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**Datasheet for the decision
of 17 June 2009**

Case Number: T 1630/08 - 3.3.01

Application Number: 91908435.0

Publication Number: 0594612

IPC: C07J 9/00

Language of the proceedings: EN

Title of invention:

A substance for lowering high cholesterol level in serum and a method for preparing the same

Patentee:

Raisio Benecol Ltd.

Opponent:

-

Headword:

Sitostanol esters/RAISIO

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"Admission of claims amended after the remittal to the first instance (yes)"

"Binding effect of an appeal decision limited to the ratio decidendi"

"Inventive step (yes) - non obvious solution"

Decisions cited:

G 0004/93, T 1206/01, T 0796/02, T 0609/94

Catchword:

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Case Number: T 1630/08 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 17 June 2009

Appellant: Raisio Benecol Ltd.
(Patent Proprietor) Raisionkaari 55
FI-21200 Raisio (FI)

Representative: Kirsch, Susan Edith
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
16 June 2008 concerning maintenance of European
patent No. 0594612 in amended form.

Composition of the Board:

Chairman: P. Ranguis
Members: C. M. Radke
D. S. Rogers

Summary of Facts and Submissions

- I. An opposition was filed against European patent no. 0 594 612 based on grounds under Article 100(a), (b) and (c) EPC.

The opposition division, in its first decision posted on 11 October 2001, revoked the patent. It deemed that the subject-matter of the claims did not involve an inventive step in view of the disclosure of document (D9) if combined with that of documents (D6) and (D7).

The patent proprietor filed an appeal against this decision.

With the decision T 1206/01 of 23 September 2004, the board rendered its first decision in this matter, deciding:

- to set aside the decision of the opposition division revoking the patent,
 - that claims 1 and 2 of the second auxiliary request met the requirements of Article 123(2) and (3) EPC and that they were clear according to Article 84 EPC, and
 - to remit the case to the first instance for further prosecution based on the second auxiliary request filed during the oral proceedings before the board.
- II. The only opponent withdrew its opposition with a letter dated 23 January 2008.

- III. In the proceedings before the opposition division following the board's decision T 1206/01, the opposition division issued a second decision posted on 16 June 2008 in which it
- decided not to admit the claims of the main request and of auxiliary requests 1 to 3 (all four requests filed with a letter dated 01 April 2008) to the proceedings; and
 - decided that the patent amended according to auxiliary request 4 filed with a letter dated 01 April 2008 met the requirements of the EPC.

The opposition found that the patentee had withdrawn auxiliary request 10, which contained product claims, before the board of appeal in appeal T 1206/01, thereby depriving said board of the opportunity to decide on them. The reintroduction of such claims after the remittal of the case to the opposition division was considered to be an abuse of the proceedings.

- IV. The second decision of the opposition division was based on the following sets of claims, all filed with a letter dated 01 April 2008:

Claims 1-5 of the Main Request,
claims 1-4 of Auxiliary Request 1,
claims 1-3 of Auxiliary Request 2,
claims 1-3 of Auxiliary Request 3, and
claims 1 and 2 of Auxiliary Request 4.

- (a) Claims 1 and 2 of the main request and the auxiliary requests 1 to 4 are identical and read as follows:

"1. A process for the preparation of a substance comprising a β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture in which free β -sitostanol is esterified with a fatty acid ester or a fatty acid ester mixture in the presence of an interesterification catalyst, wherein no substances other than free stanol, a fatty acid ester or a fatty acid ester mixture and a catalyst are used in the esterification reaction."

"2. A process according to claim 1, characterized in that the reaction is carried out at a temperature of approx. 90-120°C and under a vacuum of approx. 0.67-2.0 kPa."

These claims are identical to the claims of the second auxiliary request on the basis of which the decision T 1206/1 remitted the case to the opposition division (see point I above).

(b) Claim 3 to 5 of the Main Request filed with the letter dated 01 April 2008 read as follows:

"3. A substance for use in lowering cholesterol levels in serum comprising a β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture obtainable by a process according to claim 1 or claim 2."

"4. A substance comprising a β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture for use in lowering cholesterol levels in serum, wherein the β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture is

present in an amount effective to lower the cholesterol level in serum of a subject consuming the substance."

"5. A substance comprising a β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture for use in lowering cholesterol levels in serum, wherein the β -sitostanol fatty acid ester or a β -sitostanol fatty acid ester mixture are manufactured using a process comprising an esterification reaction, wherein no substances other than free stanol, a fatty acid ester or a fatty acid ester mixture and a catalyst are used in the esterification reaction."

V. The patent proprietor filed an appeal against this second decision of the opposition division (hereinafter called the decision under appeal).

VI. The Appellant filed a Main Request with claims 1-5 with a letter dated 10 June 2009.

These claims 1-5 are identical to the claims of the main request on which the decision under appeal is based (see point IV above), with the exception that in claim 5 the term "a catalyst" was replaced by "an interesterification catalyst" (see point IV (b) above).

VII. The following documents were *inter alia* cited during the present appeal proceedings:

(D1) GB-A-1 405 346

(D6) F. H. Mattson et al., J. Nutrition, vol. 107 (1977), 1139-1146

- (D7) F. H. Mattson et al., *The American Journal of Clinical Nutrition*, vol. 35 (1982), 697-700
- (D9) T. Heinemann et al., *Atherosclerosis*, vol, 61 (1986), 219-223
- (D18) Efficacy of spreads enriched with stanol-stearate esters on blood cholesterol levels, Annex I to opponent's letter dated 27 June 2000
- (D28) T. A. Miettinen et al., *American Journal of Epidemiology*, vol. 131, no. 1 (1990), 20-31
- (D37) Representation of "ball and stick" models of the molecular structures of sitosterol and sitostanol, presented by the opponent at the oral proceedings before the opposition division on 19 September 2001
- (D39) Representation of "ball and stick" models of the molecular structures of sitostanol, sitosterol and cholesterol, filed by the patent proprietor with the letter dated 21 February 2002 setting out the grounds for appeal in the case T 1206/01
- (D40) L. Swell et al., *Proc. Soc. Exp. Biol. Med.*, vol. 87 (1954), 216-218
- (D47) B. Borgström and H. L. Brockman (ed.), *Lipases*, Elsevier, Amsterdam/NL, 1984, 185-204
- (D48) H. Brockerhoff and R. G. Jensen, *Lipolytic Enzymes*, Academic Press, New York/US, 1974, 176-193
- (D63) Doctoral thesis of S. J. Avart, Drexel University, June 1985, pages i-x and 1-107

VIII. The arguments of the Appellant may be summarised as follows.

- (a) Following the board's decision in T 1206/01, it had the right to add claims 3 to 5 to the set of

claims of the second auxiliary request that was remitted to the opposition division because claim 11 of the main request before the board in T 1206/01 had not been withdrawn and was never objected to by the board and thus was not res judicata. The case law of the board of appeals did not object to the filing of new claims unless they contravened the ratio decidendi of the decision of the board (see T 609/94, point 2.1 of the reasons).

- (b) The subject-matter of claims 3 to 5 of the Main Request was novel as document (D1) does not disclose the hydrogenation of the sitosterol ester.
- (c) Starting from document (D9) as the closest prior art the person skilled in the art would not have replaced β -sitostanol by its esters as he would not have expected that these esters would be hydrolysed as fast as the respective β -sitosterol esters by cholesterol esterase, because
 - the conformations of these compounds are not similar (see documents (D37) and (D39), and
 - cholesterol esterase is substrate specific (see document (D40)).

The hydrolysis of the sterol and stanol esters to the active species had to be fast for an efficient lowering of cholesterol absorption (which takes place in the upper part of the small intestine).

It was not obvious to use a larger amount of stanol ester as document (D6) teaches that amounts of sterol esters larger than 4% by weight in the

dietary fat do not lead to a higher efficiency in lowering the cholesterol absorption.

- IX. The Appellant requested
- that the decision under appeal be set aside,
 - that claims 1-5 of the Main Request filed with a letter dated 10 June 2009 be admitted to the proceedings, and
 - that the patent be maintained on the basis of this set of claims.
- X. At the end of the oral proceedings the decision of the Board was announced.

Reasons for the Decision

1. The appeal is admissible.
2. *Admission of the amended Claims*
 - 2.1 In its reasons for rejecting the main request and auxiliary requests 1 to 3 (see point III above), the opposition division referred to the decision T 796/02 of 1 April 2004. In this decision it is stated that "... it amounts to an abuse of procedure to withdraw a request with broader claims in proceedings before the board of appeal, in order to avoid that a negative decision be taken on it by the board, but then to re-introduce those broader claims before the opposition division, having obtained remittal of the case for further prosecution on the basis of much more limited claims." (see point 13 of the reasons for the decision).

2.2 The Appellant defended the patent in suit during the first appeal proceedings (T 1206/01) on the basis of the claims of the main request, auxiliary requests 1 and 2. The respective decision of the board of 23 September 2004 gives reasons why the main request could not be granted (see point 2.1 of the reasons for the decision). Hence, this main request was not withdrawn before the board before the decision in T 1206/01 was reached. This main request comprised claims 1 to 12 filed on 23 August 2004, claim 11 reading as follows:

"11. A substance comprising an amount of a β -sitostanol fatty acid ester or a mixture of β -sitostanol fatty acid esters effective to lower the cholesterol level in serum of a subject consuming the substance for use in lowering cholesterol levels in serum."

The scope of this claim is equivalent to that of claim 4 of the main request in these proceedings and is broader than that of claims 3 and 5 (relating to a first medical use) on which the decision under appeal is based (see point IV(b) above).

Therefore, the Appellant did not withdraw any broader claims during the appeal T 1206/01. Thus the facts of this case do not support a finding of an abuse of proceedings under the principles set out in T 796/02.

2.3 Hence, it remains to be determined whether or not there are further reasons preventing the Board from admitting the amended claims of the Main Request into the proceedings, namely whether or not the decision

T 1206/01 prevents the Board from admitting claims 3 to 5 of the Main Request.

- 2.3.1 In the appeal T 1206/01 the board decided to remit the case to the first instance "for further prosecution on the basis of the second auxiliary request submitted at the oral proceedings on 23 September 2004."

The expression "on the basis of" does not strictly exclude any amendments in the set of claims, such as the addition of claims (see the decision T 609/94 of 27 February 1997, the headnote and points 2.1 to 2.3 of the reasons).

- 2.3.2 Decision T 609/94 states that such claims may be admitted unless they contravene the *ratio decidendi* of the decision of the board by which the case was remitted.

In the T 1206/01 decision, the board considered that the term "solvent-free" in amended claim 1 of the main request and the term "adapted to provide ... at a daily dose of 0.2 - 20 g/d" in amended claim 1 of the first auxiliary request contravened the requirements of Article 123(2) EPC and rejected these requests.

These terms objected to by the board in the decision T 1206/01 do not form part of the wording of any of the claims of the present Main Request.

Hence, the admission of the claims of the Main Request does not contravene the *ratio decidendi* of decision T 1206/01.

2.4 In view of these reasons the Board exercised its discretion to admit the claims of the Main Request into the proceedings.

3. *Reformatio in peius*

3.1 Claims 1 and 2 of the Main Request are identical to the claims that the decision under appeal decided met the requirements of the EPC, namely with claims 1 and 2 of auxiliary request 4 filed with a letter dated 01 April 2008 (see points III and IV above).

3.2 "If the patent proprietor is the sole appellant against an interlocutory decision maintaining a patent in amended form, neither the Board of Appeal nor ... may challenge the maintenance of the patent as amended in accordance with the interlocutory decision." (decision G 04/93, OJ EPO 1994, 875, point 1 of the order).

3.3 The patent proprietor being the sole Appellant, the Board may not challenge the decision of the opposition division that claims 1 and 2 of the Main Request meet the requirements of the EPC. Therefore, the Board will only examine the remaining claims of the Main Request.

4. *Article 123 EPC*

Claims 3 to 5 have their basis in original claims 1 and 8 and page 6, line 34, to page 7, line 2 of the application as filed.

These claims do not extend the protection with respect to claim 11 as granted.

Hence, these claims do not contravene the requirements of Article 123(2) and (3) EPC.

5. *Novelty*

5.1 Claims 3 to 5 of the Main Request are directed to β -sitostanol fatty acid esters for use in lowering cholesterol levels in serum.

5.2 This subject-matter differs from that disclosed in
- document (D1) disclosing in example 2 the esterification of β -sitosterol with sunflower oil fatty acid ethyl ester; and from that disclosed in
- document (D9) disclosing β -sitostanol but not its esters.

Nor do any of the other prior art documents cited in the opposition and appeal proceedings disclose β -sitostanol fatty acid esters.

5.3 Therefore, the subject-matter of claims 3 to 5 of the Main Request is novel.

6. *Inventive step*

6.1 *Closest prior art*

The closest prior art is normally a prior art document disclosing subject-matter with the same objectives and having the most relevant technical features in common with the claimed invention.

The objective of claims 3 to 5 is to lower the serum levels of cholesterol (see points IV (b) and 5.1 above).

Document (D1) has a different objective, namely "... to protect free sterols contained in vegetable and animal oils and fats against possible changes during processing in a simple and effective manner and equally to convert higher proportions of added free sterols into a readily soluble form." (see page 2, lines 12-18). Thus it does not qualify as the closest prior art.

Document (D9) reports that β -sitostanol when administered to patients with hypercholesterolemia lowers their serum cholesterol levels (see the summary). Hence it has the same objectives as present claims 3 to 5 and is considered to represent the closest prior art.

6.2 *The problem to be solved*

The patent in suit mentions on page 4, lines 8-11, that the results listed in Table 1 on page 6 "... show that an intake of β -sitostanol ... - i.e in the form of fatty acid esters - reduced the absorption of plant sterols more effectively than did free β -sitostanol taken in the same dosage."

Table 1 on page 6 shows that a β -sitostanol ester more effectively lowers the serum levels of campesterol as does the respective amount of free β -sitostanol.

According to page 2, lines 37-38 "Usually the campesterol concentrations in serum in particular

reflect the degree of absorption (10, 11, 12)", where reference 11 is identical with document (D28) (see page 7, lines 56-57 of the patent in suit). This statement is confirmed in document (D28) which concludes that the serum levels of plant sterols, and in particular campesterol, reflect the absorption efficiency of dietary cholesterol (see the left column on page 29, the second sentence in the bottom paragraph).

Therefore, the results listed in Table 1 of the patent in suit, namely the higher decrease in the serum level of campesterol, does indeed show that a β -sitostanol ester is at least as effective as β -sitostanol in lowering the absorption of dietary cholesterol.

Hence, the problem posed in the patent was to provide a dietary cholesterol absorption inhibitor which is at least as effective as β -sitostanol (which is disclosed in document (D9)).

In view of the test results listed in Table 1 of the patent in suit, the Board has no doubt that this problem is solved over the whole breadth of the claims.

6.3 *Solution of the problem*

- 6.3.1 Document (D7) discloses that β -sitosterol and its oleic acid ester decrease the absorption of dietary cholesterol (see the abstract). The document comments as follows on the finding that the ester is less effective than the sterol:

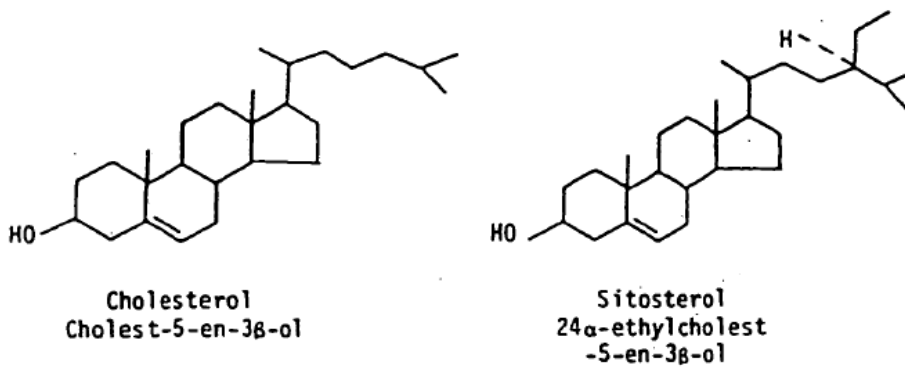
- "One possibility is that the sterol ester was incompletely hydrolyzed in the lumen of the intestine. Only when it is present as the free sterol can β -sitosterol ... decrease cholesterol absorption." (see (D7), the penultimate paragraph on page 699).
- 6.3.2 Hence, documents (D9) and (D7) inform the person skilled in the art that β -sitostanol and β -sitosterol decrease cholesterol absorption, and that β -sitosterol esters have the same effect only to the extent that the ester bond is hydrolysed in the lumen of the intestine to yield free β -sitosterol.
- 6.3.3 Therefore, the person skilled in the art could only expect β -sitostanol esters to be as effective as the free β -sitostanol in decreasing the absorption of cholesterol, if the esters were quickly and completely hydrolysed in the lumen of the intestine, i.e. more quickly and completely than those of β -sitosterol.
- 6.3.4 The enzyme catalysing the hydrolysis of sterol esters in the lumen of the intestine is pancreatic cholesterol esterase (see document (D47), the first sentence of chapter 1 on page 185). This enzyme is rather unspecific (see document (D47), the paragraph bridging pages 188 and 189; document (D48), the third paragraph on page 192; document (D63), the second paragraph on page 79).

Hence, the person skilled in the art who had the task of providing a dietary cholesterol absorption inhibitor which was at least as effective as β -sitostanol would not have considered testing β -sitostanol esters if he expected that these esters were not hydrolysed in the

presence of pancreatic cholesterol esterase more quickly and completely than β -sitosterol esters.

6.3.5 Document (D40) reports on the hydrolysis of certain butyric acid esters in the presence of pancreatic cholesterol esterase. After two hours 77.4 % of dihydrocholesterol butyrate, 92.6 % of cholesterol butyrate and 92.0 % of β -sitosterol butyrate are hydrolysed (see Table I on page 217).

Cholesterol and β -sitosterol have the following formulae



(see document (D63), page 14).

The formula of dihydrocholesterol differs from that of cholesterol, and that of β -sitostanol differs from that of β -sitosterol only in that the carbon-carbon double bond is hydrogenated to form a single bond.

Due to the fact that the butyrates of cholesterol and β -sitosterol show almost the same rate of hydrolysis, the person skilled in the art would conclude that the difference in structure between these two molecules - namely the absence or presence of the 24 α -ethyl group - has practically no effect on the hydrolysis rate.

However, cholesterol butyrate is hydrolysed considerably faster than dihydrocholesterol butyrate. The person skilled in the art would thus conclude that the hydrogenation of the double bond would lead to a decrease in the rate of hydrolysis. Consequently, he would expect that the rate of hydrolysis also decreased when a β -sitosterol ester was replaced by the respective dihydro- β -sitosterol ester, i.e. the β -sitostanol ester.

For these reasons, the person skilled in the art would have expected that a β -sitostanol ester would hydrolyse more slowly and thus to be a less effective cholesterol absorption inhibitor than the respective β -sitosterol ester.

6.3.6 Consequently, the person skilled in the art in charge of providing a dietary cholesterol absorption inhibitor which is at least as effective as β -sitostanol would not test β -sitostanol esters as he would expect due to the disclosure of document (D40) that such esters would not hydrolyse speedily and completely enough *in vivo* to set free completely the active agent, i.e. β -sitostanol, in the lumen of the intestine where the absorption of cholesterol occurs.

6.3.7 Therefore, the subject-matter of claims 3 to 5 of the main Request is based on an inventive step.

7. *Other grounds for opposition*

7.1 *Article 100(b) EPC*

The opponent raised grounds under Article 100(b) EPC relating to certain features of the process claims. No argument that the information in the patent in suit did not enable the person skilled in the art to prepare β -sitostanol esters was put forward by the opponent. Therefore, this objection does not apply to claims 3 to 5 of the Main Request.

The allegation of the opponent that the β -sitostanol esters did not lower blood cholesterol levels was based on experimental evidence (D18). However, the sitostanol ester enriched spread administered to the patients according to document (D18) differed from the control spread not only in the presence of sitostanol ester; it also had a different triglyceride content and a considerably lower content of polyunsaturated fatty acids (28 vs. 35 percent by weight; see the penultimate page of the document). The experimental results thus are not strictly comparative and cannot support the opponent's arguments.

7.2 *Article 100(c) EPC*

7.2.1 Amendments in the claims

The objection raised related to the reference to the term "medicament" in claim 10 as granted. It does not apply to the present claims which do not contain this term.

7.2.2 Amendments in the description

As the opposition division pointed out in its decision posted on 11 October 2001, the amendments objected to were merely concerned with bringing the English translation into conformity with the original Finnish text of the application (see point 2.3 of the reasons of the decision). Hence, these amendments are admissible under Article 14(2) EPC, both in the 1973 and the 2000 versions.

8. *Adaptation of the description to the amended claims*

The Board is satisfied that the amended pages of the description received during the oral proceedings of 17 June 2009 adapt the description to the amended claims and remove an obvious error.

9. Consequently, the patent as amended according to the Main Request meets the requirements of the EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. Claims 1 to 5 of the Main Request filed with the letter dated 10 June 2009 are admitted into the proceedings.
3. The case is remitted to the department of first instance with the order to maintain the patent as amended in the following version:

Description:

Pages 2 and 4 to 8 of the patent specification;
amended pages 3 and 9 of the patent specification
received during the oral proceedings on 17 June 2009.

Claims:

Claims 1 to 5 of the Main Request filed with the letter
dated 10 June 2009.

The Registrar:

The Chairman:

M. Schalow

P. Ranguis