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**Datasheet for the decision
of 30 June 2014**

Case Number: T 0010/10 - 3.3.07

Application Number: 97927372.9

Publication Number: 0914818

IPC: A61K9/20, A61K47/10, A61K47/26,
A61J3/10

Language of the proceedings: EN

Title of invention:
INTRAORALLY RAPIDLY DISINTEGRABLE TABLET

Patent Proprietor:
KYOWA HAKKO KOGYO CO., LTD.

Opponent:
Teijin Pharma Limited

Headword:

Relevant legal provisions:
EPC Art. 56
RPBA Art. 13(1), 13(3)

Keyword:
Inventive step - main request (no)
Late-filed requests 1 to 4 - admitted (yes)
Inventive step - auxiliary requests 1 to 4 (no)
Late-filed requests 5 to 8 - admitted (no)

Decisions cited:

Catchword:



**Beschwerdekammern
Boards of Appeal
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Case Number: T 0010/10 - 3.3.07

**D E C I S I O N
of Technical Board of Appeal 3.3.07
of 30 June 2014**

Appellant: KYOWA HAKKO KOGYO CO., LTD.
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 2 November 2009
revoking European patent No. 0914818 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman J. Riolo
Members: A. Usuelli
P. Schmitz

Summary of Facts and Submissions

- I. The appeal of the patent proprietor (appellant) lies against the decision of the opposition division to revoke European patent No. 914 818.
- II. The patent was opposed on the grounds of lack of inventive step (Article 100(a) EPC), insufficiency of disclosure (Article 100(b) EPC) and extension of the subject-matter beyond the content of the application as filed (Article 100(c) EPC). The following documents were among those cited during the opposition proceedings:

D4: EP 553 772

D14: Pharmaceutical Research, 1993, Vol. 10, 3, 351-355

D15: Pharmaceutisch Weekblad Scientific edition, 1983, 5, 165-171

D30: Experimental data No. 3

D39: Experimental data No. 1

- III. The decision of the opposition division was based on a single set of claims filed with letter of 17 July 2009.

Claim 1 of this set of claims read as follows:

"1. A pharmaceutical tablet for oral disintegration, comprising:
sugar alcohol or saccharide each having an average particle diameter of not more than 30 μm , an active ingredient, and a disintegrant selected from the group consisting of crospovidone, croscarmellose sodium, and low substituted hydroxypropylcellulose, wherein the sugar alcohol or the saccharide is in the amount of 60 to 95% by weight of the tablet, and the disintegrant is in the amount of 1-10% by weight of the tablet."

- IV. In its decision the opposition division came to the following conclusions:
- a) The subject-matter of the claims met the requirements of Article 123(2) EPC.
 - b) The closest prior art D4 disclosed rapidly disintegrating oral tablets that differed from the pharmaceutical tablets claimed in the opposed patent in that a different disintegrant was used. The "experimental data No. 1" submitted by the patentee during the examination phase contained data comparing tablets comprising only 5% disintegrants rather than 15% as disclosed for instance in example 19 of document D4. Thus, these data could not be taken into account for the assessment of inventive step because they were not based on the disclosure of document D4. The objective technical problem was to be seen in the provision of "alternative rapidly dissolving oral pharmaceutical tablets with acceptable hardness". Documents D14 and D15 disclosed the disintegrants of claim 1 as being pharmaceutically effective. The replacement of the disintegrants of D4 with the alternative agents disclosed in D14 and D15 was therefore obvious.
- V. The appellant lodged an appeal against that decision. With the statement setting out the grounds of appeal sent on 12 March 2010, he maintained as main request the set of claims filed on 17 July 2009 and submitted two auxiliary requests.
- VI. In a communication sent on 07 April 2014, the board submitted a preliminary opinion concerning *inter alia* the inventive step of all the requests and the

compliance of the amendments introduced in the auxiliary requests with the requirements of Article 123(2) EPC.

VII. With letter of 28 April 2014 the appellant filed a new auxiliary request 1 and renamed the auxiliary requests submitted on 12 March 2012 as auxiliary requests 2 and 3.

VIII. On 27 June 2014, the appellant submitted seven new requests named auxiliary requests 2 to 8 and withdrew the previous auxiliary requests 2 and 3.

IX. Claim 1 of auxiliary request 1 read as follows:

"1. A pharmaceutical tablet for oral disintegration, comprising:
D-mannitol having an average particle diameter of not more than 30 μm , an active ingredient, and a disintegrant selected from the group consisting of crospovidone, croscarmellose sodium, and low substituted hydroxypropylcellulose, wherein D-mannitol is in the amount of 60 to 95% by weight of the tablet, and the disintegrant is in the amount of 1 to 10% by weight of the tablet."

Claim 1 of auxiliary request 2 was based on claim 1 of auxiliary request 1 with the introduction of the indication that the tablets were obtained by compressing a dried granulated mixture.

Claim 1 of auxiliary request 3 differed from claim 1 of auxiliary request 2 in the introduction of the requirement that the tablets disintegrated in the mouth within one minute.

Claim 1 of auxiliary request 4 was based on claim 1 of auxiliary request 1 with the introduction of the indication that the tablets disintegrated in the mouth within one minute.

Claim 1 of auxiliary requests 5 and 6 was based on claim 1 of the main request with the amendment that the disintegrants were limited respectively to croscarmellose sodium and low substituted hydroxypropylcellulose (auxiliary request 5) or low substituted hydroxypropylcellulose (auxiliary request 6).

Claim 1 of auxiliary requests 7 and 8 was based on claim 1 of auxiliary request 1 with the amendment that the disintegrants were limited respectively to croscarmellose sodium and low substituted hydroxypropylcellulose (auxiliary request 7) or low substituted hydroxypropylcellulose (auxiliary request 8).

X. The opponent (respondent) replied to the grounds of appeal with a letter dated 2 August 2010. On 5 February 2014 he communicated his decision not to attend the oral proceedings.

XI. On 30 June 2014 oral proceedings were held before the board.

XII. As far as relevant for the present decision, the appellant's arguments can be summarised as follows:

Inventive step

- a) The problem underlying the invention was to be seen in the provision of improved pharmaceutical

formulations that disintegrated rapidly in the oral cavity while maintaining acceptable physical properties such as hardness and ease of manufacture. Document D4 represented the closest prior art for the assessment of inventive step. There were ample data showing the surprising effects due to the combination of small-sized sugar with the specific disintegrants selected by the inventors. In particular, the results of the experiments described in D30 and D39 showed that the tablets of the invention exhibited improved properties in terms of time required for oral disintegration and hardness as compared to those of D4. These surprising properties were not suggested by document D15. This document differentiated between water-soluble and water-insoluble superdisintegrants. According to D15, the water-soluble croscarmellose sodium exhibited disappointing disintegration properties. Sodium starch glycolate, which was one of the preferred disintegrants according to D15, disintegrated very slowly when used in formulations according to the invention. Hence, the teaching of document D15 could not be generalised to any formulation. This document did not suggest replacing traditional disintegrants such as starch with one the superdisintegrants disclosed therein.

- b) According to the teaching of D4 it was mandatory to add at least some water prior to compression. Drying the granules before compression was regarded as detrimental to the effects on disintegration time, as could be seen from the data disclosed in respect of reference example 3. Contrary to the teaching of document D4, according to the invention drying the granules before

compressing was favourable for producing a rapidly disintegrating tablet. Thus, the claimed tablets were to be considered inventive also in view of the process used for their preparation. This applied in particular to the tablets defined in claim 1 of auxiliary requests 2 and 3, which incorporated the features relating to their preparation.

Admissibility of the auxiliary requests

- c) Auxiliary request 1 was submitted on 28 April 2014 in reply to the communication sent by the board. It was based on the main request with the restriction that the sugar was D-mannitol. This amendment had a basis for instance in claim 3 as filed, and it was in conformity with the requirements of Rule 80 EPC.
- d) Auxiliary requests 2 to 4 were submitted on 27 June 2014 in response to the concerns expressed by the board in its communication as to the basis under Article 123(2) EPC for the feature "obtained by compressing a dried mixture". These requests contained only minor amendments as compared with previous auxiliary requests 2 and 3. For these requests too, the requirements of Article 123(2) EPC and Rule 80 EPC were met.
- e) Claim 1 of auxiliary requests 5 to 8 filed on 27 June 2014 included a narrower definition of the disintegrant. These requests were filed with the purpose of overcoming the objections under Article 56 EPC.

XIII. As far as relevant for the present decision, the respondent's arguments can be summarised as follows:

Inventive step

- a) The only difference between the tablets claimed in the opposed patent and the tablets disclosed in the closest prior art D4 was that the latter tablets did not comprise 1 to 10% of a disintegrant as defined in claim 1 of the main request. The tablets of D4, such as the one of example 19, met the requirements of adequate hardness and fast dissolution time. Accordingly, the objective technical problem was to be seen in the provision of an alternative tablet having adequate hardness and fast dissolution time. The patentee did not provide any suitable comparative data to support the argument that the tablets of the patent had improved properties. The disintegrants used in the tablets of the opposed patent were known to be effective disintegrants from document D15. This document would have taught the skilled person that the conventional disintegrants used in D4 could be replaced by lower amounts of crospovidone with the expectation of improvements in the hardness and disintegration time. Hence, the claimed tablets were obvious in the light of the combination of documents D4 and D15.

- b) The process for preparing the tablets could not render the subject-matter of claim 1 of the main request inventive, since this claim had no process features. Furthermore, a process for compressing a dried mixture was already disclosed in reference example 3 of D4. The reason why the tablet

obtained in this example had a slow disintegration time was simply because it did not contain a superdisintegrant. Additionally, document D15 too disclosed a process for preparing tablets by compression of a dried mixture. Tablets made by this method which contained a superdisintegrant disintegrated quickly. Accordingly, it was not surprising that the tablets of the invention, which also contained a superdisintegrant and were made by a method analogous to that described in D15, had a fast disintegration time.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be maintained according to the main request filed on 17 July 2009, or alternatively according to auxiliary request 1 filed on 28 April 2014, or according to one of auxiliary requests 2 to 8 filed on 27 June 2014.

XV. The respondent requested that the appeal be dismissed.

Reasons for the Decision

Main Request

1. *Inventive Step*

1.1 The invention addresses the problem of providing tablets which disintegrate rapidly in the oral cavity ([0001] of the patent specification).

1.2 The board agrees with the opposition division and with the parties that document D4 can be considered to represent the closest state of the art. This document too relates to tablets which disintegrate in the oral cavity (page 3, line 1). Said tablets contain a

carbohydrate, such as a sugar alcohol, in an amount from 10 to 90% (page 3, lines 30-32) and having a particle size preferably in the range of 20 to 70 μm (page 4, lines 48-49). As an optional component, the tablets of document D4 can contain also a disintegrant. A list of suitable disintegrants is disclosed on page 5 (lines 15 to 18). None of the three disintegrants specified in claim 1 of the main request is mentioned in this passage of D4. Furthermore, the general disclosure of D4 does not provide any indication as to the amount of disintegrants.

- 1.3 According to the appellant, the technical problem in the light of document D4 is the provision of tablets which exhibit improved properties in terms of the time required for oral disintegration and hardness.
- 1.4 As a solution to this problem the patent in suit proposes a tablet for oral disintegration according to claim 1 which is characterized in that it contains a disintegrant selected from the group consisting of crospovidone, croscarmellose sodium, and low substituted hydroxypropylcellulose, in the amount of 1-10% by weight of the tablet.
- 1.5 The appellant relied on the experimental reports D30 and D39 to demonstrate the improved properties of the tablets according to the invention over the tablets disclosed in document D4. Both reports relate to experiments comparing the hardness and the disintegration time of tablets according to the opposed patent, and tablets containing the disintegrants of D4. In D30 the tablets contain lactose as sugar while in D39 the sugar is mannitol. In both experiments the amounts of sugar and disintegrant are respectively 89.5% and 5%. Document D30 includes also data

concerning a tablet containing a disintegrant disclosed in document D15, namely sodium starch glycolate.

- 1.6 The results of the experimental reports indicate that the tablets having a composition in accordance with the opposed patent have a shorter disintegration time than the tablets containing one of the disintegrants mentioned in D4. The results concerning the hardness of the tablets appear less conclusive since the tablets according to the patent are not always performing better than the tablets containing the disintegrants of D4.

To the benefit of the appellant, and in view of the conclusions on obviousness below, the board considers that the results disclosed in documents D30 and D39 make it credible that the technical problem defined in 1.3 above has been solved by the provision of the tablets according to claim 1.

- 1.7 The question to be answered is whether the proposed solution would have been obvious to the skilled person in the light of the prior art.

Document D15 relates to tablets prepared by wet granulation containing lactose and a so called "super disintegrant". Four different super disintegrants are used including crospovidone and croscarmellose sodium, which are among the disintegrants listed in claim 1 of the opposed patent. Tablets containing 4% of a super disintegrant have been prepared and tested for their crushing strength and disintegration time. The properties of these tablets have been compared then with the properties of tablets containing 20% of potato starch which is a conventional disintegrant used in

various examples of D4 (see instance examples 2,7 and 19).

- 1.7.1 The results disclosed in Table IV with regard to the crushing strength, unequivocally show the better hardness for all the tablets containing 4% of a super-disintegrants as compared with the tablet containing 20% of potato starch.
- 1.7.2 As to the disintegration time, the tablet containing 4% of crospovidone disintegrates in 23 seconds or 26 seconds depending on the position of the disintegrant (intragranular or extragranular). These disintegration times are clearly shorter than those shown for the tablet with 20% of potato starch which disintegrates in 96 (intragranular) or 215 (extragranular) seconds.

The disintegration time of tablets containing 4% intragranular croscarmellose sodium is slightly above the time determined for tablets with 20% potato starch (110 vs 96 seconds). When the disintegrant is extragranular, the tablet with croscarmellose sodium disintegrates faster than the one with potato starch (149 vs 215).

- 1.7.3 Altogether, the results of Table IV demonstrate the better performance in terms of hardness and disintegration time, for the tablets containing crospovidone or croscarmellose sodium as compared with the tablets containing potato starch. In this respect it must also be observed, especially with regard to the comparison of the data concerning intragranular croscarmellose sodium and potato starch, that the amount of super-disintegrants in the tablets is always much lower than the amount of potato starch (4% vs 20%).

- 1.8 In the light of the above, the board concludes that a person skilled in the art faced with the problem of improving the hardness and disintegration time of the tablets disclosed in D4, would find in document D15 a clear incentive to replace the conventional disintegrant used therein with croscarmellose sodium.

- 1.9 The appellant argued that according to the teaching of document D15, croscarmellose sodium exhibited disappointing disintegration properties. Furthermore, sodium starch glycolate which was one of the preferred disintegrants according to D15, provided a slow disintegration when used in a formulation according to the invention, as shown in D30. Hence, in his opinion certain results obtained by the authors of D15 can not be generalized to any formulation.
 - 1.9.1 As to the disintegration time of croscarmellose sodium, it is noted that while the tablet containing this super-disintegrant disintegrates slowly when compared to the tablets containing a different super-disintegrant, it maintains a better disintegration profile vis-à-vis the tablet with potato starch (see 1.7 above). Hence, the observation of the appellant does not affect the conclusion that the skilled person would regard the replacement of a conventional disintegrant with croscarmellose sodium as a suitable solution of the technical problem.

 - 1.9.2 Having regard to the argument concerning sodium starch glycolate, indeed the experimental results of D30 appear to indicate that tablets containing this compound may not disintegrate so rapidly as suggested by document D15. There is no apparent explanation for

this deviation especially having regard of the fact that the formulations tested in D30 and D15 appear very similar. It is in any case observed, that the results shown in D30 with regard to the hardness of the tablet containing sodium starch gylcolate, and the results of D30 and D39 in respect to hardness and disintegration time of crospovidone and croscarmellose sodium, are in line with the teaching of D15 in the sense of confirming the improved properties of the super disintegrants over the conventional disintegrants. In the board's opinion a single deviating result would not justify a skeptical attitude towards the teaching of D15. Hence, the argument of the appellant is not convincing.

- 1.10 The appellant has also submitted some arguments based on the features of the manufacturing process, in order to support the presence of an inventive activity for the tablets of claim 1.

However, claim 1 is a product claim which is not limited by any process feature. Hence, these arguments are not relevant in the context of the assessment of the inventive activity of the subject-matter of claim 1.

- 1.11 In view of the above, the board concludes that claim 1 of the main request does not fulfil Article 56 EPC.

Auxiliary Request 1

2. Admissibility

- 2.1 This request was submitted on 28 April 2014, i.e. after filing of the grounds of appeal and when oral proceedings had already been arranged. The

admissibility of this request is therefore at the board's discretion (Articles 13(1) and 13(3) of the Rules of Procedure of the Boards of Appeal (RPBA), Supplementary publication to OJ EPO 1/2014, 44).

- 2.2 Auxiliary request 1 was submitted as a reaction to the observations made by the respondent to the statement of grounds of appeal and to the communication sent by the board. The request is based on the claims of the main request with the limitation that the sugar alcohol or saccharide is D-mannitol, as for claim 3 of the main request. The amendment has a basis for instance in claim 3 of the application as filed. Thus, the subject-matter of auxiliary request 1 does not involve any complexity and does not raise any new issue.

In view of the above, auxiliary request 1 is admitted into the proceedings.

3. *Inventive step*

- 3.1 As mentioned above, claim 1 of this request differs from claim 1 of the main request only in that the sugar alcohol or saccharide is specified to be D-mannitol.
- 3.2 The selection of this specific sugar does not result in any additional property or effect of the pharmaceutical tablets. Moreover, document D4 provides the teaching that mannitol is a suitable sugar for orally disintegrable tablets, so that this amendment does not add any further distinguishing feature to the claim vis-à-vis the closest state of the art.

Hence, the subject-matter of this request is obvious for the same reasons given with respect to the main request.

Auxiliary requests 2 to 4

4. *Admissibility*

4.1 Auxiliary requests 2 to 4 were submitted on 27 June 2014, that is three days before the oral proceedings. The admissibility of these requests is therefore subject to the discretion of the board.

4.2 The appellant argued that auxiliary requests 2 to 4 represented a response to the comments made by the board in its communication of 14 March 2014 having regard to the basis under Article 123(2) EPC for the feature "obtained by compressing a dried mixture", which was included in the then pending auxiliary requests 2 and 3 filed on 28 April 2014.

4.3 The amendments introduced in these requests are indeed in relation to the contested feature. Claim 1 of auxiliary requests 2 and 3 differs from claim 1 of the previous auxiliary requests 2 and 3 only in that the feature "obtained by compressing a dried mixture" has been amended to read "obtained by compressing a dried granulated mixture". Claim 1 of auxiliary request 4 corresponds to claim 1 of the previously pending auxiliary request 3 the sole difference being the deletion of the feature "obtained by compressing a dried mixture".

4.4 In the light of the above, the board holds that the subject-matter of auxiliary request 2 to 4 is not complex and the admission of these requests does not cause undue procedural delays. Hence, auxiliary requests 2 to 4 are admitted into the proceedings.

5. *Inventive step - Auxiliary request 2*

5.1 Claim 1 of this request differs from claim 1 of auxiliary request 1 on the additional feature "obtained by compressing a dried granulated mixture".

5.2 The appellant argued that according to document D4 it is mandatory to add some water before compressing the granules into tablets. In contrast to that, in the process of the invention the granules are dried before compression.

There is however no evidence proving that the method for producing the tablet imparts any additional properties to the latter. Hence, the pharmaceutical tablet of claim 1 of this request is not different from the pharmaceutical tablet of claim 1 of auxiliary request 1. Already for this reason, it must be concluded that also auxiliary request 2 does not comply with the requirements of Article 56 EPC.

5.3 In addition and independently from the previous considerations, it is noted that also according to the processes disclosed on page 167 of D15 (2nd complete paragraph) and in Reference example 3 of D4, the granules are dried before compression. Hence, the process as such does not appear to involve any inventive activity.

The appellant has argued that the skilled person would be discouraged by the teaching of D4 to carry out a drying step before compression since the disintegration time of the tablets of Reference Example 3 is too high. However, no reason is given in document D4 to explain the high disintegration time of the tablet of Reference Example 3. In the board's opinion there are no

objective reasons for assuming that the slow disintegration of this tablet is to be attributed to the drying step made before the compression. Hence, this argument is not convincing.

Accordingly, the subject-matter of auxiliary request 2 does not involve an inventive step in the sense of Article 56 EPC.

6. *Inventive step - Auxiliary request 3*

6.1 Claim 1 of this request differs from claim 1 of auxiliary request 2 on account of the introduction of the feature that the tablet "disintegrates in the mouth within one minute".

Since also document D4 discloses various tablets which disintegrate in the mouth within one minute (see Tables 22-1 and 22-2 and page 6, line 16), the feature introduced in auxiliary request 3 can not establish the presence of an inventive step.

Thus, also this request does not comply with Article 56 EPC.

7. *Inventive step - Auxiliary request 4*

7.1 Claim 1 of this request is based on claim 1 of auxiliary request 3 with the deletion of the feature "obtained by compressing a dried granulated mixture".

This request fails to comply with Article 56 EPC for the same reason given in respect to the auxiliary request 3.

Auxiliary requests 5 to 8

8. *Admissibility*

8.1 These requests were submitted together with auxiliary requests 2 to 4 on 27 June 2014.

8.2 In the accompanying letter, the appellant briefly illustrates the amendments introduced in the claims without however providing any comment as to the patentability of the subject-matter. The limitations to the list of disintegrants introduced in all the requests suggest that the appellant's aim was possibly to overcome the outstanding issues under Article 56 EPC. This was indeed confirmed by the appellant during the oral proceedings.

In this respect, the board notes that the objections raised by the respondent during the appeal proceedings with regard to the requirement of inventive step are based on the same facts and arguments discussed before the opposition division. Also, the comments submitted by the board in its communication of 14 March 2014, in particular with regard to the selection of D4 as the closest prior art and the observation that the disintegrants represent the distinguishing feature, are in line with the conclusions reached by the opposition division in its decision.

Notwithstanding the absence of any relevant change as to the factual and legal basis underlying the objection under Article 56 EPC, the appellant decided to file, only one working day before the oral proceedings, new requests in which for the first time limitations have been introduced in the list of disintegrants. These requests could already have been presented with the statement of the grounds of appeal, because the appellant was already aware of the criticality of the

feature concerning the disintegrants. Admitting these requests at this late stage would oblige the board to open a new discussion on inventive step during the oral proceedings in order to assess the relevance of these limitations. This could also imply the need to analyse documents so far disregarded during the appeal proceedings, and in the absence of the respondent, who did not attend the oral proceedings. This task would be rendered more difficult by the fact that no explanation has been given by the appellant before the oral proceedings as to why the subject-matter of auxiliary requests 5 to 8 should be considered to meet Article 56 EPC.

In the board's opinion, this all runs counter to the requirement of procedural economy (see Article 13(1) RPBA).

In view of the above, auxiliary requests 5 to 8 are not admitted into the proceedings.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



M. Schalow

J. Riolo

Decision electronically authenticated