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Datasheet for the decision of 10 September 2019

Case Number: T 2080/16 - 3.3.07

Application Number: 07123922.2

Publication Number: 1920763

IPC: A61K9/00, A61K47/28

Language of the proceedings: EN

Title of invention:
Pharmaceutical compositions for inhalation

Patent Proprietor:
Vectura Limited

Opponent:
Gallafent, Alison

Headword:
Pharmaceutical compositions for inhalation/Vectura Limited

Relevant legal provisions:
EPC Art. 108, 100(b), 54, 56
EPC R. 99(2)

Keyword:

Opponent's appeal admissible - Yes
Main request - Sufficiency of disclsoure (Yes)
Main request - Novelty (Yes)
Main request - Inventive step (Yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 2080/16 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 10 September 2019

Appellant: (Patent Proprietor)	Vectura Limited 1 Prospect West Chippenham, Wiltshire SN14 6FH (GB)
Representative:	Clarke, Christopher John Vectura Limited Intellectual Property Department One Prospect West Chippenham Wiltshire SN14 6FH (GB)
Appellant: (Opponent)	Gallafent, Alison Alison Gallafent Ltd 21 Bridge St Llandeilo SA19 6BN (GB)
Representative:	FRKelly 27 Clyde Road Dublin D04 F838 (IE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 12 July 2016 concerning maintenance of the European Patent No. 1920763 in amended form.**

Composition of the Board:

Chairman	J. Riolo
Members:	D. Boulois
	Y. Podbielski

Summary of Facts and Submissions

I. European patent No. 1 920 763 was granted on the basis of a set of 26 claims.

Independent claims 1 and 15 read as follows:

"1. Microparticles for use in a pharmaceutical composition for pulmonary administration, comprising particles of an active substance having, on their surfaces, particles of a hydrophobic material suitable for promoting the dispersal of the active particles on actuation of an inhaler and suitable for delaying the dissolution of the active substance, wherein the hydrophobic material comprises a metal stearate."

"15. A method of preparing microparticles exhibiting delayed dissolution for use in a pharmaceutical composition for pulmonary administration, comprising the step of combining particles of an active substance with particles of a hydrophobic material in a spray drying step, wherein the hydrophobic material comprises a metal stearate."

II. The patent was opposed under Article 100 (a), (b) and (c) EPC on the grounds that its subject-matter lacked novelty and inventive step, was not sufficiently disclosed, and extended beyond the content of the application as filed. Said patent was a divisional of application No 01 998 329.5 published as EP 1 337 241.

III. The appeal lies from the decision of the opposition division that the patent as amended met the requirements of the EPC. The decision was based on the sets of claims filed with letter of 28 April 2016 as main request and auxiliary request 1, and auxiliary

request 2 filed during the oral proceedings of 28 June 2016.

The subject-matter of claim 1 of auxiliary request 2 was identical to claim 1 of the main request with the further added feature "wherein the coating covers at least 50% of the total surface area of the active particles". Claim 14 corresponded to claim 15 of the main request with the further specification specifying that the claimed method was for preparing "microparticles according to any of claims 1 to 13".

IV. The documents cited during the opposition proceedings included the following:
D8: WO 00/53158
D9: WO 87/05213
D10: US 5 972 388

V. According to the decision under appeal, the claimed invention was sufficiently disclosed, in view of the examples of the contested patent.

The main request did not meet the requirements of novelty in view of D8 and D9. D10 was however not novelty-destroying. The same conclusion applied to auxiliary request 1.

As regards the novelty of auxiliary request 2, there was no clear and unambiguous disclosure in D8 and D9 that the coating of magnesium stearate covered at least 50% of the total surface area of the active particles. Hence, claim 1 was novel over D8 and D9.

D10 was seen as the closest prior art, instead of D8 which had the preference of the opponent. D10 disclosed an active substance encapsulated in a cellulose ether

membrane. The distinguishing feature of claim 1 was the presence of a coating of metal stearate that covers at least 50% of the total surface area of the active particles. In the absence of any effect, the problem was seen as the provision of alternative type of microparticles displaying delayed dissolution in the airways. There was no explicit or implicit indication in D8-D10 that a coating of metal stearate covering at least 50% of the total surface area would be a suitable solution to the technical problem. The subject-matter of claim 1 of auxiliary request 2 was inventive for this reason.

VI. The patent proprietor and the opponent (hereinafter respectively the appellant-proprietor and the appellant-opponent) filed an appeal against said decision.

VII. With its statement setting out the grounds of appeal dated 22 November 2016, the appellant-proprietor submitted a main request and auxiliary requests 1 to 8.

Independent claim 1 of the main request read as follows, difference(s) compared with claim 1 as granted shown in bold:

"1. Microparticles for use in a pharmaceutical composition for pulmonary administration, comprising particles of an active substance having, on their surfaces, particles of a hydrophobic material **present as a coating on the surface of the particles of active substance** and suitable for promoting the dispersal of the active particles on actuation of an inhaler and suitable for delaying the dissolution of the active substance, wherein the hydrophobic material comprises a metal stearate."

The independent process claim 14 was identical to claim 15 as granted.

VIII. A communication from the Board was sent to the parties. In this it was considered in particular that the main request was not inventive over D10, and that this applied also to the auxiliary requests.

The Board also noticed that the appellant-opponent's arguments as to inventive step related only to the subject-matter of auxiliary request 2 maintained in the opposition proceedings.

IX. In its submission dated 6 September 2019, the appellant-opponent informed the appellant-proprietor and the Board that it would not be attending the oral proceedings.

X. Oral proceedings took place on 10 September 2019. At the beginning of the oral proceedings the appellant-proprietor submitted a new main request and new auxiliary requests 1-6 to replace the requests previously filed in writing.

Claim 1 of the main request was identical to claim 1 as filed with the statement of grounds of appeal, and the main request did not comprise any process claims anymore.

XI. The arguments of the appellant-proprietor, as far as relevant to the present decision may be summarised as follows:

Admissibility of the opponent's appeal

The statement of grounds of appeal should set out clearly and concisely the reasons why it was requested that the decision under appeal be reversed, amended or upheld, and should specify expressly all the facts, arguments and evidence relied on. The purpose of the statement was to contest the reasoning of the decision under appeal. The statement had to give the legal or factual reasons for setting aside the decision on which the appeal is based. An appeal which did not explain why the impugned decision was wrong was inadmissible.

The opponent's statement of grounds of appeal did not meet these requirements:
- as regards sufficiency, the statement raised two completely new arguments, which clearly could not be responsive to the decision.
- as regards novelty, the statement failed to explain why the opponent considered that the opposition division's interpretation of the disclosure of D9 was incorrect.
- as regards inventive step, although the statement challenged the opposition division's choice of closest prior art, this in itself was not sufficient to explain why the opponent considered that the Opposition Division's decision on inventive step was wrong. Regardless of which document was taken as the starting point, to make out his case of lack of inventive step, the opponent had to show why the skilled person would have modified the teaching of D8 and D10 to introduce a coating of magnesium stearate which covers at least 50% of the surface of the active particles.

Sufficiency of disclosure

Claim 1 did not need to include a limitation to a particular blending, since sufficiency of disclosure

required that the patent, not the claims, discloses the invention. In any case, claim 1 specified the presence of a coating, which was the technical feature of the particles which resulted from the use of an effective method. Moreover, the patent disclosed sufficient examples, embodiments or variations across the scope of the claims. Finally, as regards the amount of hydrophobic material to be used, the specification, in particular paragraph [0028] and the examples, provided clear guidance about the suitable amounts of hydrophobic material. Furthermore, the skilled person would have known that the amount can be adjusted according to the desired extent of dissolution delay.

Novelty

In Example 2 of D9, most of the magnesium stearate was trapped inside the conglomerate and could not come into contact with the active agent, BDP. It would not be able to form a coating on the BDP, because blending did not apply a sufficiently high degree of force. For these reasons, it was clear that Example 2 of D9 could not produce active particles which had a coating of magnesium stearate.

Inventive Step

D1O clearly related to exactly the same technical problem as the patent, i.e. to provide microparticles with delayed dissolution. D8 was concerned with a different problem, namely modifying the surface properties of carrier particles in order to reduce the adhesion of the active agent. The problem addressed by the patent was neither derivable nor recognisable from the disclosure of D8. The opposition division was correct to conclude that D10 represented the closest

prior art, and that the claims are inventive for the reasons set out in the decision.

The distinguishing feature of claim 1 of the main request over D10 was that the microparticles had a coating of metal stearate on their surfaces. The problem was the provision of an alternative microparticle.

D10 mentioned in column 10, lines 29-36, that a solution of cellulose ether and medicament had to be spray-dried, to which it was possible to add a lubricant such as magnesium stearate. Such a process involving a solution could not produce microparticles within the scope of the claims, since one would not obtain particles having a coating of magnesium stearate on their surfaces.

This is the reason why the process claims had been suppressed from the main request. A spray-drying process was not able to provide particles of active agent coated with magnesium stearate and was not consistent with the product claims of the main request.

There was no incentive in D10 to provide a coating of magnesium stearate over the active particles, and the claimed product was inventive over D10.

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

Sufficiency of disclosure

Claim 1 did not include any limitation as to the blending method to be used, while not all blending

methods were effective in production of the claimed particles, over the whole area covered by the claims.

Moreover, given that the amount of hydrophobic material, in this case a metal stearate, might be as low as 0.01%, the skilled person would have immediately realized that this is not enough to form a coating and that he could not have used this low amount. This amount of hydrophobic material was also an essential feature which had to be present in the claims.

The claims should disclose any feature essential for carrying out the invention in sufficient detail to render it apparent to the skilled person how to put the invention into practice, and neither the blending method, nor the amount of hydrophobic material were defined in the claim or described in sufficient detail in the description in order for the skilled person to provide a coating covering at least 50% of the total surface area of the active particles as was claimed.

Novelty

Example 2 of D9 was novelty destroying. When carrying out the teaching of Example 2 of D9, the skilled person would mix thoroughly the micronised BDP and magnesium stearate in the conglomerate until homogeneous in a powder mixer; and so inevitably arrive at a result falling within the terms of the claim.

Inventive step

D8 had to be considered as closest prior art instead of D10. D8 actually corresponded to a similar purpose/use as the claimed invention, namely reducing upper respiratory tract deposition of delivered particles

capable of penetrating into the lower lungs. Moreover, D8 already taught the carrier particles are mixed with suitable amounts, preferably from 0.05 to 2% by weight, of additives, such as metal stearates. The distinguishing feature between the claimed invention and the disclosure of D8 was that the coating covers at least 50% of the total surface area of the active particles.

However, there was no evidence of a technical result occurring at and above the critical value of 50% of the total surface area of the active particles. Accordingly, the objective technical problem had to considered to be the provision of alternative microparticles for use in a pharmaceutical composition for pulmonary administration. The solution was obvious in view of D8.

XIII. Requests

The appellant-proprietor requested that the decision under appeal be set aside and the patent be maintained according to the sets of claims filed as main request or alternatively on the basis of one of auxiliary requests 1-6 filed during the oral proceedings of 10 September 2019. The appellant-proprietor further requested that the appeal of the appellant-opponent not be held admissible.

The appellant-opponent requested in writing that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. Admissibility of the appeal of the opponent

1.1 The board is of the view that the appeal is admissible for the reasons set out below.

1.2 The admissibility of the appeal depends on the conformity of the notice of appeal with Article 108, third sentence, EPC, combined with Rule 99(2) EPC.

According to these provisions, in the statement of grounds of appeal the appellant must indicate "the reasons for setting aside the decision impugned, or the extent to which it must be amended, and the facts and evidence on which the appeal is based".

1.3 An appeal by an opponent is admissible if the grounds of appeal contain at least one reason for setting aside the impugned decision, as required by Rule 99(2) EPC. This is clearly the case with the present opponent's appeal, at least with regard to the grounds of novelty and inventive step.

The objections as regards novelty presented by the opponent in its notice of appeal were based on example 2 of D9, and the objections as regards inventive step were based on the choice of D8 as the closest prior art, instead of D10 as decided by the opposition division in its decision. Said objections were already presented during the opposition proceedings by the opponent, and were not followed by the opposition division in its conclusions as regards the request which was maintained in the opposition proceedings.

The presentation of these objections in the grounds of appeal constitute clearly reasons for setting aside the decision impugned as required by Rule 99(2) EPC.

1.4 Hence, the statement of grounds of appeal of the opponent constitute a clear answer to the decision of the opposition division and the appeal is thus admissible.

2. Main request – Sufficiency of disclosure

2.1 Claim 1 relates to microparticles comprising particles of an active substance having, on their surface, particles of a metal stearate present as a coating.

Sufficiency of disclosure within the meaning of Article 100(b) EPC must be assessed on the basis of the patent as a whole, including the description and the claims, and not of the claims alone. The description of the patent specification gives information as to the nature of the coating and the process used to obtain such discontinuous or continuous coating (see par. [0047] [0054]-[0056] and [0059]-[0061]). The description specifies in particular that blending processes involving a high degree of force were required to prepare the claimed microparticles, and gives specific examples thereof in the description and in the examples. The description provides also several examples of particles coated with magnesium stearate, and several explicit specific blending processes and various amounts of magnesium stearate to prepare said particles. There is thus no reason to doubt the possibility to prepare the claimed microparticles, all the more so as the description of the contested patent provides enough teaching showing how to obtain them.

2.2 The Board can in particular not follow the argument of the appellant-opponent that the blending method and the amount of metal stearate were essential features wich should have been present in claim 1. Indeed, according to the appellant-opponent, not all blending methods are effective in producing the claimed particles, and a skilled person would immediately realize that an amount as low as 0.01% of a metal stearate, as presented in the description, would not be enough to form a coating.

First, said objection amounts in fact to an objection on insufficiency of disclosure in view of possible non-working embodiments; such objection can only be directed to an invention claimed in terms of an effect or purpose to achieve, which is not the case here.

Moreover, claim 1 relates to a product and it is therefore only necessary to investigate whether the patent specification has provided enough information to the skilled person for him to reliably determine if at least one method enables the manufacture of such product. This is undeniably the case, and the fact that not all blending methods would be effective in the production of the claimed particle, as mentioned by the appellant-opponent, is irrelevant as regards the claimed product.

With regard to the amount of metal stearate, claim 1 does not comprise any restriction with this regard. The description of the contested patent mentions that "the microparticles will usually comprise at least 0.01% by weight of the hydrophobic material and will preferably comprise at least 1%, more preferably at least 5% and optionally at least 15% by weight of the hydrophobic material, based on the total weight of the microparticles" with the restriction that "the

microparticles comprise not more than 80%, more preferably not more than 60%, more preferably not more than 40% by weight of the hydrophobic material, based on the total weight of the microparticles" (see par. [0028] of the specification). The skilled person would therefore have no difficulty to determine the necessary amount of metal stearate to obtain continuously or discontinuously coated microparticles.

2.3 The patent therefore discloses the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

3. Main request - Novelty

3.1 D8 and D9 were mentioned as novelty-destroying documents by the opposition division in view of respectively examples 3 and 2 of these documents.

3.2 D8 relates to carrier particles having their surface modified with magnesium stearate by a mild blending method, in order to reduce the drug-carrier interparticle forces (see pages 6-9). D8 discloses in example 3 particles for pulmonary administration comprising BDP, lactose and magnesium stearate, wherein lactose and magnesium stearate are first mixed in a Turbula mixer for two hours and finally micronized BDP powder was added to the carrier and also blended under mild conditions (30 minutes at 32 rpm) in a Turbula rotating mixer. Given the process steps disclosed in example 3 and the general disclosure of D8 dealing with carrier particles having their surface modified with magnesium stearate, it is not technically credible that the active agent becomes coated with magnesium stearate as shown in example 3, but is is rather immediately

apparent that it is indeed the carrier lactose which is coated with magnesium stearate.

3.3 D9 discloses the preparation of a lactose and magnesium conglomerate and its further mixing with an active agent, as shown in examples 1 and 2. As for D8, D9 does not disclose an active agent coated by magnesium stearate, but relates to the preparation of a excipient in the form of conglomerate of a water-soluble vehicle, in particular lactose, with a suitable lubricant, such as magnesium stearate. D9 is not concerned with coated particles of active agent.

3.4 Consequently, the main request meets the requirements of Article 54 EPC.

4. Main request - Inventive step

4.1 The invention relates to microparticles for use in a pharmaceutical composition for pulmonary administration comprising a particle of active substance having, on its surface, particles of a hydrophobic material for delaying the dissolution of the active substance.

4.2 The opposition division considered D10 as closest prior art, while the appellant-opponent's choice is D8.

4.2.1 D8 relates to the modification of the surface properties of the carrier particles by the use of a conventional mixer which allows to modify said surface properties of the carrier, preferably lactose (see D8, pages 6, 8). The purpose is to modulate the interaction of the carrier particles with the micronised drug particles, to give sufficient adhesion force to hold the active particles to the surface of the carrier particles during manufacture and in the delivery device

before use, but that force of adhesion should be low enough to allow the dispersion of the active particles in the respiratory tract (see D8, page 4, second par. and page 6, two last par.). The carrier may be mixed under mild conditions, and not by a milling process, with 0.05 to 2% by weight of stearate to reduce the drug-carrier inter particle forces, and increase the respirable fractions. Example 3 shows the preparation of such composition by mixing lactose with 0.25% by weight of magnesium stearate, and mixing the obtained powder with BDP in a Turbula mixer for 30 minutes at 32 rpm. This document does therefore clearly not appear to relate to the coating of active agents or even to the purpose of the contested patent and cannot constitute the closest prior art.

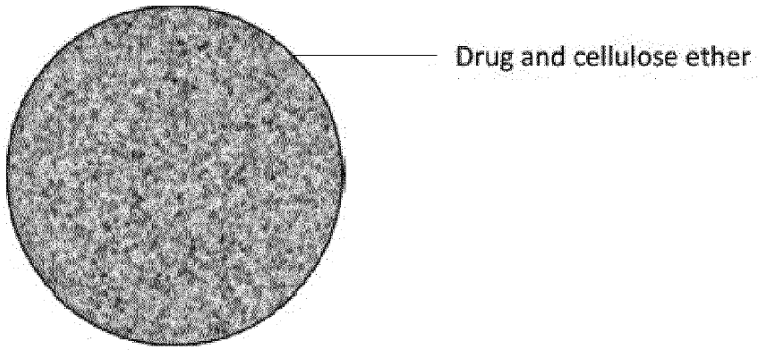
4.2.2 D10 discloses aerosol particles which have a good retention and provide a sustained release of the active agent, and relates thus to the same technical problem as the contested patent. The active agent particles are spray-dried with a lower alkyl cellulose ether, such as HPC or HPMC (col. 7, l. 20-25 and the examples). Said document further suggests that the properties of the powder can be improved by adding in a solution to be spray dried a lubricant such as magnesium stearate, a surfactant such as soybean lecithin, an anti-static agent, a stabilizer, and an odor-changing agent.

The process used in D10 is a spray-drying process and when suggesting the improvement of the properties of the particles by the addition of a lubricant such as magnesium stearate, D10 mentions that the addition of said lubricant is made to a solution to be dried (see col. 10, l. 29-36). All examples of D10 disclose indeed the spray drying of a solution of cellulose ether and active substance, with solvents such as ethanol, water

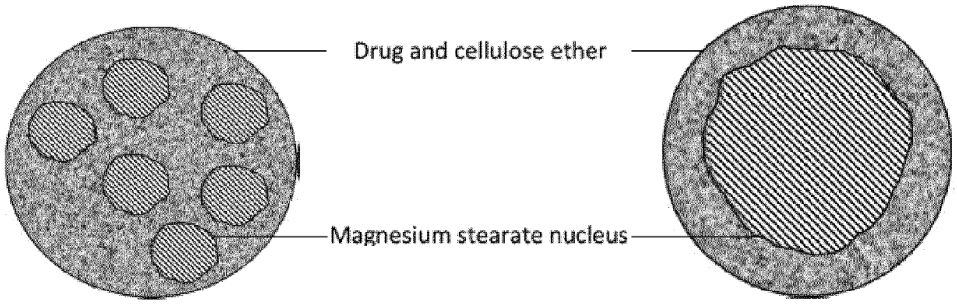
or dichloromethane. Magnesium stearate is not soluble in any of the solvents listed in D10, and it could only be added as a solid and would remain in suspension.

With this disclosed spray-drying process, the active particles cannot have a coating of magnesium stearate on their surface, but have rather the following structures:

(a) Particles obtained by the dissolved drug and cellulose

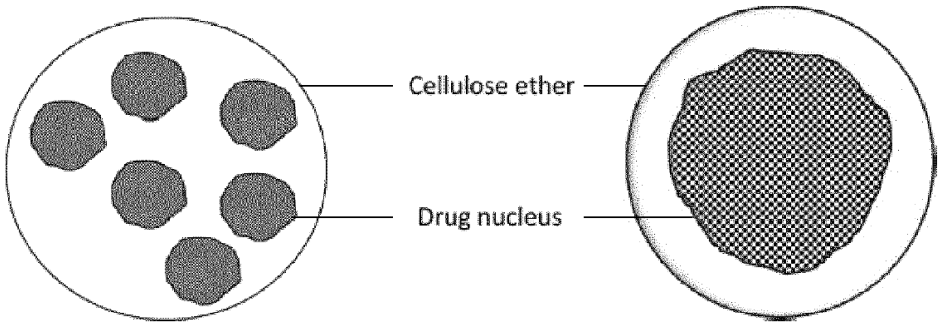


(b) Particles obtained by the suspended magnesium stearate and dissolved drug and cellulose



Alternatively, D10 discloses also a spray-drying process of an active substance suspended in a solution of the cellulose ether, without however mentioning or suggesting the addition of further excipients, such as a lubricant, or disclosing examples according to this variant (see col. 9, lines 47-60). The particles

obtained with spray-drying the suspended drug and dissolved cellulose ether relate indeed to particles of active substance coated with the cellulose ether and having a delayed dissolution and their structure is as follows:



Consequently, D10 discloses coated particles of active substance, but does not disclose a coating of metal stearate on the surface of microparticles.

4.2.3 D10 appears to relate to the same problem as the contested patent and to have the highest number of technical features in common with the claimed invention, and should be considered as the closest prior art for this reason.

4.3 The problem appears to be the provision of an alternative microparticle, suitable for delaying the dissolution of the active substance, as agreed by the appellant-proprietor.

4.4 As a solution to this alleged problem, claim 1 of the main request proposes particles of a hydrophobic material present as a coating on the surface of the particles of active substance, wherein the hydrophobic material comprises a metal stearate.

4.5 The patent demonstrates in its examples 3 and 4, and in the corresponding dissolution curves of Figures 2, 3 and 4, that microparticles of an active substance coated with a metal stearate show an improved delayed dissolution over uncoated particles of active substances. The contested patent provides therefore sufficient convincing evidence supporting the alleged effect.

4.6 The question remaining is whether the skilled person, starting from the teaching of D10, would arrive at the subject-matter of claim 1 of the main request in an obvious manner in order to solve the problem posed.

There is no direct suggestion in D10 to provide particles coated with a metal stearate, and in the situation wherein the addition of magnesium stearate is suggested as lubricant, the spray-drying process used does not lead to the provision of coated particles of active substances (see point 4.2.2 above).

As admitted by the appellant-proprietor, it appears in any case that the spray-drying process of an active substance and a metal stearate, especially of a suspension thereof, would not be able to provide the claimed coated microparticles.

The solution is also not obvious in view of D8, which discloses the coating of the carrier for another purpose than the contested patent, namely to reduce the drug-carrier inter particle forces, and increase the respirable fractions.

D9 also discloses the formation of an agglomerate of the lubricant with the excipient and not with the active substance, and does so for a different purpose,

namely for increasing the flow properties of the powder.

The claimed solution, namely the provision of particles of a hydrophobic material present as a coating on the surface of the particles of active substance, wherein the hydrophobic material comprises a metal stearate, is therefore not obvious.

4.7 Consequently, the main request meets the requirements of Article 56 EPC.

5. Adaptation of the description

The spray-drying process which was the subject-matter of claims 15-20 as granted is not part any more of the claimed invention, and the description still remains to be adapted correspondingly.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of the main request filed during the oral proceedings before the Board and a description to be adapted thereto.

The Registrar: The Chairman:

B. Atienza Vivancos J. Riolo

Decision electronically authenticated