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**Datasheet for the decision  
of 24 June 2014**

**Case Number:** T 0602/10 - 3.3.07

**Application Number:** 00956180.4

**Publication Number:** 1196146

**IPC:** A61K9/14, A61K9/72

**Language of the proceedings:** EN

**Title of invention:**

POWDER PARTICLES WITH SMOOTH SURFACE FOR USE IN INHALATION  
THERAPY

**Patent Proprietor:**

CHIESI FARMACEUTICI S.p.A.

**Opponent:**

NORTON HEALTHCARE LIMITED

**Headword:**

**Relevant legal provisions:**

EPC Art. 100(b)

**Keyword:**

Sufficiency of disclosure - (no)

**Decisions cited:**

**Catchword:**

see point 1.7



**Beschwerdekammern  
Boards of Appeal  
Chambres de recours**

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

Case Number: T 0602/10 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 24 June 2014**

**Appellant:** CHIESI FARMACEUTICI S.p.A.  
(Patent Proprietor) Via Palermo, 26/A  
43100 Parma (IT)

**Representative:** Adam, Holger  
Kraus & Weisert  
Patent- und Rechtsanwälte  
Thomas-Wimmer-Ring 15  
80539 München (DE)

**Appellant:** NORTON HEALTHCARE LIMITED  
(Opponent) Regent House  
5-7 Broadhurst Gardens  
Swiss Cottage  
London NW6 3RZ (GB)

**Representative:** Gillard, Richard Edward  
Elkington and Fife LLP  
Thavies Inn House  
3-4 Holborn Circus  
London EC1N 2HA (GB)

**Decision under appeal:** **Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
21 January 2010 concerning maintenance of the  
European Patent No. 1196146 in amended form.**

**Composition of the Board:**

**Chairman** J. Riolo  
**Members:** A. Uselli  
P. Schmitz

## Summary of Facts and Submissions

- I. The appeals of the patent proprietor and of the opponent lie against the decision of the opposition division announced at the oral proceedings on 26 November 2009 to maintain European patent No 1 196 146 in amended form.
- II. The patent had been opposed under Articles 100(a), (b) and (c) EPC on the grounds that its subject-matter lacked novelty and inventive step, the invention was not sufficiently disclosed and its subject-matter extended beyond the content of the application as filed.
- III. The documents filed during opposition proceedings included the following:
- D1: US 5,254,330
  - D5: AAPS PharmSciTech, 2004; 5(4), Article 60
  - D11: Report PMSQ1204 dated 18 September 2009
  - D14: Advances in Pharmaceutical Sciences, Volume 6, 1992
- IV. The decision was based on four sets of claims consisting of a main request filed on 18 January 2008 and three auxiliary requests filed during oral proceedings.

Claim 1 according to the main request read as follows:

"1. Particles for use as a carrier in the preparation of pharmaceutical formulations for the pulmonary administration of micronized active ingredients by means of a powder inhaler, wherein the median diameter of said particles is greater than 90  $\mu\text{m}$ , the surface

rugosity is less or equal to 1.1 upon determination of the fractal dimension as described on page 14, line 15- page 15, line 11 and their surface is coated with an additive selected from lubricants, anti-adherents and soluble polymers."

V. The decision of the opposition division can be summarised as follows:

- a) All the requests fulfilled the requirements of Article 100(b) EPC since the issues raised by the opponent with regard to the determination of the surface rugosity were questions of clarity rather than sufficiency.
- b) The main request and the first auxiliary request did not comply with Article 54 EPC. The subject-matter of the second auxiliary was novel but did not comply with Article 56 EPC.
- c) The subject-matter of auxiliary request 3 was considered to meet the requirements of the Convention.

VI. Both parties lodged an appeal against that decision. With the statement setting out the grounds of appeal the appellant-patent proprietor and the appellant-opponent submitted respectively the following documents:

D17: Experimental Report of Professor Bettini

D18: Statement of Dr Mark Hooper dated 26 October 2010

VII. In the statement setting out the grounds of appeal dated 21 May 2010, the appellant-patent proprietor requested that the patent be maintained on the basis of

the main request or auxiliary requests 1 to 3 filed therewith. In a subsequent letter sent on 23 May 2014 he submitted two new sets of claims as auxiliary requests 4 and 5.

The main request was identical to the one underlying the impugned decision.

Claim 1 of auxiliary request 1 read as follows:

"1. Particles for use as a carrier in the preparation of pharmaceutical formulations for the pulmonary administration of micronized active ingredients by means of a powder inhaler, wherein the median diameter of said particles is greater than 90  $\mu\text{m}$ , the surface rugosity is less or equal to 1.1 upon determination of the fractal dimension as described on page 14, line 15- page 15, line 11 and their surface is coated with an additive selected from lubricants, anti-adherents and soluble polymers, wherein the lubricant is magnesium stearate, sodium benzoate, or sodium stearyl fumarate, wherein the anti-adherent is leucine or isoleucine and wherein the soluble polymer is hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, polyvinylpyrrolidone, polyethyleneglycol or a cyclodextrin."

Auxiliary request 2 was identical to the request maintained by the opposition division (previous auxiliary request 3). Claim 1 of this request read as follows:

"1. Particles for use as a carrier in the preparation of pharmaceutical formulations for the pulmonary administration of micronized active ingredients by means of a powder inhaler, wherein the median diameter of said particles is greater than 90  $\mu\text{m}$ , the surface

rugosity is less or equal to 1.1 upon determination of the fractal dimension as described on page 14, line 15- page 15, line 11 and their surface is coated with an additive selected from lubricants and soluble polymers, wherein the lubricant is magnesium stearate, sodium benzoate, or sodium stearyl fumarate obtainable by a process comprising the step of subjecting the particles of a carrier to repeated stages of wetting with a solvent and drying, wherein the solvent contains an additive selected from lubricants and soluble polymers and comprising carrying out the repeated stages of wetting and drying in a high-speed granulator, said high-speed granulator consisting of a cylindrical mixing chamber (container) in which a rotating paddle (impeller) and a spray nozzle, wherein said high-speed granulator is capable of operating in controlled conditions of temperature and pressure."

Claim 1 of auxiliary request 3 read as follows:

"1. Particles for use as a carrier in the preparation of pharmaceutical formulation for the pulmonary administration of micronized active ingredients by means of a powder inhaler, wherein the median diameter of said particles is greater than 90  $\mu\text{m}$ , the surface rugosity is less or equal to 1.1 upon determination of the fractal dimension as described on page 14, line 15- page 15, line 11 and their surface is coated with an additive selected from lubricants, anti-adherents and soluble polymers, wherein the lubricant is magnesium stearate, sodium benzoate, or sodium stearyl fumarate, wherein the anti-adherent is leucine or isoleucine and wherein the soluble polymer is hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, polyvinylpyrrolidone, polyethyleneglycol or a cyclodextrin obtainable by a process comprising the step of

subjecting the particles of a carrier to repeated stages of wetting with a solvent and drying, wherein the solvent contains an additive selected from lubricants, anti-adherents and soluble polymers and comprising carrying out the repeated stages of wetting and drying in a high-speed granulator, said high-speed granulator consisting of a cylindrical mixing chamber (container) in which a rotating paddle (impeller) and a spray nozzle, wherein said high-speed granulator is capable of operating in controlled conditions of temperature and pressure"

Claim 1 of auxiliary requests 4 was based on claim 1 of auxiliary requests 2 with the introduction of the limitation that the additive is dissolved or dispersed in the solvent and is present in an amount between 0.05 and 2%.

Claim 1 of auxiliary requests 5 was based on claim 1 of auxiliary requests 3 with the addition of the same limitation introduced in auxiliary request 4.

VIII. Oral proceedings were held on 24 June 2014.

IX. As far as relevant for the present decision, the arguments of the appellant-opponent can be summarised as follows:

*Sufficiency of disclosure*

The standard method used for determining the rugosity of a surface at the filing date of the opposed patent was the air permeametry. This method was applied for instance in documents D1 and D14. In the opposed patent a new method for determining the rugosity was introduced, without however providing the adequate

level of information for its implementation. In particular, there was no teaching in the patent on how the SEM image was to be produced and which software for the image analysis was used. The description was silent with regard to certain SEM settings such as the contrast, the magnification and the resolution. Concerning the contrast, it was shown in report D11 that changing this parameter had a direct effect on the level of grey. With regard to the magnification, it was clear from D17 that variations of this parameter resulted in different values of the fractal dimension. Having regard to the software, no information at all was given in the opposed patent. Since the surface rugosity was presented as a key feature of the invention, there was a fundamental deficiency deriving from the absence of adequate instruction as to how to determine this parameter. Contrary to the position taken by the opposition division, the lack of adequate information in the opposed patent with regard to the method for determining the surface rugosity was to be seen as a problem of sufficiency of disclosure rather than clarity.

- X. As far as relevant for the present decision, the arguments of the appellant-patent proprietor can be summarised as follows:

*Sufficiency of disclosure*

The method for determining the rugosity of the particle's surface was clearly and unambiguously defined in paragraph [0040] of the patent specification. As outlined in this passage, the surface rugosity was quantified by measuring the fractal dimension of the line expressing the variation in grey level of the surface's image, as a function of the



position on the surface of the crystal. The image of the particle's surface was obtained with the scanning electron microscope (SEM). As explained by Professor Bettini in his declaration (D17), changing some settings of the SEM, such as the magnification, had no substantial influence on the surface rugosity value. Furthermore, some of these settings were disclosed in the figures of the patent. In addition, from the figures it was possible to read the word "JEOL" that identified the SEM apparatus. With this microscope, the contrast and the resolution could not be adjusted. Several software programs were known before the priority date which could have been used for determining the surface rugosity. All these programs provided a line showing the variation of the grey level and calculated the fractal dimension of this line. It was of no importance that the specific software used was not mentioned in the patent, because any of them would have been suitable for calculating the fractal dimension. Therefore, the skilled person would have been able to quantify the fractal dimension even if the software for the image analysis was not mentioned in the patent. Lastly, the specification described how to obtain carrier particles having the required surface rugosity. Hence, by applying the smoothing process described in paragraph [0040] and in example 1, the skilled person would have obtained particles having a surface rugosity within the scope of the claims. This applied in particular to the product claims of auxiliary requests 2 to 5, which incorporated the process features that led to the obtention of particles with the desired rugosity. The requirement of sufficiency of the disclosure was therefore met.

XI. The appellant-patent proprietor requested that the decision under appeal be set aside and that the patent

be maintained on the basis of the main request or auxiliary requests 1 to 3 filed with the statement setting out the grounds of appeal dated 21 May 2010, or of auxiliary requests 4 or 5 filed with letter dated 23 May 2014.

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

### **Reasons for the Decision**

#### *Main Request - Sufficiency of disclosure*

1. The objection put forward by the appellant-opponent is based exclusively on the argument that the patent does not provide the skilled person with adequate information for the measurement of the surface rugosity in accordance with the method defined in claim 1.
- 1.1 As explained in paragraph [0040] of the patent, the method adopted by the inventors for measuring the surface rugosity is based on the determination of "the variation in grey level of the image relating to the surface of the particle". This determination is carried out in two steps. The first step is the acquisition of an image of the surface of the particles with a scanning electron microscope (SEM). The second step is performed by means of a software which generates a line expressing the level of grey as a function of the position on the surface of the crystal and calculates the fractal dimension of this line. The value of the fractal dimension expresses the rugosity of the surface. It is equal to 1 for smooth particles and it increases with the increase in rugosity.

1.2 From the analysis the relevant prior-art documents, it emerges that the standard method used before the priority date for determining rugosity was the air permeametry method. This method is used in document D1 (col. 3, lines 7-8) and document D14 (page 174, lines 21 to 23), and it is also mentioned in the opposed patent as a known method for evaluating rugosity.

There is no prior-art document in which the rugosity is determined according to the same method used in the opposed patent. The sole document referring to the fractal dimension as a quantitative measurement of the rugosity is D5, which was published more than 4 years after the filing date of the opposed patent.

1.3 In the light of the above, the question arises as to whether the information contained in the patent would on its own enable the skilled person to determine the rugosity, in the absence of any other supporting teaching derivable from the prior art. In this respect, the appellant-opponent said there was a lack of technical information in respect to both steps of the method, namely the acquisition of the image with the SEM apparatus and the analysis of the image by means of software.

1.4 As to the acquisition of the image, the description of the patent does indeed not contain any information with regard to some settings of the SEM apparatus, such as the contrast, the magnification and the resolution.

1.4.1 Having regard to the first of these parameters, namely the contrast, the data contained in report D11 of Dr Hooper show that the same sample could provide different images if different conditions of contrast are used. In particular, as underlined also in the

second report of Dr Hooper D18, the contrast has a direct impact on the degree of brightness of the pixels, rendering "the lighter pixel more light and the darker pixel more dark", thereby affecting the differences in the level of grey (D18, page 4). Thus, modifications of the contrast result in variations of the level of grey which is the relevant parameter for the calculation of the fractal dimension.

- 1.4.2 In the report of Professor Bettini submitted by the appellant-patent proprietor (D17), it is affirmed that a change in the contrast would not affect the difference between upper and lower level of grey (page 8). It is however not explained why the results experimentally shown in D11 clearly indicate the contrary.
- 1.4.3 During the oral proceedings, the appellant-patent proprietor eventually modified its line of reasoning with regard to the effect of the contrast and submitted for the first time in the proceedings that with the SEM used for acquiring the images, i.e. a JEOL microscope, the contrast cannot be changed.
- 1.4.4 From the above it must be concluded that either the images of the surface are taken with the same apparatus used by the inventors, or else, if a different SEM is used, the value of the fractal dimension could vary according to the contrast used. There is however no indication in the description of the patent that a specific apparatus has to be used. The name "JEOL" appears only in the corner of some figures without any indication as to its meaning.
- 1.4.5 No information is given in the description of the patent also with regard to two other parameters

relating to the acquisition of the image, namely the resolution and the magnification.

- 1.4.6 Concerning the resolution, again the appellant-proprietor declared for the first time during the oral proceedings that this parameter cannot be changed when a JEOL apparatus is used.
- 1.4.7 As to the magnification, it can be derived from Figures 1a, 1b, 1c, and 2 of the patent that images of the surface of lactose were taken at magnifications of X130 and X250. The data disclosed in report D17 (page 7) show that the fractal dimension of images obtained at the magnifications of X130 and X250 for a sample of lactose are respectively 1.213 and 1.179. According to claim 1, the particles must have a rugosity less than or equal to 1.1. Since a perfectly smooth particle has a rugosity of 1, the range of rugosity defined in claim 1 calculated in terms of fractal dimension is of only 0.1 units. Thus, although the difference in rugosity obtained at the magnifications of X130 and X250 may appear small in absolute terms, it is not negligible when compared with the amplitude of the range defined in claim 1. Accordingly, the same carrier particle could be considered to have the required rugosity or not, depending on the magnification used for acquiring the image of the surface.
- 1.5 With regard to the second step of the method for determining the rugosity, namely the analysis of the image, the Board observes that no information whatsoever is given in the patent. The skilled person faced with the problem of performing the invention would therefore be left with the task of finding the appropriate software.

- 1.6 The above analysis underlines the fact that the patent provides a rather qualitative description of the method for determining the rugosity, and that important technical information has been omitted.
- 1.7 The proprietor having deliberately decided to use a method for determining the rugosity which is different from the one commonly used in the state of the art, it was his duty to provide full information with regard to the means and the procedures for implementing said method. It is true that the requirement of sufficiency of disclosure does not impose on the applicant the burden of providing details concerning aspects well-known to the skilled person. But it is the Board's conviction that the extent of the information omitted from the application must be commensurate with the general knowledge in the technical field concerned. In general terms, when the issue of sufficiency concerns the description of a method for determining a parameter, the less common the method the more accurate the information provided in the description should be. In the present case, in the absence of any known prior-art work applying the same method used in the patent for measuring the rugosity, the skilled person has to rely primarily on the teaching of the patent to put the method into practice. In such a situation, important pieces of information such as the mandatory use of a specific instrument or the definition of important settings for using such an instrument must be clearly disclosed in the patent to avoid uncertainties and guesswork.
- 1.8 The appellant-patent proprietor argued also that the patent discloses in example 1 and paragraph [0040] of the description a method for reducing the rugosity of the particles. By applying this method, the skilled

person would inevitably obtain particles having a degree of rugosity within the range defined in claim 1.

However, a surface rugosity which is less than or equal to 1.1 upon determination of the fractal dimension, is a feature of claim 1, and it is therefore an essential part of the invention in that it makes it possible to identify the particles having the desired properties. Article 100(b) EPC imposes the requirement to disclose the invention in a manner which is sufficiently clear and complete for it to be carried out by a skilled person. Applied to the present case, this means that the skilled person should be enabled *inter alia* to determine the rugosity of the particles obtained according to the process described in the patent, since this aspect is an essential part of the definition of the invention. Accordingly, the argument of the appellant-patent proprietor is unconvincing.

- 1.9 In view of the above, the Board concludes that there is a fundamental lack of technical information concerning the determination of the rugosity by the method defined in claim 1.

As a consequence, the Board decides that the main request does not comply with the requirements of Article 100(b) EPC.

*Auxiliary requests 1 to 5*

2. Claim 1 of all these requests includes the requirement that the particles must have a surface rugosity which is less than or equal to 1.1 upon determination of the fractal dimension. Accordingly, the considerations set out above in respect to the main request apply also to the auxiliary requests.

- 2.1 With regard to claim 1 of auxiliary requests 2 to 5, the appellant patent-proprietor argued that the requirements of Article 100(b) EPC were met also in view of the incorporation in the claim of the features relating to the preparation of the particles. However, claim 1 of these requests likewise includes the feature relating to the rugosity. Thus, as explained in 1.8 above, carrying out the invention defined in these requests involves also determining the rugosity of the particles, and the patent does not contain an enabling disclosure for this task. Hence, the argument of the appellant-patent proprietor is not convincing.
- 2.2 In view of the above, the Board concludes that also auxiliary requests 1 to 5 do not meet the requirements of Article 100(b) EPC.



**Order**

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

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



M. Cañueto Carbajo

J. Riolo

Decision electronically authenticated