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**Datasheet for the decision
of 12 May 2016**

Case Number: T 2236/14 - 3.3.07
Application Number: 08462008.7
Publication Number: 2072041
IPC: A61K9/16, A61K9/28, A61K31/565
Language of the proceedings: EN

Title of invention:

Method for preparing film-coated tablets containing
drospirenone as active agent

Patent Proprietor:

Richter Gedeon Nyrt.

Opponents:

Bayer Pharma Aktiengesellschaft /
Bayer Intellectual Property GmbH

Relevant legal provisions:

EPC Art. 56, 100(a)
RPBA Art. 13

Keyword:

Inventive step - reformulation of the technical problem
Late-filed auxiliary requests - admitted (no)



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Case Number: T 2236/14 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 12 May 2016

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 29 September
2014 rejecting the opposition filed against
European patent No. 2072041 pursuant to Article
101(2) EPC.**

Composition of the Board:

Chairman J. Riolo
Members: D. Semino
W. Ungler

Summary of Facts and Submissions

I. European Patent No. 2 072 041 was granted on the basis of 3 claims, independent claim 1 reading as follows:

"1. Process for the preparation of film-coated tablets containing drospirenone active agent which comprises dissolving drospirenone in ethanol, then dripping continuously or periodically the solution obtained onto the surface of the fluid bed in a fluidizing equipment without spraying pressure while controlling the temperature of the product obtained removing the solvent molecules from the wet material by a hot airflow, and the cores obtained are film-coated with an organic and/or aqueous solution or dispersion of a film-forming polymer."

II. A notice of opposition was filed in which revocation of the patent in its entirety was requested.

III. During opposition proceedings, the following documents *inter alia* were cited:

D7: Experimental data submitted to the EPO on 10 October 2005 in connection with the prosecution of EP-A-1 380 301

D8: EP-A-1 380 301

D10: Hall, Business Briefing: Pharamtech 2004, pages 1-5

D16: Record sheet filed by the patent proprietor with letter of 16 December 2013

D17: A.R. Gennaro et al., "Remington's Pharmaceutical Sciences", Eighteenth Edition, 1990, pages 591-595

D19: US-A-5 926 082

D20: US-A-4 894 177

- IV. The decision of the opposition division rejecting the opposition was announced at the oral proceedings on 17 July 2014. With regard to inventive step, the decision can be summarised as follows:

The process of granted claim 1 differed from the disclosure in D7 in that the solution of drospirenone was dripped onto the surface of the fluidised bed instead of sprayed. As no evidence was available to show a reduction in the loss in active agent, nor an improvement in homogeneity, the technical problem was the provision of an alternative. The technical effect related to this problem was maintenance of the same dissolution profile in view of the dissolution data shown in the letter of the opponent dated 15 May 2014 and taken *inter alia* from D7 and D16. It was not obvious to replace spraying with dripping, as documents D19 and D20 were fundamentally different from the opposed patent and as it was unexpected that dripping led to the same dissolution profile in view of D10 and D17. In any case, the rapid dissolution could not represent a constraint to the technical problem, which was the provision of a mere alternative having the same or a similar effect.

- V. The opponents (appellants) lodged an appeal against that decision, contesting the findings of the opposition division *inter alia* as far as lack of inventive step was concerned. In this context, it was *inter alia* submitted that the technical problem put forward by the proprietor was not solved across the entire scope of the claims (pages 14 to 17, in particular last sentence on page 16); this analysis included the statement that "the dissolution properties of a film-coated tablet is highly dependent on the film-coating material *per se*" (last but one paragraph on page 15) followed by an analysis of the

influence of the coating material (last paragraph of page 15 and page 16).

- VI. With the reply to the statement setting out the grounds of appeal the patent proprietor (respondent) countered the arguments of the appellants and took position on the issues raised by the appellants, including on the achievement of an effect for the entire scope of the claims (pages 8 and 9 of the reply).
- VII. In a communication sent in preparation of oral proceedings, the Board summarised the points to be dealt with, and with regard to the formulation of the technical problem addressed the issues of whether rapid dissolution of the tablets could be seen as implied or related to the problem as initially presented and could be considered as credibly achieved by the claimed process (see point 3.3 in particular). In this context it was mentioned *inter alia* that "it does not seem credible that, with no limitation on the coating, a rapid dissolution is achieved by the claimed process".
- VIII. With a reply to that communication dated 12 April 2016 the respondent filed two set of claims as auxiliary requests 1 and 2.

Claim of auxiliary request 1 corresponded to granted claim 1 with the addition "wherein the film-forming polymer is selected from the group consisting of acrylic acid, methacrylic acid, methoxyethylacrylate, cellulose acetate, ethylene oxide and polyethylene oxide, ethylene vinyl acetate copolymer, methyl cellulose, polyvinyl acetate, polyvinyl alcohol, polyvinyl pyrrolidone, polytetrafluorethylene and polyvinylidene chloride". In claim 1 of auxiliary request 2, the film-forming polymer was limited to "polyvinyl alcohol".

- IX. With letter of 21 April 2016 the appellants filed a further document (D28: R. Voigt, "Lehrbuch der pharmazeutischen Technologie" 6. Auflage, VHC, 1987, pages 470-474).
- X. Oral proceedings were held on 12 May 2016.
- XI. The arguments of the appellants, as far as relevant to the present decision, can be summarised as follows:

Granted claim 1 - inventive step

- a) The reformulation of the technical problem as the provision of an alternative process for providing a film-coated tablet having the same rapid dissolution as the tableted disclosed in document D7 was not allowable, as the obtainment of the rapid dissolution was not implied or related to the problem initially proposed. On the contrary, the patent conveyed the general impression that the tablets should not dissolve rapidly (paragraph [0020]), while the passages indicated by the respondent did not address the issue of rapid dissolution. In particular, the fact that drospirenone was in amorphous form was not a feature of the claim. Moreover, it was not plausible that all tablets prepared according to the claimed process exhibited rapid dissolution without any limitation of the parameters of the process, such as the size of the drops, and of the film-coating material, so that the problem was not credibly solved across the entire scope of the claims. Actually, the process conditions were not even indicated for the product whose dissolution rate was given in D16. The correct technical

problem with respect to D7 as the closest prior art was the provision of a further process for preparing a drospirenone-containing film-coated tablet. The replacement of spray-coating with drip-coating, which constituted the only difference with respect to the disclosure of D7, was obvious in view of document D19, which described spraying and dripping as being equally suitable for applying an active agent, including a drug substance, onto the surface of carrier particles in a fluidised bed system. How the fluidisation was accomplished (i.e. by means of air or by magnetic forces) was not relevant to how the active agent was applied. Moreover, claim 1 was not limited to fluidisation by air stream. In any case it was known that better dissolution of low-soluble drugs was obtained, if the drug was deposited on the surface of inert carrier particles (see e.g. D28), independently of how deposition was accomplished. For these reasons, the process of claim 1 did not involve an inventive step.

Auxiliary requests - admittance

- b) There was no justification for filing the auxiliary requests only after the communication of the Board and shortly before the oral proceedings, as the Board had not raised any new objection, nor any new point in that communication, but it had only emphasised issues which had been fully covered in the previous proceedings. While a reaction could be appropriate and justified if a communication raised new issues, it was abusive and against the Rules of Procedure not to react to the statement of grounds of appeal, but do it only when the preliminary opinion of the Board repeated some

arguments discussed therein. Moreover, the amended requests did not solve the inventive step issue, as they did not specify any process conditions, nor the achievement of any effect. On that basis, the requests should not be admitted.

XII. The arguments of the respondent, insofar as relevant to the present decision, can be summarised as follows:

Granted claim 1 - inventive step

- a) The process of granted claim 1 differed from the disclosure in D7 as closest prior art in that spraying of the solution of drospirenone onto the surface of the fluidised bed was replaced by dripping. The technical problem was the provision of an alternative process for preparing a drospirenone-containing film-coated tablet with dissolution of the active from the tablets core in the same rapid manner as in D7. The fact that dissolution was as rapid as in the tablets of D7 was shown in the figure submitted by the opponents during opposition proceedings showing the data in D7 and D16. The comparison was perfectly appropriate as the only relevant difference was the replacement of spraying by dripping. As to the coating, a water-soluble coating was used in both cases, while a comparison using coatings with different solubility did not make sense. No counter-data existed to show that the attainment of the result was not possible across the entire scope of the claims. The relevance of rapid dissolution was derivable from the patent, which specified that drospirenone was substantially insoluble in water (paragraph [0016]) and that the aim of the process was to eliminate disadvantages

of the processes of the prior art (paragraph [0012]). In addition, the indication that, similarly to the spraying method, by means of dripping drosiprenone was in amorphous form in the tablets (paragraph [0017]), gave a further indication that rapid dissolution was obtained, as it was known e.g. from D28 that spraying normally resulted in an amorphous form of the active which was characterised by an increase in dissolution rate with respect to the crystalline form. The skilled person would not have expected to obtain the same dissolution properties when replacing spraying by dripping, as he would imagine that, due to the larger droplet size, agglomerates would form and dissolution would be hindered. Document D19 contained no hint that dripping resulted in rapid dissolution. In any case, even if looking for a further process, the skilled person would not consider combining the teaching of D7 with the one of D19, as the claimed process made use of fluidising equipment significantly different from the one in D19, which employed magnetic forces, and as in D19 the liquid could be sprayed or dripped before, after or during fluidisation. In view of that, the claimed process was inventive.

Auxiliary requests - admittance

- b) The auxiliary requests should be admitted into the proceedings, as they were a reaction to the preliminary opinion of the Board, as they were filed sufficiently in advance of the oral proceedings and as they were so similar to the granted claims that their consideration did not require any undue effort. Indeed, while the opposition division had not given any relevance to

the coating, it was clear from the communication of the Board that the material of the coating was an important issue. As the purpose of the communication was to address the essential points of discussion, it should be allowable to react to it. Moreover, the limitation in auxiliary request 1 was taken from granted claim 2 and the one in auxiliary request 2 limited the coating to the one used in the tests in D16, so that there was no surprise for the appellants.

XIII. The appellants requested that the decision under appeal be set aside and the patent be revoked. Furthermore, they requested that auxiliary requests 1 and 2 be not admitted into the proceedings.

XIV. The respondent requested that the appeal be dismissed or that the decision under appeal be set aside and the patent be maintained according to auxiliary requests 1 or 2 filed with letter of 12 April 2016.

Reasons for the Decision

Admittance of D28

1. Document D28 was filed by the appellants shortly before the oral proceedings before the Board. However, both parties made use of the document in their argumentation and neither of them contested its admittance into the proceedings. In view of this, the Board sees no reason not to admit the document with the consequence that document D28 is admitted into the proceedings.

Granted claim 1 - inventive step

2. There was agreement between the parties both in the choice of document D7 as the closest prior art and in the identification of the difference between the process of claim 1 and the one disclosed therein, namely the replacement of spraying of the solution of drospirenone in ethanol onto the surface of the fluid bed with dripping of the solution. The Board concurs with this analysis.

2.1 Indeed D7 contains experimental data relating to the prosecution of document D8 and discloses in its examples 1 and 2 the preparation of tablet cores by charging a fluidised bed granulator with corn starch, modified starch and lactose, activating the fluid bed, spraying an ethanolic solution of *inter alia* drospirenone onto the bed while drying by heating the air stream of the fluidised bed, granulating with magnesium stearate and pressing the resulting granulate into tablet cores. The tablet cores of examples 1 and 2 are coated in example 3 of D7 following the procedure in example 1 of D8, namely by coating with an aqueous solution of hydroxypropyl-methylcellulose and macrogol combined with an aqueous suspension of talc, titanium dioxide and ferric oxide (paragraph [0045] of D8).

2.2 As to the formulation of the technical problem, the problem described in the patent is that of eliminating the disadvantages of the processes described in the technical literature (paragraph [0012]), which are outlined in the preceding paragraphs ([0009] to [0011] in particular) and concern primarily lack of homogeneity of the product obtained and a large loss of active agent. There is nothing in the analysis of the disadvantages of the technical literature that points

explicitly or implicitly to the need or the relevance of a rapid dissolution of the drug.

- 2.3 The sentence relative to the solubility of drospirenone in water in paragraph [0016] ("the drospirenone is substantially insoluble in water") is present in the context of the selection of the solvent to be used in the preparation process and is neither related to disadvantages of the processes of the prior art, nor to desired properties of the product obtained.
- 2.4 As to the statement that the drospirenone active agent obtained by the claimed process is in an amorphous state (last sentence of paragraph [0017]), it also does not identify the desire or the need of obtaining a certain dissolution profile, all the more as it refers to a result which is not present in granted claim 1. While it may be known (e.g. from document D28) that drospirenone in amorphous state has a better solubility than the same agent in crystalline state, this is not the only feature of the product which determines the drug dissolution profile, so that a plain statement that the agent is in amorphous form at the end of the procedure cannot be understood as an indication that it is desired to have a dissolution profile which is as rapid as the one of prior art products.
- 2.5 On that basis, while the obtainment of a homogeneous product and a small loss of active agent are identified as objective of the patent in suit and could form the basis for the formulation of the technical problem, maintenance of a rapid dissolution is neither implied, nor related to the problem initially suggested, so that it cannot be taken into account in the formulation of the technical problem.

- 2.6 On top of that, the process of claim 1 is so broadly formulated in terms of the distinguishing feature ("dripping") with no specification of any process condition, nor any limitation on how dripping is accomplished, that it cannot be credible that, independently of how dripping is conducted, a rapid dissolution profile is obtained. In this respect, it is worthwhile mentioning that also the description contains very little information about how dripping is accomplished, that even the example on which dissolution data are given in D16 has no information about how dripping is conducted and that no result or effect is mentioned in the claim. While under other circumstances counter-examples could be needed to doubt the presence of an effect, in the present case the complete lack of detail about the dripping step renders not credible that certain dissolution properties are obtained in the absence of any evidence on the side of the proprietor that, independently of how dripping is accomplished, a rapid dissolution profile is obtained.
- 2.7 As to the objectives present in the patent, there are neither data, nor arguments on the side of the respondent concerning the obtainment of any effect related to homogeneity of the product or loss of active agent with respect to the process of D7.
- 2.8 In view of that, the technical problem is to be formulated as the provision of a further process for the preparation of film-coated tablets containing drospirenone.
- 2.9 As the problem is simply the provision of a further process, the skilled person would consider any feature proposed in the prior art as a possible alternative or equivalent to the features of the claims for a similar

process as an obvious measure not requiring any inventive activity. This is indeed the case for dripping, which is listed in D19 together with spraying as one of the possible methods for providing liquid into a chamber to be contacted with moving particles of a fluidised bed (column 2, lines 42-50).

- 2.10 The further arguments of the respondent regarding the lack of relevance of document D19 are not considered as convincing by the Board. Indeed document D19 concerns the application of liquids to particulates in fluidised bed (field of the invention, column 1, lines 6-10). While fluidisation takes place by magnetic forces in D19, the methods listed in the cited passage are said to be suitable for providing liquid to a chamber in order to come into contact with moving particles with no restrictions on how the particle movement is generated. In addition, the fact that spraying and dripping are mentioned with reference to moving particles makes it clear that they are suitable for application of the liquid during fluidisation. Finally, at several instances reference is made in D19 to the production of pharmaceutical products (column 1, lines 17-18; column 3, lines 14-16; column 9, lines 3-10 including the indication that the active ingredient may be carried by the liquid and remain on the surface after removal of the liquid).
- 2.11 Therefore, the skilled person, starting from the process of D7 and looking for a further process would take into consideration the teaching of D19 and replace spraying with dripping. For these reasons, the process of granted claim 1 does not involve an inventive step.

Auxiliary requests - admittance

3. Auxiliary request 1 and 2 were filed one month before the oral proceedings before the Board with a reply to the communication of the Board. In claim 1 of both requests amendments were introduced concerning the definition of the film-forming polymer of the coating.
- 3.1 While it is true that the Board expressed doubts on the credibility that a rapid dissolution could be achieved with no limitation on the coating (point VII, above), the appellants had expressed similar doubts in the statement of grounds (see point V, above), on which the respondent had already taken position in their letter of reply (see point VI, above).
- 3.2 On that basis, the communication of the Board did not confront the respondent with new grounds or evidence, nor with new arguments, which could justify a reaction only at that stage.
- 3.3 In this respect it is worthwhile noting that a communication of the Board is not compulsory and is not normally meant to raise new issues, but rather serves to concentrate the attention of the parties on the disputed points and cannot be seen as a justification for filing new requests, in particular when, as in the present case, it mentions arguments which have already been debated and on which both parties have already taken position.
- 3.4 With regard to the specific amendments, they do not address the critical issues concerning the formulation of the technical problem which have led to the conclusion that granted claim 1 does not involve an

inventive step (in particular points 2.2 to 2.8, above), so that their admission does not seem appropriate in view of procedural economy, independently of their complexity and of whether the amendments could be expected or not.

- 3.5 In view of this, the Board finds it appropriate to exercise its discretion under Article 13 RPBA by not admitting auxiliary requests 1 and 2 into the proceedings.

Conclusion

4. As granted claim 1 is found not to involve an inventive step and the auxiliary requests are not admitted into the proceedings, there is no reason for the Board to decide on any other issue and the patent is to be revoked.

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:



S. Fabiani

J. Riolo

Decision electronically authenticated