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Datasheet for the decision of 17 February 2016

Case Number: T 2197/11 - 3.3.01

Application Number: 00961529.5

Publication Number: 1218001

IPC: A61K31/205, A61K9/14, A23L1/305

Language of the proceedings: EN

Title of invention:
ULTRAFINE L-CARNITINE, METHODS OF PREPARING THE SAME, COMPOSITIONS CONTAINING THE SAME, AND METHODS OF USING THE SAME

Patent Proprietor:
SIGMA-TAU Industrie Farmaceutiche Riunite S.p.A.

Opponents:
Lonza Ltd
Mitsubishi Rayon Co. Ltd.

Headword:
Size-reduced L-carnitine acid fumarate/SIGMA-TAU

Relevant legal provisions:
EPC Art. 54, 56, 123(2)
RPBA Art. 12

Keyword:
Requests and documents filed with the statement of grounds of appeal: admitted (yes)
Document admitted by opposition division: discretion correctly exercised (yes)
Oral submission by inventor (yes)
Main request and first to third auxiliary requests: Novelty (yes)
Main request and first to third auxiliary requests: Inventive step (no) - obvious modification
Fourth to sixth auxiliary requests: Amendments - extension beyond the content of the application as filed (yes)
Seventh auxiliary request: admitted (no)

Decisions cited:
G 0007/93, G 0004/95, T 0990/96, T 0467/08, T 0131/03

Catchword:

Europäisches Patentamt
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Case Number: T 2197/11 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 17 February 2016

Appellant: (Patent Proprietor)	SIGMA-TAU Industrie Farmaceutiche Riunite S.p.A. Viale Shakespeare, 47 00144 Rome (IT)
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Respondent 1: (Opponent 1)	Lonza Ltd Münchensteinerstrasse 38 4052 Basel (CH)
Representative:	Steglich, Gregor Banse & Steglich Patentanwaltskanzlei Herzog-Heinrich-Straße 23 80336 München (DE)
Respondent 2: (Opponent 2)	Mitsubishi Rayon Co. Ltd. 6-41, Konan 1-chome Minato-ku Tokyo 108-8506 (JP)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 1 August 2011 revoking European patent No. 1218001 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman A. Lindner
Members: G. Seufert
M. Blasi

Summary of Facts and Submissions

I. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division revoking European patent No. 1 218 001.

II. The present decision refers to the following documents:

(3a) US 4,602,039
(7) WO 99/38505
(8) Arzneiformenlehre, fourth edition, Wissenschaftliche Verlagsgesellschaft, Stuttgart, 1985, page 529
(9) WO 99/27925
(14T) Partial Translation of passages from A. Otsuka *et al.*, Textbook of Pharmaceutics, 1997, one page
(15) Pharmaceutics, The Science of Dosage Form Design, second edition, Churchill Livingstone, 2002, pages 169 to 172
(17) "Quality Expert Interim Report, Workability characteristics of Ultrafine L-carnitine fumarate Vs L-carnitine fumarate", dated 12 July 2010, signed by L. Fabrizi, pages 1 to 13
(18) "Hygroscopicity of Ultrafine L-Carnitine tartrate Vs L-Carnitine tartrate", dated 29 March 2011, signed by L. Fabrizi, pages 1 to 4
(18a) US 5,073,376
(21) Handbook of Pharmaceutical Excipients, 1986, "Colloidal Silicon Dioxide", pages 253 to 256
(22) Declaration by L. Fabrizi, dated 17 May 2011, two pages
(23a) SciFinder®: Substance information: L-carnitine acid fumarate (ID 4), 2011, two pages

(23b) SciFinder®: Substance information: L-carnitine fumarate (ID 7), 2011, two pages

(24a) Biosint, Certificate of Analysis, L-carnitine fumarate dated 21 July 2010, one page

(24b) BIOSINT, Material Safety Data Sheet, L-Carnitine fumarate, dated 9 March 2004, pages 1 to 4

(25a) "Synthesis of L-carnitine fumarate", pages 1 to 3, dated 12 December 2011

(25b) "Particle Size Distribution Estimation by Analytical Sieving", L-carnitine acid fumarate ultrafine, one page

(25c) "Comparison of L-carnitine acid fumarate ultrafine and L-carnitine acid fumarate", two pages

(25d) "Angle of repose" of samples B1 to B3, pages 1 to 2

(26a) Product information: "Aerosil 300 fumed silica", http://www.alibaba.com/product-free/111474600/Aerosil_300_fumed_silica.html, one page

(26b) OECD SIDS, "Synthetic Amorphous Silica and Silicates", UNEP publications, pages 1, 2 and 11

(27) Declaration by R. Chopra, dated 7 March 2003, pages 1 to 6

(30) Evonik Industries, "Sipernat® and Aerosil® - an Essential in Industrial Powder Technology", Technical Information 1360, twelve pages

(31) Evonik Industries, "Sipernat® and Aerosil® as Flow Aid and Anticaking Agent", twelve pages

(36) Pharmaceutical Dosage Form, Tablets, second edition, Vol. 2, 1990, Marcel Dekker, Inc., New York, pages 107 to 112

(42) Pubchem database, Substance information l-carnitine fumarate, ten pages, attached to the board's communication accompanying the summons

III. Notices of opposition were filed by opponents 1 and 2 (respondents 1 and 2) requesting revocation of the patent in suit in its entirety on the grounds of lack of novelty, lack of inventive step and insufficiency of disclosure (Article 100(a) and (b) EPC).

IV. The opposition division held that the subject-matter of claims 1 and 7 of the main request was anticipated by document (7), which disclosed micronised acetyl-L-carnitine. The same applied to claim 1 of the auxiliary requests 1 to 3. The subject-matter of auxiliary request 4, after amendment, was considered to be novel, but was held to be obvious starting from document (9) as the closest state of the art. The same applied to auxiliary request 5. Auxiliary requests 6 and 7 were considered to contravene Article 123(2) EPC, as they encompassed a composition which had no basis in the application as originally filed. The opposition division also decided to admit documents (18) and (22) into the proceedings.

V. With the statement of grounds of appeal, the appellant filed a main request, first to sixth auxiliary requests and documents (23a) to (27).

The main request consists of five claims with claim 1 reading as follows:

"1. L-carnitine acid fumarate or L-carnitine tartrate having a particle size such that it passes through a 100 USBS mesh sieve."

Independent claims 2 and 3 are directed to a method of preparing these compounds and a composition comprising them.

The first auxiliary request differs from the main request in that independent claim 3 and its dependent claims have been deleted.

The second auxiliary request differs from the main request in that L-carnitine tartrate has been removed from the claims.

The third auxiliary request differs from the main request in that L-carnitine tartrate has been removed from claims 1 and 2, and independent claim 3 and its dependent claims have been deleted.

The fourth auxiliary request consists of three claims with independent claim 1 reading as follows:

"1. A composition, comprising:
L-carnitine acid fumarate, and
food grade fumed silica having an overall surface area of 190-475 m^2/g and a tapped density of 80-275 g/l, wherein said L-carnitine acid fumarate has a particle size such that it passes through a 100 USBS mesh sieve."

The fifth auxiliary request consists of a single claim reading as follows:

"1. A composition consisting of:
L-carnitine acid fumarate having a particle size such that it passes through a 100 USBS mesh sieve; and food grade fumed silica having an overall surface area of 190-475 m^2/g and a tapped density of 80-275 g/l."

The sixth auxiliary request differs from the fifth auxiliary request in that the following features were added to the claim:
"wherein the composition is obtainable by:

(1) subjecting L-carnitine acid fumarate having a particle size such that it does not pass through a 100 USBS mesh sieve to size reduction to obtain size-reduced L-carnitine acid fumarate; and

(2) subjecting said size-reduced L-carnitine acid fumarate to sieving through a 100 USBS mesh sieve and selecting that portion which passes through said 100 USBS mesh sieve; and

(3) blending said portion which passes through said 100 USBS mesh sieve with hydrophobic food grade fumed silica having an overall surface area of 190-475 m^2/g and a tapped density of 80-275 g/l."

VI. With reply to the statement of grounds of appeal, respondent 1 filed a number of documents, including documents (18a), (30) and (31).

VII. In a communication accompanying the summons to oral proceedings the board expressed its preliminary opinion. In particular, the board raised concerns as to whether the amendments in the fourth to sixth auxiliary requests complied with Article 123(2) EPC. With regard to inventive step, it was indicated that one of the issues to be discussed at the oral proceedings would be whether the experimental data provided by the appellant were pertinent in demonstrating that the alleged advantages had their origin in the distinguishing feature.

VIII. By letter of 29 January 2016, respondent 2 informed the board that it would not be attending the oral proceedings.

IX. At the oral proceedings before the board, the appellant filed a seventh auxiliary request, which consists of a single claim reading as follows:

"1. A method of preparing a composition consisting of: L-carnitine acid fumarate having a particle size such that it passes through a 150 USBS mesh sieve; and food grade fumed silica having an overall surface area of 190-475 m^2/g and a tapped density of 80-275 g/l, the method comprising the following steps:

(1) milling L-carnitine acid fumarate having a particle size such that it does not pass through a 150 USBS mesh sieve to obtain size-reduced L-carnitine acid fumarate; and

(2) subjecting said size-reduced L-carnitine acid fumarate to sieving through a 150 USBS mesh sieve and selecting that portion which passes through said 150 USBS mesh sieve; and

(3) blending said portion which passes through said 150 USBS mesh sieve with food grade fumed silica having an overall surface area of 190-475 m^2/g and a tapped density of 80-275 g/l."

X. The arguments of the appellant, as far as they concern the decisive issues, can be summarised as follows:

- Requests and documents filed with the statement of grounds of appeal and document (18)

The sets of claims filed with the statement of grounds of appeal were not intended to change the subject-matter and to create a fresh case, as alleged by respondent 1, but were an attempt to resolve the confusion which originated from the name "L-carnitine fumarate" used in example 1 of the patent in suit and document (17). The weight ratio mentioned in example 1 corresponded to the 1:1 salt of L-carnitine and fumaric acid (i.e. L-carnitine acid fumarate). It was also clearly stated in document (17) that the L-carnitine salt that was used

therein had been prepared according to example 8 of document (3a), which disclosed the preparation of L-carnitine acid fumarate. The confusion arose from the fact that the provider BIOSINT used the name "L-carnitine fumarate" for its 1:1 salt, as was apparent from the indicated CAS registry number in documents (24a)/(24b) and (23a).

The submission of documents (25a) to (25d) was a genuine attempt to overcome deficiencies in the experimental evidence of documents (17) and (18) emphasised in the decision under appeal. The flow behaviour was derivable from the patent in suit and could therefore be relied upon to support an inventive step. The experiments described in documents (25a) to (25d) were reproducible and the results, in particular the comparison between samples B0 and B3, showed that the improvement in flow behaviour had its origin in the distinguishing feature.

- Oral submissions by the inventor

With regard to inventive step, incentives and disincentives for reducing the particle size needed to be carefully considered. In this framework, the hygroscopicity of the target substance was particularly relevant. Mr Hassen's comments concerned the alleged lack of hygroscopicity mentioned in the closest state of the art and how this alleged lack was actually perceived in the pharmaceutical and food industry.

- Novelty

The subject-matter of claim 1 of the main request was novel over documents (3a) and (18a). None of these documents directly and unambiguously disclosed L-carnitine acid fumarate or L-carnitine tartrate having

the claimed particle size. Document (15) was not pertinent in this context, because the size reduction and sieving steps described therein resulted in a much wider range of particle sizes than presently claimed. For the same reasons, the subject-matter of claim 1 of the first to third auxiliary requests was novel.

- Inventive step

The subject-matter of claim 1 of the main request involved an inventive step. Starting from document (3a), the problem to be solved by the present invention was the provision of L-carnitine acid fumarate with improved flow behaviour and very low hygroscopicity.
Documents (25a) to (25d), in particular the comparison of sample B3 with sample B0 in document (25c), were evidence that this problem had been successfully solved. Document (25a) was a faithful reproduction of example 8 of document (3a). There was also no justification for the assumption that different mixing conditions, which allegedly could affect the flow behaviour, were applied in samples B3 and B0. Contrary to the statement in document (3a), the L-carnitine acid fumarate disclosed therein was still quite hygroscopic and caused problems in the formulation of capsules or tablets, whereas document (17) showed the extremely low hygroscopicity of L-carnitine acid fumarate according to the invention. The person skilled in the art had no incentive to reduce the particle size, as it was known that fine powders tended to cake more than coarser material and therefore flowed badly. Additional disincentives were high energy, time and equipment costs and potential disadvantages linked to size reduction such as possible degradation by oxidation and adsorption of unwanted moisture due to an increase in surface area. Furthermore, an increase in bioavailability was only expected for poorly soluble

compounds, which was not the case for the claimed compound. The same reasoning applied to claim 1 of the first to third auxiliary requests.

- Amendments

The subject-matter of the fourth auxiliary request found its basis in claims 7 and 9, page 5, lines 8 to 10, page 7, lines 1 to 5 and example 1 of the application as originally filed. Claims 7 and 9 disclosed the combination of L-carnitine acid fumarate having the required particle size with a pharmaceutical carrier. The passages on pages 5 and 7 disclosed the presence of silica, which was a suitable pharmaceutical carrier, and the working example illustrated how the invention was put into practice. In particular, it disclosed suitable types of silica with the required surface area and tapped density. On page 8, lines 13 to 14 the presently claimed fumed food grade silica was mentioned. The process steps in claim 1 of the sixth auxiliary request were based on claim 4, page 7, line 27 and example 1.

- Admission of the seventh auxiliary request

The seventh auxiliary request was an appropriate reaction to the preceding discussion. In particular, it addressed the board's objection with respect to the mesh size.

XI. The arguments of respondent 1, as far as they concern the decisive issues, can be summarised as follows:

- Requests and documents filed with the statement of grounds of appeal and document (18)

The appellant's requests filed with the statement of grounds of appeal should be held inadmissible. They were directed to a different compound compared to the requests submitted during the opposition proceedings, required an additional search and delayed the proceedings without any justification.

Documents (18) and (25a) to (25d) should also not be admitted into the proceedings. The former was filed without justification only two months before the oral proceedings before the opposition division and deprived respondent 1 of the possibility to check or reproduce its examples or to carry out counter-experiments. Documents (25a) to (25d) were not a fair attempt to address the deficiencies in documents (17) or (18). The new experimental data were unconvincing, incomplete, and therefore not verifiable, and concerned a different invention, because the flow behaviour, relied upon in support of an inventive step, was not derivable from the patent in suit. Their submission only served to delay the proceedings.

- Oral submissions by the inventor

Mr Hassen should not be allowed to make oral submissions taking into account the decision G 4/95. In particular, the subject-matter of his submission was not sufficiently specified.

- Novelty

The subject-matter of claim 1 of the main request was not novel over documents (3a) and (18a). The claimed particle size was the direct consequence of the use of L-carnitine acid fumarate and L-carnitine tartrate in the pharmaceutical compositions, in particular the

tablets, described in these documents. Size reduction was standard practice and a prerequisite in the preparation of tablets, as was apparent from document (15), which disclosed several size-reducing methods with subsequently performed sieving steps. It was inherent in the powder and tablets disclosed in documents (3a) and (18a) that at least a fraction passed through a 100 mesh sieve. Furthermore, the claimed subject-matter was not novel because the claimed particle size was not sufficiently far removed from the known range, taking into account the disclosure in paragraph [0017] of the patent in suit. Moreover, in analogy to decision T 990/96, the particle size, by definition, could not confer novelty upon a known compound. The same arguments applied to the subject-matter of claim 1 of the first to third auxiliary requests.

- Inventive step

Starting from document (3a) as the closest prior art, the problem to be solved was the provision of an alternative L-carnitine acid fumarate. The patent in suit contained no evidence that the claimed subject-matter was associated with any technical effects, let alone unexpected effects. The only example of the patent in suit contained silica, a well-known flow enhancer and anticaking agents, as was apparent from documents (21), (30) and (31). It could not be used to demonstrate technical effects which had their origin in the particle size, which was the sole distinguishing feature of claim 1 of the main request. Any improvement in flow behaviour or hygroscopicity, although not demonstrated at all in the working example, would be due to the presence of silica. Document (17) was unsuitable as evidence, mainly because silica was present in the

example reflecting the invention. Documents (25a) to (25d) were also not pertinent. They did not contain a proper reproduction of the prior art. Moreover, all samples described therein contained silica and therefore could not be used to demonstrate technical effects that would have their origin solely in the particle size. The silica to be used as flow aid or anticaking agent was usually adjusted to the powder to be treated. The results in documents (25c) could therefore also be explained by the fact that the specific silica that had been used was better suitable for the compound of sample B3 than for the compound of sample B0. In addition, the L-carnitine acid fumarate of sample B3 was not only sieved, but also milled and thereby homogenised. This would also have had a significant effect on the flow behaviour. Size reduction was common practice in the pharmaceutical field or food industry. Therefore it was an entirely obvious measure for any skilled person. It was also common general knowledge that size reduction could lead to a number of advantages, in particular to improvements in bioavailability or miscibility, as was apparent from a number of documents, including document (36). The person skilled in the art therefore had strong incentives for reducing the particle size of known L-carnitine acid fumarate. The same reasoning also applied to claim 1 of the first to third auxiliary requests.

- Amendments

The fourth auxiliary request did not comply with the requirement of Article 123(2) EPC. Its subject-matter was a combination of features which was not directly and unambiguously disclosed in the application as filed. In particular, L-carnitine acid fumarate was combined with a specific type of silica. However, this type of silica

was only disclosed in combination with other features, including a specific particle size, none of which were present in claim 1 of the fourth auxiliary request. The same objection applied to the fifth and sixth auxiliary requests.

- Admission of the seventh auxiliary request

The seventh auxiliary request should not be admitted into the proceedings. Its submission was not appropriate and only delayed the proceedings. It had already been indicated in the reply to the statement of grounds of appeal and in the board's communication accompanying the summons that example 1 on which the appellant relied in this context was not a proper basis for the amendments in the fourth to sixth auxiliary requests. The appellant had the possibility to address this issue, but failed to do so, even in its reply to the board's communication.

XII. Respondent 2 did not provide any arguments or comments.

XIII. The appellant requested that the decision under appeal be set aside and the patent be maintained in amended form on the basis of the set of claims of the main request, or alternatively, of one of the first to sixth auxiliary requests, all filed with the statement of grounds of appeal, or further alternatively, of the seventh auxiliary request filed during the oral proceedings.

XIV. Respondent 1 requested that the appeal be dismissed.

XV. Respondent 2 requested in writing that the appeal be dismissed.

XVI. At the end of the oral proceedings the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. As communicated in advance to the board (see point VIII above), respondent 2, who did not submit any comments or observations with regard to the substantive issues, did not attend the oral proceedings before the board, to which it had been duly summoned. The board decided to continue the proceedings pursuant to Rule 115(2) EPC and Article 15(3) RPBA.

3. Procedural matters

3.1 Requests

3.1.1 According to respondent 1, the appellant's requests submitted with the statement of grounds of appeal should be held inadmissible, as they were directed to a different compound and therefore concerned subject-matter which had not been dealt with in the opposition proceedings.

3.1.2 The board, however, concurs with the appellant and considers the sets of claims filed with the statement of grounds of appeal as a genuine attempt to resolve the confusion which originated from the use of the name "L-carnitine fumarate" rather than the more apt name "L-carnitine acid fumarate" in example 1 of the patent in suit and in document (17) (see point X above). The data provided in the patent in suit (see page 4, lines 45 to 50) are consistent with the 1:1 salt, which was not

contested, irrespective of the name "L-carnitine fumarate" being used. In fact, the name "L-carnitine fumarate" can be used for both 1:1 and 2:1 salts, as confirmed by document (42). It is also apparent that already in the opposition proceedings the appellant attempted to defend the patent in suit by relying on advantages associated with the 1:1 salt disclosed therein and accordingly provided document (17), which compared the 1:1 salt of example 8 of document (3a) with the 1:1 salt of example 1 of the invention (see decision under appeal, point 14.3.4 on pages 6 and 7 and point 6.6.2, second paragraph on page 15). The subject-matter of the amended requests therefore does not deviate to such an extent from the line of defence followed during the opposition proceedings that the decision under appeal is rendered nugatory or that the board or respondent 1 is faced with a fresh case. The necessity for an additional search, as alleged by respondent 1, is not apparent to the board.

3.1.3 Therefore, the board decided to take the appellant's main request and first to sixth auxiliary requests into account for the appeal proceedings, i.e. not to hold the requests inadmissible (see Article 12(4) RPBA).

3.2 Document (18)

3.2.1 In exercising its discretion under Article 114(2) EPC, the opposition division decided to admit document (18) into the proceedings. This decision was challenged by respondent 1, who argued that it did not have sufficient time to reproduce the experiments described therein or to carry out counter-experiments.

3.2.2 If a discretionary decision of the opposition division is challenged, it is not the task of the board to review

all the facts and circumstances as if it were in the place of the opposition division and to decide whether or not it would have exercised such discretion in the same way. The board should only overrule the way in which the opposition division has exercised its discretion if it comes to the conclusion that it has done so without taking into account the right principles, or that it had exercised its discretion in an unreasonable way and has thus exceeded the proper limit of its discretion (see G 7/93, OJ EPO 1994, 775, point 2.6 of the Reasons).

3.2.3 The admission of the documents was discussed with the parties in the oral proceedings before the opposition division. This was not contested. The board also notes that document (18) was filed within the time limit set by the opposition division in an attempt to address the division's objection that the alleged effect had not been shown over the whole scope of the claims. As such it can be considered relevant for the assessment of inventive step. Furthermore, after the filing of document (18), respondent 1 did not indicate its intention to submit its own experimental data and that more time was needed for that purpose. Nor did respondent 1 request postponement of the oral proceedings. Hence, the board concludes that the opposition division exercised its discretion to admit document (18) correctly and in a reasonable way.

3.2.4 The Board also notes that it can reject a party's submission within the framework of Articles 12 and 13 RPBA. However, since document (18) was admitted into the proceedings by the opposition division, it cannot be eliminated from the appeal proceedings pursuant to Article 12(4) RPBA, according to which the board has the power to hold inadmissible facts, evidence

or requests which were not admitted in the first instance proceedings (see also T 467/08, point 1.2.2 of the Reasons). For the same reasons, namely document (18) already forming part of the appeal proceedings, the provisions of Article 13 RPBA cannot be relied on as they concern amendments to a party's case after the filing of the grounds of appeal or the reply to it. Hence, document (18) cannot be disregarded by the board.

3.3 Documents (25a) to (25d)

3.3.1 Documents (25a) to (25d) were filed with the statement of grounds of appeal, in direct response to the opposition division's decision revoking the patent. In the decision under appeal, the opposition division criticised the experimental evidence submitted by the appellant in support of an inventive step. In particular, the division considered that this evidence was not suitable to demonstrate that the alleged effects had their origin in the distinguishing feature, namely the particle size (see page 15, point 6.6.2, fourth paragraph of the decision under appeal). According to the appellant, this deficiency was remedied in documents (25a) to (25d), particularly in view of the comparison between samples B0 and B3. In these circumstances, the board is of the opinion that the submission of documents (25a) to (25d), filed at the earliest possible moment in the appeal proceedings, was a legitimate attempt by the appellant to address the objections raised in the decision under appeal and further support its position with respect to inventive step. Whether or not these documents would provide conclusive evidence was an issue to be considered in the assessment of inventive step.

3.3.2 Hence, the board decided to take documents (25a) to (25d) into account in the proceedings (Article 12 RPBA).

3.4 Documents (23a)/(23b), (24a)/(24b), (26a)/(26b) and (27)

3.4.1 Respondent 1 requested not to admit these documents, without, however, providing any reason in support of its request. The board also saw no reason to exclude these documents from the appeal proceedings. They were filed with the statement of grounds of appeal and therefore form part of the basis of the appeal proceedings as a matter of principle (Article 12(1a), 12(2) and 12(4) RPBA).

3.4.2 Accordingly, documents (23a)/(23b), (24a)/(24b), (26a)/(26b) and (27) were taken into account in the proceedings.

3.5 Oral submissions by the inventor

3.5.1 By letter of 18 January 2016, the appellant notified the board that the inventor, Mr Hassen, would attend the oral proceedings and requested permission for Mr Hassen to make oral submissions under the control of the representative. At the oral proceedings, respondent 1 requested that Mr Hassen should not be allowed to speak.

3.5.2 According to decision G 4/95 of the Enlarged Board of Appeal (OJ EPO 1996, 412), oral submissions by a person accompanying the professional representative can only be made with the permission of and under the discretion of the EPO. In exercising its discretion the board should consider certain main criteria such as whether a request for permission has been made sufficiently in advance of the oral proceedings, the name and qualification of the

accompanying person has been stated, the subject-matter of the proposed oral submissions has been sufficiently specified and the board is satisfied that the oral submissions are made under the continuing responsibility and control of the professional representative. A request made shortly before the date of the oral proceedings should, in the absence of exceptional circumstances be refused, unless the other party agrees (see G 4/95, *supra*, Order).

The board notes that the attendance of Mr. Hassen was notified sufficiently in advance of the oral proceedings and it was requested that he be permitted to make oral submissions. This was not contested. Mr Hassen's qualifications were not explicitly mentioned in the written request. However, there were no doubts that Mr Hassen as the sole inventor was qualified to speak on technical issues concerning the invention. This was also conceded by respondent 1. The specification of the subject-matter previously indicated in writing was relatively short and referred to "submissions relating to technical issues, under the control of the undersigned representative, should this become necessary or desirable". At the oral proceedings, the appellant's representative further specified that Mr Hassen should comment on the alleged lack of hygroscopicity mentioned in the prior art document (3a), in particular, how this alleged lack was perceived in the food and pharmaceutical industry at the time the invention was made.

3.5.3 In the board's judgment, hearing Mr Hassen on this specific and restricted point, which was linked to his perception of the technical problem to be solved, did not place respondent 1 at any disadvantage. It could expect to hear technical arguments by the inventor on

the invention and aspects of the relevant prior art. Furthermore, respondent 1 was accompanied by its own technical expert and was therefore in a position to adequately react to Mr Hassen's submissions, if this was considered to be necessary. The board also considered that the admission of the oral submissions in the present case was not in contradiction to the aim of the guiding criteria set out in the decision G 4/95, namely that the provisions establishing the scheme of professional representation for parties to proceedings laid down in Article 133 et seq. EPC should not be undermined, and that the other party should not be taken by surprise and should have adequate and proper opportunity to reply.

3.5.4 For the aforementioned reasons, the board allowed Mr Hassen to make oral submissions as an accompanying person on the point indicated by the representative.

Main request and first to third auxiliary requests

4. Novelty (Article 54 EPC)

4.1 Claim 1 of the main request is directed to L-carnitine acid fumarate or tartrate with a particle size such that it passes through a 100 USBS mesh sieve. A 100 USBS mesh sieve has openings of 149 µm, which was not contested.

According to respondent 1, the subject-matter of claim 1 of the main request was anticipated by documents (3a) and (18a).

4.2 Document (3a) discloses L-carnitine compounds, including L-carnitine acid fumarate, which are suitable for preparing oral dosage forms such as tablets (see example 8 and column 7, lines 33 to 36), and

document (18a) discloses L-carnitine tartrate for oral use in the form of tablets, capsules or powder (see column 1, lines 6 to 8 and lines 57 and 58, examples 1 and 4). However, none of these documents discloses any particle size. Nor is there any experimental evidence on file that compounds having the claimed particle size are inevitably obtained in the examples of documents (3a) and (18a). Example 4 of document (18a), directed to the formation of a tablet, mentions a mixing and sieving step for L-carnitine tartrate without, however, providing any information as to the specific conditions used in these steps, in particular the size of the openings of the sieve.

4.3 The appellant's argument that the claimed particle size was an inherent feature of the powder and the tablets disclosed in documents (3a) and (18a) is not accepted in the absence of conclusive evidence. Document (15), on which respondent 1 relied as evidence that size reduction was a common measure in the preparation of pharmaceutical dosage forms and a prerequisite for the preparation of tablets, describes size reduction methods which result in a wide range of particle sizes (e.g. from 100 to almost 100000 µm for cutter mills and about 10 to almost 10000 µm for hammer mills; see document (15), figures 11.5 and 11.8). Therefore, this document cannot serve as evidence that the tablets or the powder mentioned in documents (3a) and (18a) inevitably have a particle size such that they pass through a 100 mesh sieve. In this respect, it should be noted that in the board's judgement, claim 1 is directed to L-carnitine acid fumarate and L-carnitine tartrate which pass through a 100 USBS mesh sieve. It does not encompass a product where merely a fraction passes through such a sieve, irrespective of the statement in

the description that "substantially all" of the carnitine salt passes through a 100 USBS mesh sieve.

4.4 The board also does not accept respondent 1's argument that the claimed particle size could not confer novelty because it was not sufficiently far removed from the particle size in documents (3a) and (18a). Neither document (3a) nor document (18a) discloses a specific particle size. Paragraph [0017] of the patent in suit, on which respondent 1 relied in this context, mentions the preparation of L-carnitine and salts thereof according to methods described in three different documents, including document (3a). The same paragraph also states that "[s]uch piocedures *[sic]* typically yield L-carnitine having a size of such that greater than 10 % by weight of the L-carnitine is retained by a 50 mesh sieve and more than 40 % by weight is retained by a 100 mesh sieve". However, from this general statement it cannot be directly and unambiguously deduced that L-carnitine acid fumarate of document (3a) and L-carnitine tartrate of document (18a) - the latter is not even mentioned in said paragraph - have a particle size such that 60 % by weight pass through a 100 USBS mesh sieve, as argued by respondent 1. Such a particle size is a purely arithmetic possibility, which has not been corroborated by any evidence.

4.5 With regard to respondent 1's argument that in the present case the appellant has the burden of proof regarding novelty, the board notes the following:

In opposition appeal proceedings the onus of proof for lack of novelty rests primarily with the opponent. However, the board notes that according to established jurisprudence of the boards of appeal in cases where the claimed subject-matter is defined by an unusual

parameter, the patent proprietor has to contribute to establishing to what extent this parameter distinguishes the claimed subject-matter from the prior art, once the opponent has established a strong presumption that this parameter is inherently disclosed in the prior art (see for example T 131/03, headnote and point 2.7 of the Reasons).

The board concurs with the appellant that particle size is not an unusual parameter. Moreover, for the reasons set out in points 4.3 and 4.4 above, respondent 1 has not established a strong presumption that the claimed particle size is inherently disclosed in the prior art. Therefore, respondent 1's argument that the onus of proof has shifted to the appellant is not accepted.

4.6 With regard to decision T 990/96 cited by respondent 1, the board is of the opinion that this decision is not relevant to the present case. In T 990/96 there was no doubt that the product (i.e. the compound) was known *per se* in the art as part of a composition. The question, which has to be decided in the present case, is whether the product (i.e. the L-carnitine acid fumarate or L-carnitine tartrate with the claimed particle size) has actually been made available to the public within the meaning of Article 54 EPC, either explicitly or as the inevitable result of the examples of document (3a) and (18a). Decision T 990/96 is of no relevance to answering this question. The Board therefore sees no need to discuss this decision in further detail.

4.7 Since the feature of the particle size as defined in claim 1 of the main request is not directly and unambiguously disclosed in documents (3a) and (18a), these documents are not detrimental to the novelty of the presently claimed L-carnitine salts.

4.8 The board therefore concludes that the subject-matter of claim 1 of the main request, and by the same token the subject-matter of claim 1 of the first to third auxiliary requests, is novel within the meaning of Article 54 EPC.

5. Inventive step (Article 56 EPC)

5.1 The board, in accordance with both parties, considers document (3a) as a suitable starting point for the assessment of inventive step.

5.2 In the light of this document, the appellant defined the problem to be solved as the provision of L-carnitine acid fumarate with improved flow behaviour and very low hygroscopicity.

The proposed solution was the L-carnitine acid fumarate with the claimed particle size.

As evidence that the technical problem had been solved, the appellant mainly relied on documents (25a) to (25d), in particular on samples B3 and B0 and their respective flow behaviour demonstrated by measuring the Angle of Repose (see documents (25c) und (25d)). According to the appellant, samples B3 and B0 differed only in their respective particle size. Hence, in the appellant's opinion, the requirement that the nature of the comparison with the closest prior art must be such that the alleged advantage or effect is convincingly shown to have its origin in the distinguishing feature was complied with.

5.3 The board notes that the parties were divided on the question whether the alleged improvement in the flow

behaviour - a technical effect that is not explicitly mentioned anywhere in the patent in suit - can be taken into account in the formulation of the technical problem. However, this question can be left open, since even if the flow behaviour were a property derivable from the patent in suit, it has not been shown that its alleged improvement has its origin in the distinguishing feature compared to the closest state of the art for the reasons set out in points 5.4 and 5.5 below.

5.4 The sole feature distinguishing the L-carnitine acid fumarate of claim 1 of the main request or claim 1 of the first to third auxiliary requests from the closest state of the art is the particle size. Nevertheless, in documents (25c) and (25d), the appellant has chosen to compare L-carnitine acid fumarate samples which differ not only in their particle size (B3 with a particle size as claimed; B0, B1 and B2 with a particles size that passes through a 14.63 mesh sieve, see document (25a) page 3), but also in that silica is present in all samples. No convincing reasons have been provided by the appellant as to why it has carried out its comparative tests with the addition of silica instead of simply comparing the size-reduced L-carnitine acid fumarate sample with a sample where no particle size reduction step was performed before mixing both with silica.

It is true that in document (25c) the same type of silica in the same amount was used in the allegedly inventive sample B3 and the comparative sample B0 (see page 1, first and last column and page 2, first and last paragraph) and that therefore these samples appear to differ only in their particle size. Nevertheless, contrary to the appellant's view, this comparison does not properly demonstrate that the alleged advantage has its origin in the particle size, because a potentially

different influence of silica - a well-known flow-aid and drying agent (see document (21), points 1, 2 and 17) - on the flow behaviour of compounds with different particle sizes cannot be excluded. At best, the comparison shows that the presence of silica advantageously affects the flow behaviour of L-carnitine acid fumarate having a smaller particle size compared to the flow behaviour of L-carnitine acid fumarate having a larger particle size. These results cannot be extended to L-carnitine acid fumarate particles where no flow-aid is present. For this reason alone, the appellant's comparative data in documents (25c) and (25d) are not suitable for demonstrating that the alleged improvement in flow behaviour has its origin in the sole distinguishing feature, namely the particle size.

5.5 Document (17), filed by the appellant during the opposition proceedings in order to demonstrate improved flow behaviour and hygroscopicity of the claimed product, is not pertinent either. It compares L-carnitine acid fumarate of the claimed particle size blended with silica with L-carnitine acid fumarate prepared according to example 8 of document (3a), where no silica is present (see "Samples" on page 1 of document (17) and document (22), page 1, third paragraph). Since the flow-conditioning, anti-adherent and drying properties of silica will undoubtedly have an effect on the properties of L-carnitine acid fumarate, the data in document (17) cannot be used to demonstrate any advantage or effect based solely on the difference in particle size.

5.6 The patent in suit also mentions improvements in bioavailability and miscibility. However, it does not provide any evidence in this respect and documents (17) and (25c)/(25d) either do not address this issue

(documents (25c)/(25d)) or are not suitable as evidence (document (17)) for the reasons set out in points 5.4 and 5.5 above).

5.7 Document (27) refers to improvements being achieved by using the appellant's "ultrafine L-carnitine acid fumarate" instead of conventional L-carnitine acid fumarate. However, in the absence of any information regarding the products, in particular, in the absence of any information as to the presence or absence of silica in the ultrafine product, any advantages which may have been experienced cannot be attributed to the difference in particle size. Therefore, this document cannot be relied on to demonstrate improvements based solely on the particle size.

5.8 It follows from the above that the alleged improvements in flow behaviour, hygroscopicity, miscibility and/or bioavailability have not been convincingly established. According to the jurisprudence of the boards of appeal alleged but unsupported advantages cannot be considered in the determination of the technical problem underlying the invention. Consequently, the technical problem as defined by the appellant needs to be redefined in a less ambitious way, namely as the provision of further L-carnitine acid fumarate.

The board is satisfied that this problem has been solved.

5.9 It then remains to be decided whether or not the proposed solution is obvious in view of the prior art.

Size reduction and size reducing methods, for example milling, are commonly known and applied in the field of pharmaceuticals as illustrated for example by

documents (8), (14t), or (36). The selection of L-carnitine acid fumarate with a particle size such that it passes through a specific mesh sieve has not been shown to result in any technical benefit vis-à-vis the closest state of the prior art. It is neither critical nor purposive, but merely represents an arbitrary selection of no particular technical significance. Such a selection does not require inventive ingenuity.

5.10 According to the appellant, the person skilled in the art with the purpose of improving the flow behaviour of L-carnitine acid fumarate would not have considered reducing the particle size, as it was known in the art that fine powders flowed badly (see documents (30), fourth page, right column, second point under "Reasons for caking and bad flowability", document (31), page 5, point 3.1, first paragraph). Furthermore, particle size reduction would also have increased the hygroscopicity of L-carnitine acid fumarate. This was also confirmed by document (27), which stated in point 10 that "L-carnitine in any form is not a candidate for size reduction, since the frictional heat generated during the particle reduction process may induce the humid state relatively to the ambient air temperature and thereby produce sticking".

5.11 However, as set out in points 5.4 and 5.5. above, no improvements in flow behaviour or hygroscopicity have been demonstrated for the presently claimed L-carnitine acid fumarate, and the technical problem to be solved is merely the provision of a further L-carnitine acid fumarate. The appellant's argument that the skilled person in an attempt to improve the flow behaviour or hygroscopicity would not have reduced the particle size is therefore not pertinent.

5.12 The appellant also argued that the skilled person had no incentive to reduce the particle size, since it was time-consuming, increased energy and equipment costs and led to a number of disadvantages, including possible degradation and adsorption of moisture (see document (36), page 112, lines 15 to 36, in particular, lines 21 to 23).

5.13 However, the selection of a potentially less advantageous size-reduced L-carnitine acid fumarate does not require inventive ingenuity, if, as in the present case, it merely amounts to tolerating clearly predictable disadvantages. Furthermore, as is apparent from document (36), size reduction creates a number of advantages (see points 1 to 8 on pages 110 to 112) and a number of disadvantages (see points 1 to 5 on page 112). It belongs to the routine work of a person skilled in the art to decide under the given circumstances whether the potential advantages outweigh potential disadvantages and which of the potential disadvantages he is prepared to accept. Inventive skills are not required in this respect.

5.14 For the aforementioned reasons, the board concludes that the subject-matter of claim 1 of the main request and claim 1 of the first to third auxiliary requests does not involve an inventive step within the meaning of Article 56 EPC. Accordingly, these requests must be refused.

Fourth to sixth auxiliary requests

6. Amendments (Article 123(2) EPC)

6.1 The application as originally filed, as referred to herein, is the international application published as WO 01/17525.

6.2 Claim 1 of the fourth auxiliary request is directed to a composition comprising L-carnitine acid fumarate and food grade fumed silica of a particular overall surface area and tapped density. The acid fumarate has a particle size such that is passes through a 100 USBS mesh sieve (see point V above).

According to the appellant this claim had its basis in claims 7 and 9, taking into consideration the disclosure on page 5, lines 8 to 10, page 7, lines 1 to 5 and example 1 as originally filed.

6.3 The board does not agree.

6.3.1 Claim 7 as originally filed is directed to a composition comprising (A) L-carnitine with the claimed particle size and (B) a pharmaceutically acceptable excipient or carrier, and claim 9, which refers back to claim 7, lists a considerable number of specific L-carnitine compounds, including L-carnitine acid fumarate. The pharmaceutically acceptable excipient or carrier is not defined in any of the claims as originally filed.

6.3.2 On page 5, lines 8 to 10 of the description as originally filled it is stated that suitable excipients or carriers are described in Remington's Pharmaceutical Hand Book. Specific excipients, such as silica, let alone silica with the required overall surface area and tapped density, are not disclosed in this context. Nor is there any reference in this context to L-carnitine acid fumarate.

Page 7, lines 1 to 5 discloses a particular embodiment for a particular purpose, namely the combination of a specific fine particle size (**200 Mesh**) and **coating** with hydrophilic or hydrophobic silicas, especially for formulations that use other finely particled ingredients or for improvement in shelf life. Furthermore, no reference to L-carnitine acid fumarate, fumed silica or a particular overall surface or tapped density is made in this context.

6.3.3 The first part of the example (see page 7, line 24 to page 8, line 2) refers to L-carnitine acid fumarate having various particle sizes (i.e. it passes through a **100** USBS mesh sieve or through **150 to 200** mesh sieve). Particles are then blended with food grade **hydrophilic and/or hydrophobic fumed or precipitated silica** of the type available from Degussa Inc. having the required surface area and tapped density. A direct and unambiguous disclosure of food grade fumed silica with L-carnitine acid fumarate passing through a 100 mesh sieve cannot be found in the general part of the example.

6.3.4 The second part of the example (page 8, lines 3 to 15) discloses a specific ultra-fine L-carnitine acid fumarate with particular analytical properties. In lines 13 to 14 it is stated that the product "Passes 150 mesh conditioned with fumed food grade silica". A product that passes through a 100 mesh sieve as presently claimed, however, does not necessarily pass through a 150 mesh sieve, since the openings in a 150 mesh sieve are smaller (see document (25b)). The presently claimed L-carnitine acid fumarate and the L-carnitine fumarate on page 8 are therefore not necessarily identical. Thus, the disclosure on page 8 is not a proper basis for the amendment in claim 1 of the

fourth auxiliary request. Furthermore, the board notes that the passage on page 8 refers to L-carnitine acid fumarate with further properties, such as a specific water content or rotation, none of which is present in claim 1 of auxiliary request 4.

6.3.5 It follows from the above that none of the aforementioned passages in the application as originally filed clearly and unambiguously discloses the composition according to claim 1 of the fourth auxiliary request.

6.4 The board therefore concludes that claim 1 of the fourth auxiliary request, and for the same reason claim 1 of the fifth and sixth auxiliary requests do not comply with Article 123(2) EPC.

Seventh auxiliary request

7. Admission into the appeal proceedings (Article 13(1) RPBA)

7.1 The seventh auxiliary request was filed at the latest possible stage of the appeal proceedings, namely during the oral proceedings, following the discussion of the fourth to sixth auxiliary requests and the announcement of the board's conclusion that these requests did not comply with the requirements of Article 123(2) EPC.

7.2 The appellant justified the late filing of this auxiliary request as a direct reaction to the preceding discussion and an attempt to overcome the board's objections concerning the issue of the mesh size.

7.3 However, objections under Article 123(2) EPC were already raised in the respondent's reply to the

statement of grounds of appeal. In particular, it was pointed out that the combination of claim 1 of auxiliary request 4 had no basis in example 1, on which the appellant relied. The board in its communication accompanying the summons to oral proceedings shared respondent 1's concerns and indicated that the size of the mesh sieve, in particular in auxiliary requests 5 and 6, appeared to have no basis in the example on page 8 (see point 2.3 of the board's communication). Hence, if it considered it necessary, the appellant could and should have filed a request with appropriate amendments at an earlier stage in the appeal proceedings. The appellant's argument that the filing of this request was a timely and appropriate reaction to the course of the oral proceedings is therefore not accepted. In addition, the new request contains a multitude of amended features, at least one of which was taken from the description. Admitting such a request into the proceedings at this stage would not have been fair towards the respondent, because the filing of such a request was not predictable. Furthermore, the board notes that there were also doubts as to whether the new request with its many amendments fulfilled the requirements under Article 123(2) EPC and was likely to succeed, bearing in mind that the mere reformulation of the compound claim into a method claim does not appear to address clearly the key issue with regard to inventive step, namely the obviousness of size reduction.

7.4 Hence, the board, making use of its discretionary power pursuant to Article 13(1) RPBA, decided not to admit the seventh auxiliary request.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated