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**Datasheet for the decision  
of 16 May 2014**

**Case Number:** T 1570/09 - 3.3.02  
**Application Number:** 05752599.0  
**Publication Number:** 1755580  
**IPC:** A61K31/194, A61K31/198,  
A61P3/06, A61K38/03, A61K31/16  
**Language of the proceedings:** EN

**Title of invention:**

USE OF ALPHA-KETOGLUTARATE AND RELATED COMPOUNDS FOR LOWERING  
PLASMA LIPIDS

**Applicant:**

Protista Biotechnology AB

**Headword:**

Alpha-ketoglutaric acid and pharmaceutically acceptable salts  
thereof for use in increasing HDL plasma levels/PROTISTA

**Relevant legal provisions:**

EPC 1973 Art. 52(4), 54  
EPC 2000 Art. 53(c), 54(5), 56, 69

**Keyword:**

Admission of main request and first auxiliary request (Yes)  
Main request: Two independent claims for the same medical use;  
one claim under the provisions of EPC 1973 invoking legal  
fiction in G 5/83, and other claim under the provisions of  
Article 54(5) EPC 2000 (No)  
First auxiliary request: allowable (Yes)

**Decisions cited:**

G 0001/83, G 0005/83, G 0006/83, G 0002/08

**Catchword:**



**Beschwerdekammern  
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Case Number: T 1570/09 - 3.3.02

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.02**  
**of 16 May 2014**

**Appellant:** Protista Biotechnology AB  
(Applicant) Kvarngatan 2  
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**Representative:** Kortesmaa, Jarkko  
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**Decision under appeal:** **Decision of the Examining Division of the  
European Patent Office posted on 25 March 2009  
refusing European patent application No.  
05752599.0 pursuant to Article 97(2) EPC 2000.**

**Composition of the Board:**

**Chairwoman** M. C. Ortega Plaza  
**Members:** T. Sommerfeld  
L. Bühler

## Summary of Facts and Submissions

- I. European patent application No. 05752599.0, based on the international application published as WO 2005/123056, was filed with eight claims.
- II. The following documents were cited during examination and appeal proceedings:
- D1 G. Bazzano and G. S. Bazzano, *Proceedings of the Society for Experimental Biology and Medicine*, 140(1), 36-39, 1972
- D2 Leinweber et al., *Med. Klin.* 71(24), 1043-1046, 1976
- D4 A. Scriabine, *Cardiovascular Drug Reviews*, 22(2), 147-153, 1 June 2004
- D5 S. Thomas, *CPD Clinical Biochemistry*, 5(2), 41-47, 2003
- D6 Viles-Gonzalez et al., *Current Opinion in Cardiology*, 18, 286-294, 2003
- D7 F. M. Sacks, *Br. J. Cardiol.*, 10, 297-304, 2003
- E1 "Professional statement" of Mr W. Rzeski dated 25 June 2009
- E2 "Professional statement" of Mr B. Vyacheslav dated 22 June 2009
- E3 Declaration of Mr S. G. Pierzynowski dated 21 June 2011 (3 pages)
- III. The present appeal lies from a decision of the examining division refusing the patent application under Article 97(2) EPC 2000.
- IV. Claim 1 of the main request before the examining division read as follows:
- "1. Method of increasing plasma levels of high density lipoprotein (HDL) in vertebrates, such as birds and

mammals, including man, comprising administering to a vertebrate at least one member selected from the group consisting of alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof."

Claim 1 of the first auxiliary request before the examining division read as follows:

"1. Use of at least one member selected from the group consisting of alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof, for the manufacture of a pharmaceutical preparation or a food or feed supplement for increasing plasma levels of high density lipoprotein (HDL) in vertebrates, such as birds and mammals, including man."

Claim 1 of the second auxiliary request before the examining division differed from claim 1 of the first auxiliary request in that the expression "or a food or feed supplement" was deleted.

The examining division considered that the main request was not allowable since claim 1 encompassed a method of treatment excluded from patentability under Article 53(c) EPC 2000.

Furthermore, the examining division considered that the novelty of the Swiss-type claim 1 of the first auxiliary request, which sought protection for the second (or further) medical indication of alpha-ketoglutaric acid (and its pharmaceutically acceptable salts) "for increasing plasma levels of high density lipoprotein (HDL) in vertebrates" could not be acknowledged over the cited prior art (documents D1 and D2) in view of the fact that the claim's wording included not only the manufacture of a pharmaceutical

preparation, but also mentioned a food or feed supplement.

As regards claim 1 of the second auxiliary request, the examining division found that it met the requirements of Article 123(2) EPC. Furthermore, according to the examining division's findings, the subject-matter claimed in the second auxiliary request was novel over documents D1 and D2, but lacked an inventive step (Article 56 EPC 2000). In particular, document D1 represented the closest prior art. The examining division was of the opinion that although none of the available prior-art documents which formed part of the state of the art under Article 54(2) EPC 2000 disclosed alpha-ketoglutaric acid or its pharmaceutically acceptable salts for increasing HDL plasma levels, the skilled person would find the claimed invention obvious, since measuring HDL plasma levels had become "*a routine labour practice*" in 2004.

- V. The applicant (appellant) lodged an appeal against said decision and filed grounds of appeal. With its grounds of appeal the appellant filed additional documents and requested that the decision under appeal be set aside and that a "European patent be granted on the second auxiliary request presented at the oral proceedings".
  
- VI. The board sent on 25 February 2014 a summons to attend oral proceedings on 16 May 2014. A board's communication pursuant to Article 15(1) RPBA was sent together with the summons. The board expressed *inter alia* a preliminary opinion in relation to the documents forming part of the state of the art under Article 54(2) EPC 2000 serving as the basis for the examining division's decision (i.e. documents D1, D2) and introduced *ex officio* further documents, namely D4,

D5, D6 and D7, all forming part of the state of the art under Article 54(2) EPC.

The board also expressed a preliminary opinion in relation to the subject-matter initially claimed in claims 1 and 4 as originally filed.

VII. With a letter dated 16 April 2014, the appellant filed a substantive response to said board's communication.

With this letter of 16 April 2014, the appellant withdrew all its previous requests and filed a new main request and auxiliary requests 1 to 5. It also filed three additional documents concerning the "definition of HDL".

The **main request filed on 16 April 2014** has two independent claims (claims 1 and 4). Claim 1 of the main request is identical to claim 1 of the first auxiliary request before the examining division (see point IV above).

Claim 4 of the main request reads as follows:

"4. A compound selected from the group consisting of alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof, for use in increasing plasma levels of high density lipoprotein (HDL) in vertebrates, such as birds and mammals, including man".

VIII. Oral proceedings took place on 16 May 2014.

IX. At the oral proceedings before the board the appellant withdrew auxiliary requests 1 to 5 filed on 16 April 2014 and filed a new first auxiliary request. Claim 1 of the first auxiliary request filed on 16 May 2014 is identical to claim 4 of the main request.

During said oral proceedings the appellant also filed a copy of the declaration E3.

- X. The appellant's arguments as far as relevant for the present decision may be summarised as follows:

*Admission of requests and document E3*

The new first auxiliary request filed during the oral proceedings before the board should be admitted as it was a direct reaction to the discussion at the oral hearing. The amendments introduced only concerned the deletion of claims 1 to 3 of the main request and the renumbering of claims.

Document E3 should be admitted into the proceedings, even though late filed. The appellant had not thought it necessary to file it before, either as a reply to the board's communication or in response to the examining division's reasoning. Moreover, the technical data in document E3 were clear and easy to understand.

*Main request*

The appellant argued that the two independent claims, i.e. claim 1 in Swiss-type form and claim 4 as purpose-limited product claim under Article 54(5) EPC 2000, should be allowed in one single set of claims in order to preserve its legitimate interests when seeking full protection for its invention. The scope of protection conferred by the two different forms of claims was not identical. Moreover, the interpretation of the two different claim forms by the national courts of the contracting states might differ from one state to another and also deviated from the EPO's practice.



It was accepted practice before examining divisions to allow both claim types together, since the entry into force of EPC 2000.

The Enlarged Board of Appeal decision G 2/08, OJ EPO 2010, 456, solely ordered the end of the Swiss-type form with a certain time limit in the context of the answer to question 3. G 2/08 did not expressly state that before expiry of this time limit European patents could not be granted containing Swiss-type claims at the same time as purpose-limited product claims under Article 54(5) EPC 2000.

*First auxiliary request*

The appellant argued that document D4, especially Gary M. Coppola's reference on page 150, first full paragraph, which disclosed HDL elevating compounds, should be seen as the closest prior art. It had to be assumed that these compounds were the result of a research programme with the goal of discovering a drug that would elevate HDL levels. In particular, it had been investigated whether these new drugs were able to elevate HDL-C and Apo A1 for the treatment of patients with HDL-C less than 35mg/dL more efficiently than gemfibrozil. The appellant further submitted that none of the documents D4 to D7 mentioned alpha-ketoglutaric acid or its pharmaceutically acceptable salts.

The objective technical problem could thus be seen as the provision of alternative means to increase HDL.

The application as originally filed contained an animal model of hypercholesterolemia (example 2, page 14 onwards). In this model, after an induction phase of 60 days on a cholesterol and lard enriched diet, the

animals remained on the diet and were either given a placebo solution or alpha-ketoglutaric acid (AKG) basic solution or a tenfold thinned AKG basic solution for another 60 days. It could be seen from table 13 on page 16 that there was a statistically significant increase of HDL plasma level for the two tested dosages of AKG for male animals when compared to placebo. Concerning the female animals this study showed a trend that AKG administration increased HDL plasma levels. These tests results made it plausible that the problem was solved.

As further support that the problem was plausibly solved, the application as originally filed disclosed in example 3 (page 17 onwards) a study conducted on two volunteers to whom alpha-ketoglutarate calcium salt (AKG calcium salt) was administered orally. Table 16 showed that after four weeks of treatment with AKG calcium salt there was a trend showing increased HDL plasma levels, whereas after two weeks of cessation of treatment the levels of HDL plasma decreased again.

Lastly, the additional technical data presented with declaration E3 not only supported the view that the problem was plausibly solved as expected from the content of the application as filed, but also served to confirm that the problem had been actually solved, since a statistically significant increase of HDL plasma levels was reported in 60 human patients after two months of treatment with AKG calcium salt.

The skilled person would not combine the teaching in document D4 with that of documents D1 or D2, since neither document D1 nor document D2 mentioned HDL in any way. Both documents D1 and D2 were from the 1970's and only referred to total cholesterol levels.

It was also not self-evident for the skilled person that any compound known in the prior art to decrease total cholesterol was a valid candidate to increase HDL. In this context the appellant made reference to the professional statements E1 and E2, which confirmed this view.

The appellant further argued that combining documents D1 or D2 with document D4 needed hindsight, given that numerous articles disclosing a large number of different compounds decreasing total cholesterol had been published before the relevant filing date in the field of hyper-cholesterolemia. However, there was no hint in the cited prior art for choosing AKG as a solution to the stated problem.

- XI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed on 16 April 2014 or, alternatively, on the basis of the first auxiliary request filed during the oral proceedings of 16 May 2014.

### **Reasons for the Decision**

1. The appeal is admissible.
2. *Admission of requests*
  - 2.1 The main request was filed on 16 April 2014 with the appellant's response to the board's communication sent as annex to the summons to oral proceedings.

The main request represents a direct response to the board's observations made in said communication.

Therefore, the main request is admitted into the proceedings.

- 2.2 The first auxiliary request was filed at the oral proceedings before the board as a direct reaction to the discussion about the main request. The first auxiliary request differs from the main request in that independent claim 4 of the main request is claim 1 of the first auxiliary request and dependent claims 5 and 6 of the main request are dependent claims 2 and 3 in the first auxiliary request. Independent claim 1 of the main request and its dependent claims 2 and 3 have been deleted.

The filing of the first auxiliary request containing one independent claim 1, which is identical to independent claim 4 of the main request, simplifies the discussion and does not open any new issues for discussion in relation to the main request. Therefore, the first auxiliary request is admissible.

3. *Admission of document (E3)*

During the discussion about inventive step at the oral proceedings before the board, the appellant submitted a copy of the declaration of Mr Pierzynowski (E3).

The declaration E3 was signed on 21 June 2011 by Mr Pierzynowski. This declaration contains data results of a clinical study on 60 patients treated for two months with alpha-ketoglutarate calcium salt (AKG calcium salt). The test conditions and data results concerning HDL plasma levels are clear and easy to understand. Moreover, although these additional technical data could have been filed earlier, there was no objective reason to file them until the discussion

at the oral proceedings before the board took place. In particular, the decision under appeal (sent to the party on 25 March 2009) and the statement of grounds of appeal (filed on 6 July 2009) predate declaration E3. Furthermore, the examining division's decision does not question that the technical problem was plausibly solved. In fact, the examining division's decision does not even refer to the technical data in the present application. Thus, there was no need to file the additional technical data in declaration E3.

Additionally, the board introduced *ex officio* with the communication sent as annex to the oral proceedings documents D4 to D7 (they are documents which form part of the state of the art under Article 54(2) EPC) in view of the deficient development of the problem-solution approach in the examining division's decision.

At the oral proceedings before the board, the inventive step of the subject-matter claimed in independent claim 4 of the main request (claim 1 of auxiliary request 1) was discussed in detail and the board *inter alia* asked the appellant to explain the experimental results in example III of the present application, as well as the statistical significance of some of the data presented on page 20 of the present application. Only at that moment did it become appropriate to provide declaration E3 as a reaction to the board's questions. In fact, the data results of the clinical study displayed in E3 were filed in order to strengthen the appellant's position that the problem had not only been plausibly solved in the light of the data in the application, but that it had been actually solved.

Therefore, in view of the above reasons the board admits declaration E3 containing additional technical data into the proceedings.

4. *Main request*

- 4.1 It is generally known to the skilled person (see documents D5 to D7) that increasing plasma levels of high density lipoprotein (HDL) in human and animals is a medical indication for treatment, including prophylaxis, of several medical conditions and diseases.

The set of claims of the main request contains two independent claims (claims 1 and 4) concerning the further therapeutical use, defined as "increasing plasma levels of high density lipoprotein (HDL) in vertebrates, such as birds and mammals, including man", of the known substance alpha-ketoglutaric acid (and pharmaceutically acceptable salts thereof).

Therefore, claim 1 of the main request, which is drafted in Swiss-type form, and claim 4 of the main request, which is drafted as purpose-limited product claim, aim to seek protection for one and the same medical use of one and the same active drug.

- 4.2 The legal fiction in accordance with the praetorian rule introduced with Enlarged Board of Appeal decision G 1/83 (G 5/83, G 6/83), OJ EPO 1985, 60, has to be applied for conferring notional novelty to the subject-matter claimed in the Swiss-type claim 1 of the main request.

Enlarged Board of Appeal decision G 1/83 (G 5/83, G 6/83) introduced the "Swiss-type" form claim in

consideration of the fact that the provisions of EPC 1973, and in particular of its Article 54(5), allowed purpose-related product claims only for the first (generic) medical use of a known substance or composition. In other words, in accordance with the provisions of EPC 1973, claims drafted in the form of a product claim directed to a substance or composition for use in a method referred to in Article 52(4) EPC 1973 are allowable if the first medical use of a known substance or composition is novel under Article 54(5) EPC 1973. In contrast to the first medical indication of a known substance or composition in the form of such "use-related product claims" under Article 54(5) EPC 1973, there was an absence of provisions in EPC 1973 allowing purpose-limited product claims for further specific medical indications (see G 2/08, OJ EPO 10/2010, 456, points 5.8 and 5.9 of the Reasons, and G 5/83, OJ EPO 1985, 64, point 15 of the Reasons).

- 4.3 Apart from this, a body of jurisprudence has been developed over the years by the Boards of Appeal which concerns the application of the praetorian rule introduced by Enlarged Board of Appeal decision G 1/83 (G 5/83, G 6/83) to particular situations in which the "invention" for which protection was sought relied upon a new use of a substance or composition in a method of treatment referred to in Article 52(4) EPC 1973 (Article 53(c) EPC 2000).

Thus, although Swiss-type claim 1 does not explicitly employ the term "medicament" the claim's wording is appropriate to the situation in the technical field underlying the present invention at the date of filing, where the term "medicament" has to be taken in a broader sense than the classical meaning in the year 1985, when the Enlarged Board of Appeal decision G 1/83

(G 5/83, G 6/83) was issued. Additionally, it has to be stressed that the "medicament" itself (and its definition in claim 1 of the main request) does not confer notional novelty on the claimed subject-matter. The notional novelty of the subject-matter claimed in claim 1 of the main request relies on the novelty of the medical indication specified in said claim.

Such a situation is referred to in Enlarged Board of Appeal decision G 2/08, OJ, EPO 10/2010, 456, point 7.1.1 of the Reasons, second and third paragraphs:

*"Since the medicament per se was not new the subject-matter of such a claim was rendered novel by its new therapeutic application (cf. G 5/83, points 20 and 21 of the Reasons). This praetorian approach was a "special approach to the derivation of novelty" (cf. point 21 of G 5/83) and therefore constituted a narrow exception to the principles governing the novelty requirements which was not intended to be applied in other fields of technology.*

*That praetorian ruling found its cause in the fact that a claim directed to the use of the substance or composition for the treatment of the human body by therapy had to be regarded as a step of treatment (see point 18, in fine of G 5/83). A claim of that kind was forbidden. On the other hand only the first medical indication of a known composition in the form of a medicament was by virtue of Article 54(5) EPC 1973 (Article 54(4) EPC 2000) entitled to be drafted in the form of a purpose-related product claim. And since the intention of the legislator was clearly not to exclude second therapeutic indications of a known medicament from the field of patentability the so-called Swiss-*



*type claim constituted the adequate but exceptional solution."*

4.4 Moreover, following the *rationale* of Enlarged Board of Appeal decision G 2/08, as expressed in paragraph 7.1.2 of the Reasons:

*"Article 54(5) EPC now permits purpose-related product protection for any further specific use of a known medicament in a method of therapy. Therefore, as mentioned in the preparatory document (MR/24/00, point 139) the loophole existing in the provisions of the EPC 1973 was closed.*

*In other words "cessante ratione legis, cessat et ipsa lex", when the reason of the law ceases, the law itself ceases.*

*The cause of the praetorian approach ceasing, the effect must cease."*

In the present case the appellant has been able to formulate under Article 54(5) EPC 2000 an allowable purpose-limited product claim (claim 4 of the main request) which seeks protection for the same medical indication of the same substance as in the Swiss-type claim 1, and the notional novelty of claim 1 is not derived from the "medicament" itself. Therefore, there is no longer an objective reason for justifying the simultaneous presence of both claims in the set of claims to be proposed for grant. Allowing such a set of claims would cause the contradictory legal situation that the old provisions in Article 54 EPC 1973 together with Article 52(4) EPC 1973, and the new provisions in Article 54 EPC 2000 together with Article 53(c) EPC 2000 would apply simultaneously to one and the same set of claims.

Enlarged Board of Appeal decision G 2/08 announced the official end to the praetorian rule set out in G 5/83, OJ EPO 1985, 64, in its answer to question 3 as follows:

*"Where the subject-matter of a claim is rendered novel only by a new therapeutic use of a medicament, such claim may no longer have the format of a so called Swiss-type claim as instituted by decision G 5/83.*

*A time limit of three months after publication of the present decision in the Official Journal of the European Patent Office is set in order that future applicants comply with this new situation".*

Fixing an official time limit for the end of the praetorian rule merely solved any possible problems derived from the fact that at the time of the publication of G 2/08 in the OJ EPO (October 2010) many applications for which the transitional provisions governing the entry into force of EPC 2000 applied were still pending and the abolition of the praetorian rule should therefore not create a retroactive legal effect (G 2/08, point 7.1.4 of the Reasons).

However, G 2/08 does not give applicants an absolute right to draft two independent claims in one single set of claims for one and the same medical indication of one and the same substance, one claim following the praetorian rule introduced in view of the old provisions of EPC 1973, and the other claim following the new provisions in Article 54(5) EPC 2000.

- 4.5 The appellant submitted that including both claims in a single set of claims served to protect its legitimate

interests, since it was to be expected that different national courts would decide divergently on patentability of claims seeking protection for a further use in a method referred to in Article 53(c) EPC 2000.

Apart from the fact that such argumentation would rather justify the filing of two separate sets of claims (one with claims in the form of Swiss-type claims, the other with claims in the form of purpose-limited product claims) depending on the contracting states for which particular national jurisprudence was applicable, the appellant did not cite any such national decisions to support its argument.

The relevance for the present appeal case of a theoretical possibility of supposedly conflicting national decisions cannot be seen. Moreover, Article 4(3) EPC confers on the European Patent Organisation the authority to grant European patents.

The issue is whether it is allowable in view of the Enlarged Board of appeal decisions G 1/83 (G 5/83, G 6/83) and G 2/08 to have two independent claims directed to the same known substance for use in the same further method for treatment formulated in accordance with EPC 1973 on the one hand, and in accordance with EPC 2000 on the other hand. It is thus an issue of the transitional application of the law as authoritatively interpreted by the Enlarged Board of Appeal.

- 4.6 Under the circumstances depicted above, the appellant's argument that Swiss-type form claims and purpose-limited product claims confer different scopes of protection under Article 69 EPC at national level

cannot succeed as a valid justification for allowing the main request. The answer given to question 3 in G 2/08 confirms that the theoretical possibility of different interpretations of the scope of protection conferred under Article 69 EPC at national level is not stated as a reason for prolonging the life of Swiss-type form claims in those cases where there is no longer any legal reason for applying the praetorian rule in accordance with the old law (EPC 1973) instead of Article 54(5) EPC 2000.

- 4.7 The appellant also asserted that there was a practice followed by the EPO examining divisions, after the entry into force of EPC 2000, of granting both forms of claims in the same set of claims. However, the boards of appeal have to comply with the provisions of the EPC and are not bound by the interpretations and practice of the examining divisions (Article 23(2) EPC 2000).
- 4.8 Summarising, Article 54(5) EPC 2000 applies to the present case (Article 1(3) of the decision of the Administrative Council of 28 June 2001 on the transitional provisions under Article 7 of the Act revising the European Patent Convention of 29 November 2000, and thus the purpose-limited product claim 4 of the main request is allowable for seeking protection for the further (specific) medical indication of alpha-ketoglutaric acid (and pharmaceutically acceptable salts thereof).

The Swiss-type form was conceived as an exception under the old law (EPC 1973). Therefore, since Article 54(5) EPC 2000 applies to the present application and claim 4 of the main request is allowable in view of a new medical indication of a known substance, there is no longer any legal reason in the present case for

allowing Swiss-type claim 1 in the set of claims of the main request. Accordingly, the main request is not allowable.

4.9 As regards the appellant's general comments relating to the fact that a request to the Regulatory Authorities has to be submitted before commercializing products in the medical field, this situation applies to both Swiss-type claims and purpose-limited product claims. Moreover, the provisions in the EPC concern the requirements to be fulfilled in order that a patent can be granted, which are different requirements to, and independent from, those that have to be fulfilled for a product to obtain marketing authorisation from a Regulatory Authority.

5. *First auxiliary request*

Claim 1 of the first auxiliary request filed during the oral proceedings on 16 May 2014 contains one single independent claim (claim 1) which is identical to claim 4 of the main request.

As already stated in connection with claim 4 of the main request, the purpose-limited product claim 1 of the first auxiliary request is allowable under Article 54(5) EPC 2000 since it seeks protection for a further medical indication of a known substance (alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof), which is necessarily part of medical or veterinarian methods of treatment, including prophylaxis. None of the cited prior-art documents discloses the medical indication of alpha-ketoglutaric acid and its pharmaceutically acceptable salts for use in increasing plasma levels of high density lipoprotein (HDL) in vertebrates such as birds and mammals,

including man. Therefore, the novelty of claim 1 of the main request cannot be contested.

Document D4 forms part of the state of the art under Article 54(2) EPC 2000 since it was published on 1 June 2004. D4 is a publication concerning a "Meeting Report" of the 5th International Conference on HDL Cholesterol held on 8 and 9 March 2004. D4, in particular the contribution by G. M. Coppola, which discloses that the compounds SDZ45-904 and HDL376 are HDL-elevating agents for patients with HDL-C less than 3 mg/dL, represents the closest prior art (page 150 of D4).

In the light of the closest prior art the problem to be solved lies in the provision of an alternative HDL-elevating agent.

The solution defined in claim 1 of the first auxiliary request is alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof.

The application contains technical information and experimental data which support that the problem has been plausibly solved. In particular, example 2 (experiment II) discloses a study conducted on Wistar rats, 84 animals were used. After obtaining by dietary means a hyperlipidaemic profile, some of the animals were treated with placebo, and others with alpha-ketoglutaric acid. The experimental results displayed in Table 13 show a statistically significant increase of HDL plasma levels for male animals and an experimental trend for female animals.

Additionally, the results of experiment III on human volunteers and Table 16 also show that the problem is

plausibly solved since they show an experimental trend in the elevation of HDL plasma levels following four weeks' administration of AKG (calcium salt) and a decrease in HDL plasma levels after cessation of administration of AKG (calcium salt).

In fact, the clinical study in E3 is not needed to demonstrate that in the present case the problem has been plausibly solved, since the application as filed provides the skilled person with sufficient technical information in this respect. The experimental data in document E3 resulting from a clinical study in 60 patients confirms that the problem has not only been plausibly solved, but that it has also been actually solved.

Now it has to be investigated whether the proposed solution is obvious to the skilled person.

There is no hint in document D4, which reflects the technical knowledge in the field of HDL-cholesterol shortly before the effective filing date of the present application and reports on a multitude of different compound classes encompassing statins, fibrates, enzymes etc., to look in the direction of alpha-ketoglutaric acid. The thiourea derivatives, compounds SDZ45-904 and HDL376 on page 150 of document D4, are structurally remote from alpha-ketoglutaric acid.

Moreover, documents D5 to D7 illustrate the general knowledge of the skilled person at the relevant filing date of the present application. Their contents do not allow the skilled person to conclude that any compound known to reduce cholesterol levels would be useful for increasing HDL plasma levels. Furthermore, none of documents D5 to D7 refers directly or indirectly to

alpha-ketoglutaric acid (and its pharmaceutically acceptable salts).

Documents D1 and D2 were published in the 1970's. These documents teach the skilled person that alpha-ketoglutarate shows a hypocholesterolemic effect (document D1) or that ornithin-alpha ketoglutaric acid is able to reduce the levels of free fatty acids, triglycerides and cholesterol. However, the teaching in these two documents does not give any indication to the skilled person to contemplate alpha-ketoglutaric acid (and its pharmaceutically acceptable salts) as an obvious alternative to the thiourea compounds in document D4.

Therefore, the subject-matter of claim 1 of the first auxiliary request filed on 16 May 2014 involves an inventive step (Article 56 EPC).

Claims 2 and 3 are dependent on claim 1; their subject-matter therefore also involves an inventive step.

Consequently, the first auxiliary request meets the requirements of Article 56 EPC.

## **Order**

### **For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to grant a patent with the following claims and a description to be adapted thereto:



Claims 1 to 3 of the first auxiliary request filed during the oral proceedings of 16 May 2014.

The Registrar:

The Chairwoman:



S. Sánchez Chiquero

M. C. Ortega Plaza

Decision electronically authenticated