release properties due to the total or partial neutralisation of the polymer forming the enteric coating. The board emphasises that for the question of novelty of a use claim it is decisive to determine whether the claimed effect has been explicitly or implicitly disclosed in the prior art. The possible inherent presence of the claimed effect is

not to be considered when examining novelty of a use claim. In document (17), the neutralisation of the hydroxypropylmethyl cellulose phthalate by sodium hydroxide is not linked to any effects. There is thus no direct and unambiguous disclosure, whether explicit or implicit, in document (17) that the sodium hydroxide itself has a stabilising effect on the HMG-CoA reductase inhibitor.

The subject-matter of claim 1 of auxiliary request 8 is new (Articles 52(1) and 54 EPC).

4.4 *Inventive step (Articles 52(1) and 56 EPC)*

The present invention relates to HMG-CoA reductase inhibitors. Claim 1 of auxiliary request 8 is a use claim and concerns the use of certain substances "for stabilizing the HMG-CoA reductase inhibitor". An important aspect of claim 1 is the separation of the stabilising substance from the HMG-CoA reductase inhibitor.

4.4.1 *Closest prior art*

The board and the appellants agree that document (4) is the closest prior art.

Document (4) relates to stabilised pharmaceutical compositions comprising an HMG-CoA reductase inhibitor (page 2, lines 1 and 2; claim 1). It is the aim of document (4) to protect the drug substance against pH-related destabilisation (page 2, lines 40 and 41). The compositions according to document (4) comprise the drug substance and an "alkaline medium". Preferably the drug substance and the alkaline medium are in "intimate contacting association" in the composition (page 3,

lines 12 to 15). Examples of alkaline substances capable of imparting the requisite basicity include sodium, potassium or lithium hydroxide (page 3, lines 30 to 34).

Document (4) prefers the intimate contact between the drug substance and the compounds responsible for the alkaline medium. An embodiment explicitly describing a separation of the drug substance from the alkaline medium is not disclosed. The difference between the subject-matter of claim 1 and the disclosure of document (4) thus lies in the separation of the HMG-CoA reductase inhibitor and the possibly alkaline substances for stabilising said inhibitor.

4.4.2 *Technical problem*

The problem to be solved in the light of the closest prior art can be seen as the provision of an alternative galenic arrangement for stabilising an HMG-CoA reductase inhibitor.

4.4.3 *Proposed solution*

The proposed solution as defined in claim 1 of auxiliary request 8 is characterised by placing specific classes of substances that are "capable of binding and/or neutralizing carbon dioxide" in an element of a package separate from the HMG-CoA reductase inhibitor.

The patent in suit provides comparative data for stability under certain test conditions. Unstabilised pravastatin is used as a control. Two test series of pravastatin stabilised in line with document (4) were provided. In the first series, sodium carbonate was

used as the alkaline substance in intimate contact with the pravastatin, in the second series disodium hydrogen phosphate was used. Both stabilised pravastatin preparations were tested under conditions of direct exposure to carbon dioxide atmosphere and under conditions of packaging in a closed polyethylene bag in the absence of a separate substance capable of binding and/or neutralising carbon dioxide. Furthermore, both stabilised pravastatin preparations were tested under conditions falling within the subject-matter of claim 1 of auxiliary request 8: the stabilised preparations were packaged in a closed polyethylene bag and stabilised by a substance capable of binding or neutralising carbon dioxide in the form of KOH or KO_2 kept in a separate jar.

Appellant 2 has argued that not only the comparative examples, but also the examples according to the invention show a pH deterioration after 70 hours, this being indicative of a lack of stabilisation. The fact is that all examples, the comparative examples and the examples according to the invention, show a decrease in pH over time. The decrease in pH is however slower than in the case of the control, which means that a stabilising effect has been shown for the examples according to the invention. Whether or not the data in table 2 allow the conclusion to be drawn that the examples according to the invention are more stable than the comparative examples is irrelevant in view of the technical problem defined in point 4.4.2 above. Also, it is not required that absolute stabilisation be achieved. The slowing down of stabilisation for a short time suffices to show that the problem defined in point 4.4.2 has been solved. The final values and the duration of stabilisation are irrelevant.

In view of the above considerations, the board is satisfied that the problem posed has been successfully solved.

4.4.4 *Obviousness*

It remains to be investigated whether the proposed solution was obvious to the skilled person in the light of the prior art.

As outlined above, document (4) itself does not suggest separating its alkaline compounds from the HMG-CoA reductase inhibitor.

Appellant 2 cited documents (1) and (2) which, it argued, led the skilled person to the subject-matter claimed.

Both documents, (1) and (2), relate to a sodium pravastatin-containing medication called "Pravachol®". The pravastatin tablets are provided in a bottle containing a desiccant canister. An item that is responsible for stabilisation against humidity is thus provided separately from the composition comprising the HMG-CoA reductase inhibitor.

Appellant 2 pointed out that these documents disclose the provision of stabilisation means separate from the unit comprising the drug.

However, these documents relate to a very specific type of stabilisation, i.e. against humidity. None of the substances listed in present claim 1 as being capable of binding and/or neutralising carbon dioxide has been identified as a desiccant for use in pharmaceutical packaging.

The alkaline medium in document (4) is added to the drug with the aim of controlling the pH of the intimate environment of the HMG-CoA reductase inhibitor. In document (4) there is no indication that the gaseous environment is implicated in the pH-related destabilisation. Starting from the disclosure of document (4), the person skilled in the art has no incentive to look for an alternative system for stabilisation that involves the gaseous phase surrounding the composition comprising the HMG-CoA reductase inhibitor. He would thus not consult documents dealing with stabilisation against humidity, i.e. with a clear involvement of the gaseous phase, such as documents (1) and (2).

4.4.5 *Conclusion*

In view of the above, the board concludes that the subject-matter of claim 1 of auxiliary request 8 involves an inventive step. The same applies to the dependent claims. Accordingly, the subject-matter of the claims of auxiliary request 8 meets the requirements of Articles 52(1) and 56 EPC.

4.4.6 *Further arguments of appellant 2*

Appellant 2 has further argued that in view of document (18) a person skilled in the art would have seriously contemplated keeping basifying agents that pose a threat to the health of the patient, such as lithium hydroxide, separate from the composition comprising the HMG-CoA reductase inhibitor. The board cannot accept this argumentation. In the preceding paragraphs the assessment of inventive step of the invention as claimed in auxiliary request 8 starting from document

(4) is set out. The argumentation by appellant 2 presented for lithium hydroxid based on a characteristic of said chemical compound that is not common to all basifying agents described in document (4) and that is not addressed in document (4) or documents (1) and (2), can only be seen as an unallowable *ex post facto* analysis.

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 in amended form on the basis of claims 1 to 4 of auxiliary request 8 filed together with the letter of 7 September 2016, and with a description and drawings to be adapted thereto.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated