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D E C I S I O N
of 29 April 1999

Case Number: T 0674/96 - 3.3.2

Application Number: 89302767.2

Publication Number: 0335560

IPC: A61K 9/32

Language of the proceedings: EN

Title of invention:

Controlled release pharmaceutical preparation and method for producing the same

Patentee:

Tanabe Seiyaku Co., Ltd.

Opponent:

Orion-yhtymä Oy
Boehringer Ingelheim GmbH

Headword:

Preparation coated with a porous film/TANABE

Relevant legal provisions:

EPC Art. 100(b), 83
EPC R. 57a, 57(1), 58(2)

Keyword:

"Sufficiency of disclosure - yes - no undue burden in finding out process parameters for preparing the product of the invention - addition of new dependent claims in opposition proceedings - no"

Decisions cited:

T 0823/93

Catchword:

-



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Boards of Appeal

Chambres de recours

Case Number: T 0674/96 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 29 April 1999

Appellant: Tanabe Seiyaku Co., Ltd.
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Representative: -

Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 31 May 1996
revoking European patent No. 0 335 560 pursuant

to Article 102(1) EPC.

Composition of the Board:

Chairman: P. A. M. Lançon

Members: U. Oswald

M. B. Günzel

Summary of Facts and Submissions

- I. European Patent No. 0 335 560 with the title "Controlled release pharmaceutical preparation and method for producing the same" was granted on the basis of 10 claims contained in European patent application No. 89 302 767.2.
- II. Two oppositions were filed against the granted patent, one by the Respondent (Opponent 01) and one by Opponent 02 who withdrew the opposition on 10 July 1997. The patent was opposed by both Opponents for lack of novelty and lack of inventive step under Article 100(a) EPC as well as for insufficiency of disclosure of the invention under Article 100(b) EPC.

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

- (2) "BASF FINE CHEMICALS Typical formulations **Kollidon^R** VA 64 Film coating", product brochure published by BASF July 1986
- (8) International Journal of Pharmaceutics, 104 (1994), 95-106
- III. By a decision delivered orally on 30 April 1996 with the written reasons posted on 31 May 1996, the Opposition Division revoked the patent under Article 102(1) EPC. The decision was based on a set of 18 claims comprising in comparison with the set of 10 claims as granted an amended independent product claim 1 and amended independent method claim 14,

amended dependent product and method claims, and in addition new dependent claims 4, 6, 7, 10 and 15 to 18 not forming part of the set of claims as granted.

Independent claims 1 and 14 read as follows:

"1. A controlled release pharmaceutical preparation, comprising a core containing a pharmaceutically active ingredient and coated with a porous film, characterised in that the porous film

(i) has a porosity as represented by the formula:-

$$1 - \frac{(\text{total weight of film}) / (\text{total volume of film})}{(\text{true specific gravity of film})}$$

of 0.4 to 0.9 and

(ii) is formed either from a hydrophobic polymeric substance which has film-forming ability and is insoluble in water but soluble in a water-miscible organic solvent or from a combination of said hydrophobic polymeric substance and a hydrophilic polymeric substance."

"14. A method for producing a controlled release pharmaceutical preparation, which comprises the steps of:

(i) dissolving a hydrophobic polymeric substance which has film-forming ability and is insoluble in water but soluble in a water-miscible organic solvent or said hydrophobic polymeric substance and a hydrophilic polymeric substance in a water-organic solvent mixture consisting of 9 to 0.5 volumes of the organic solvent

per one volume of water, and

(ii) spray coating a core containing a pharmaceutically active ingredient with the coating solution obtained in (i) to form a porous film comprising said polymeric substance or substances on the surface of the core, said porous film having a porosity as represented by the formula:-

$$1 - \frac{(\text{total weight of film})/(\text{total volume of film})}{(\text{true specific gravity of film})}$$

of 0.4 to 0.9."

The Opposition Division took the view that the amended set of claims including the newly filed dependent claims could be regarded as "*a reaction on a ground for opposition*" and therefore did not contravene Rule 57a EPC.

Since the invention concerned a new and very complex technique of controlling the film porosity of a controlled release pharmaceutical preparation, the Opposition Division objected that the patent in suit neither included a detailed working example nor contained specific information as to which of the many working parameters had an important influence on the film porosity. Since furthermore document (8), a scientific article by the inventors of the patent in suit concerning the same products as claimed in the patent in suit, but published after the priority date of the patent in suit, clearly showed that, beside the relative humidity during the spray coating process, the spraying temperature was by far the most important

factor of all of the process parameters, the Opposition Division took the view that the person skilled in the art did not know which of the many other parameters influencing the spray coating process were to be adjusted and in particular did not know how to adjust the temperature as appropriate to each of the other parameters. Since it was necessary to perform a vast amount of trials in order to obtain the desired result, the Opposition Division concluded that the patent in suit did not fulfil the requirements of Article 83 EPC.

- IV. The Appellant lodged an appeal against the said decision, filed an auxiliary request for oral proceedings and filed grounds of appeal including additional technical information in the form of eleven appendices, *inter alia* an expert opinion (Appendix 1) and an experimental report (Appendix 6). The Respondent filed counter arguments.

After summons to oral proceedings, in a letter dated 24 March 1999, the Respondent informed the parties that no Representative would attend the oral proceedings scheduled for the 29 April 1999. Oral proceedings took place as scheduled.

- V. The Appellant took the view that the skilled person in the present case had particular knowledge in the fields of pharmaceutical technology, process engineering and polymer chemistry and that neither the Opposition Division nor the Respondent had taken proper account of the relevant common general knowledge of the skilled person thus defined and that they had mistakenly given inappropriate consideration to documents (2) and (8). Having regard to Appendix 1 to the grounds of appeal,

it was particularly pointed out that it was generally understood in the field of film coating technique when a hydrophobic polymer such as ethyl cellulose and a volatile organic solvent such as ethanol was used that the product temperature was set relatively low, preferably at around 30°C and that the skilled worker would adjust the air inlet temperature of the coating apparatus accordingly. Since according to the invention spray coating was carried out in a conventional manner and since beside the temperature parameter there was no need for a particular adjustment of any of the other parameters, the reference to "warm air" and "room temperature" according to the examples of the patent in suit gave the skilled person sufficient technical information to repeat the method of the invention with immediate success and thus allowed him to reproduce the controlled release pharmaceutical preparation of the invention. Moreover, the appendices filed with the grounds of appeal, particularly "Appendix 6", contained background information regarding the porosity of the film of the invention and provided further evidence that the experimental work underlying the determination of the total weight of the film, the total volume of the film, the true specific gravity of the film - the parameters necessary to calculate the porosity as defined in claim 1 - belonged to the common general knowledge before the priority date of the patent in suit.

VI. The Respondent submitted *inter alia* in writing that neither the description nor the worked examples of the patent in suit allowed correlations to be deduced on the one hand between porosity and drug release rate and on the other between manufacturing parameters and

porosity. The Respondent maintained the argumentation that document (8) clearly showed the criticality of the coating temperature within a small temperature range and the complex relationship between this parameter and the other process parameters as well as the composition of the coating solution. As regards the Appellant's reference to Appendix 1, it was noted that neither coacervation nor phase separation was mentioned in the patent in suit and thus the expert's analysis based on the phenomenon of coacervation as the core of the invention could not help set aside insufficiency of disclosure of the invention. The Respondent furthermore contested the relevance of the worked examples according to the so-called Yoshino Declaration (Appendix 6 to the grounds of appeal) since according to said worked examples experiments were conducted at various temperatures but the other process parameters were not kept constant as it would be necessary to investigate whether or not there was an effect of temperature change on the porosity. Accordingly, the patent in suit did not teach how to achieve a given porosity and therefore did not fulfil the requirements of Article 83 EPC.

VII. On 27 April 1999, the Appellant filed by fax as main request the set of claims **annexed** to the decision of the Opposition Division and seven auxiliary requests.

VIII. The Appellant requested at the oral proceedings that the decision under appeal be set aside and the case be remitted to the Opposition Division with the claims annexed (meant is here "annexed to the appealed decision").

The Respondent requested in writing that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. The present decision is based on the set of claims annexed to the decision of the Opposition Division (see points III. and VIII. above). As regards the allowability of the amendments which the said set of claims comprised in comparison with the set of claims as granted, the Board notes that the Respondent made no objections under Article 123 EPC. The Board considers in accordance with the decision of the Opposition Division that the requirements of Article 123(2) and (3) EPC are satisfied.

3. Having regard to the Opposition Division's decision, the point at issue is whether (or not) the patent in suit discloses **the invention** as it is now claimed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.
 - 3.1 In the present case **the invention** relates to a controlled release pharmaceutical preparation comprising a core containing a pharmaceutically active ingredient and coated with a porous film and a method for producing the same under process conditions such that the desired dissolution rate is obtained by controlling the porosity of the film. Accordingly, the **person skilled in the art** is a process engineer having

knowledge of pharmacy and hence is familiar with the whole palette of film coating methods in 1988 just before the priority date of the patent in suit. In this respect the Board can agree with the expert opinion according to Appendix 1 in so far as that coacervation is the essential phenomenon underlying the invention and that the gist of the coating process of the present invention essentially consists in inducing a certain phase separation of the solution of the film former in the course of the process for preparing the product of the invention. Furthermore, the Board is convinced that the common general knowledge of the said skilled person includes the phenomenon of coacervation and subsequent gelation which had been used in practice before the priority date of the patent in suit *inter alia* in the field of pharmacology for the preparation of microcapsules. The latter use of coacervation and gelation has not been contested by the Respondent.

The Board notes that the Respondent objected that the description of the patent in suit did not contain a reference to the phenomenon of coacervation in relation to the claimed invention but did not contest that coacervation as a special type of phase separation belonged to the common general knowledge just before the priority date of the patent in suit. Furthermore, the Respondent did not submit that the skilled person would have difficulties in choosing suitable polymeric film-forming material(s) and/or water-miscible solvents from the groups of such components referred to in the claims and further specified in the patent in suit. Moreover, it is to be noted that the experimental part of the description of the patent in suit contains detailed information about the amount of each of the

components forming the controlled release pharmaceutical preparation of the invention. The Board is therefore convinced that the skilled person after reading the description and the experimental examples of the patent in suit and when starting experimental work on the basis of the examples of the patent in suit by using the defined amounts of components would recognize that the method of producing the product of the invention involves a phase separation of the specific type of coacervation.

- 3.2 The patent in suit indeed only indicates that the said phase separation takes place during spray coating practised according to conventional coating methods while blowing warm air. It remains therefore to be considered whether the skilled person in repeating the experimental work as described in the patent in suit is confronted with difficulties not allowing him to put the present invention **completely** into practice. The Board agrees with the Respondent's submission that neither the description nor the working examples of the patent in suit contain a reference to a specific product or air temperature, degree of moisture or humidity, or contain a reference to apparatus parameters for controlling the coating process. Having regard to the evidence on file, discussed in more detail below, particularly that in the form of an expert witness of document (8), paragraph 3.2, published after the priority date of the patent in suit and analysing various factors affecting the film porosity, *inter alia* temperature and humidity (see page 101, Figure 4 and Table 3), the Board is, however, convinced that there is no lack of technical information when taking account of the content of the

patent in suit as a whole **and** the common general knowledge of the skilled person referred to above under point 3.1.

- 3.3 As regards the extent to which in the present case the common general knowledge has to be taken into account for the disclosure of the temperature of the spraying process necessary to achieve the film porosity according to the invention, as an essential fact, it is to be noted that according to most of the worked examples of the patent in suit, namely 1 to 4 and 7 to 13, the water-organic solvent system of the coating solution consists of a water/ethanol mixture in a defined ratio.

Having regard to the said use of ethanol as the solvent for the polymeric film-forming substance of the invention, the Board cannot follow the Opposition Division's and the Respondent's assumption made on the basis of *inter alia* inlet and outlet temperatures in document (2) that the reference to "warm air" in the examples of the patent in suit would direct the skilled person to the use of more elevated spraying temperatures up to 60°C. The Board is convinced that on account of the **solvent volatility of ethanol** and the knowledge of the need to induce a certain phase separation of the solution of the film former in the course of the process for preparing the product of the invention, the skilled person in a first attempt would set the product temperature during coating relatively low, eg. below 40°C or even lower. Having regard to Figure 4 of document (8), showing, as undisputed by the Respondent, below 40°C a porosity above 0.4, it is then evident that the skilled person, **without knowing the**

temperature dependence of the porosity, is even in a first attempt able to produce a product within the porosity range claimed for the product of the present invention. Accordingly, there is no reason why the skilled person should envisage a broad temperature range for the preparation of the product of the invention, and thus the functional temperature dependency of the porosity over the broad temperature range as shown in Figure 4 of document (8) can be left aside. In the light of these facts there is no reason for supposing that said Figure 4 provides evidence that the disclosure of the invention of the patent in suit lacks technical information as to the coating temperature; but on the contrary said Figure 4 can be regarded as proof that in the present case the porosity represented a true parameter characterising the product of the invention.

- 3.4 Although from a theoretical point of view the gas inlet temperature, product temperature and gas outlet temperature in a coating apparatus may exhibit or follow a complex thermodynamic relationship, the Board is convinced that the skilled person in practice would have no difficulties in finding out a suitable test arrangement in the coating apparatus for **measuring** the gas inlet and outlet temperature as well as the product temperature and thus would find out on an experimental basis an empirical relationship for controlling the coating temperature. The Respondent did not file evidence that this would involve undue burden for a skilled person measuring the temperature in a coating apparatus.

3.5 Since Table 3 of document (8) shows that the skilled person, even by doubling the value of relative humidity from 45% up to 80%, has no difficulties in preparing a product according to the invention having a porosity within the claimed range, the Board also cannot see any technical reason why the lack of information about a certain humidity to be used in the coating process for preparing the product of the invention could establish insufficiency of disclosure of the invention.

3.6 As regards the alleged lack of information of process parameters other than temperature and humidity necessary to produce the product of the invention according to a conventional coating method, it must be presupposed that in the absence of such information the porous film is spontaneously formed during the spraying process on the basis of the phase separation principle mentioned above; otherwise, the patent in suit would indeed lack sufficiency of disclosure. Document (8), however, provides confirmation of such spontaneous formation of the porous film (see "Abstract", first and second sentence as well as page 96, left column, second paragraph).

3.7 According to point 3.1 above the present invention requires not only that the core of the preparation containing the pharmaceutically active agent is coated with a porous film but that the desired dissolution rate of the controlled release pharmaceutical preparation is obtained by controlling the porosity of the film. In this respect the patent in suit clearly indicates on page 5, lines 42 to 44, that "the porosity of the porous film, as a general rule, becomes greater as the ratio of water in the water-organic solvent

mixture is increased and smaller when the ratio of the organic solvent is increased". On page 5, lines 1 to 7, the patent in suit furthermore contains information on how the thickness of the porous film may then influence the desired dissolution rate.

Such a more general description of the invention does not affect sufficiency of disclosure if the skilled person is provided with instructions which together with common general knowledge would allow the invention to be put into practice without undue burden, if necessary with reasonable experiments. There is no requirement under Article 100(b) EPC or Article 83 EPC that any person reading the patent in suit or the application documents must immediately and without the least skill be in a position identically to carry out the invention on a large industrial scale.

Although document (8) published after the priority date of the patent in suit gives proof that a porous film according to the invention is spontaneously formed during the spraying process of the invention on the basis of a well-known phase separation principle and there are in general no difficulties in producing a controlled release pharmaceutical preparation within the claimed parameter ranges, sufficiency of disclosure of the invention requires that at least at the priority date of the patent in suit the skilled person is in a position to verify that a certain porosity of the coating film according to the invention has been achieved. In other words, sufficiency of disclosure of the invention also requires that taking into account the skilled person's common general knowledge, once experimental work has been done in order to find the

specific process parameters, the invention must be repeatable for a predetermined porosity value. In this respect both the description of the patent in suit and the amended independent claims contain a reference to a formula (see page 3, lines 3 to 14 and again point III above) allowing the porosity to be calculated by measuring the total weight of the film, the total volume of the film and the true specific gravity of the film. The Appellant has filed experimental data (Appendix 6) demonstrating that porosity values within the claimed range can be achieved at different temperatures and has shown how, by applying practical methods of determination of the physical parameters contained in the said formula, the porosity of the coated film can be evaluated in a reproducible manner. The Board notes that the Respondent has neither contested the validity of the formula for calculating the porosity nor has argued that the skilled person would have difficulties in carrying out in practice the measurement of the weight, total volume and specific gravity of the film in accordance with the methods as described in said Appendix 6. In the absence of counter-evidence the Board sees no reason to doubt that the values according to Appendix 6 are representative of a measurement of the porosity of the film in situ on a core.

The Board is also convinced that the skilled person as defined under point 3.1 above is provided with all the preparation, measuring and evaluation methods referred to in Appendix 6 but provisionally observes that **the skilled person to the same extent will also apply this knowledge in relation to any prior art disclosure.**

- 3.8 The Board agrees with the Respondent's submission that the experimental work according to said Appendix 6 cannot be regarded as an exact repetition of the worked examples of the patent in suit and that Appendix 6 relates to test series with different temperatures under conditions such that the process parameters were not kept constant. However, under Article 100(b) EPC and Article 83 EPC there is no necessity for such exact repetition of experiments of the patent in suit as long as the experimental work can be regarded as being within the **scope of the invention** under discussion. Moreover, for the purpose of the present decision Appendix 6 is taken into account only to the extent that it shows that it is possible to carry out the invention at technically meaningful temperatures under conditions within the ranges of the claimed product parameters. The Board notes that the Respondent did not contest the numerical values shown in Appendix 6 and in the **absence of contrary experimental data** can only conclude that the ground of opposition under Article 100(b) EPC cannot be maintained.
- 3.9 The Opposition Division did not take a decision on novelty and inventive step of the main request. It is therefore not appropriate to discuss in detail the auxiliary requests filed on 24 April 1999 with respect to sufficiency of disclosure. The Board only observes that the same reasoning as set out above would apply to these requests being restricted in comparison with the main request forming the basis of the decision of the Opposition Division.
- 3.10 As regards the addition of dependent claims in the Appellant's request for maintenance of the patent in

amended form the Board, in the oral proceedings, has drawn the Appellant's attention to the following:

Amendments to the text of a granted patent during opposition proceedings should only be considered as appropriate and necessary within the meaning of Rules 57(1) and 58(2) EPC and therefore admissible if they can fairly be said to arise out of the grounds of opposition laid down in Article 100 EPC. This is the established jurisprudence of the Boards of Appeal (see e.g. the decisions T 295/87, OJ EPO 1990, 470, T 317/90 of 23 April 1992 and T 823/93 of 17 March 1994, both not published in the OJ of the EPO, which are of particular relevance for the present case). In the cited decisions it was held that the addition of new dependent claims having no counterpart in the granted patent is neither appropriate nor necessary to meet a ground for opposition and is therefore not admissible in opposition proceedings. The present Board shares this view.

The grounds for opposition defined in Article 100 EPC allow for objections against the patentability of the subject matter of the patent. It is clear that the Patentee must have the right to overcome such objections by an amendment of the subject-matter claimed. The addition of a dependent claim, however, leaves unimpaired the scope of the independent claim to which such dependent claim refers. It neither limits nor amends the subject-matter claimed in the corresponding independent claim. The addition of a dependent claim is therefore no response at all to an objection against the patentability of the subject matter claimed (In this respect see also T 829/93, 6.2

of the reasons). On the contrary it adds to the patent a claim for a specific embodiment of the invention which may previously have been embraced by the scope of the corresponding independent claim but which was not specifically claimed as such. Opposition proceedings are undoubtedly not a continuation of the examining proceedings. In opposition proceedings the Patentee may not continue appropriate drafting of his patent at his convenience. In the view of the Board, it has therefore rightly been emphasised in the cited decisions that opposition proceedings do not provide an opportunity to the Patentee to improve the drafting of his claims by including new subject-matter, in particular preferred embodiments of the invention, in the claims which may have adequate support in the original description but have not been previously claimed as such (T 295/87, 3. of the reasons, T 317/90, 3. of the reasons). Therefore, the fact that dependent claims may constitute valuable fall-back positions for the case that the corresponding independent claim was found unallowable later, does not justify their addition in opposition proceedings to a remaining broader independent claim (T 829/93, 6.3 of the reasons).

All three decisions cited here concerned amendments made before the entry into force of Rule 57a EPC. Therefore, the view expressed by the Opposition Division that the addition of the new dependent claims was admissible because Rule 57a was not applicable to the amendments made by the Appellant is not correct.

However, the question of novelty and inventive step of the subject-matter of the main request remains to be decided. It cannot be ruled out that the Appellant may

have to limit the subject-matter of its main claims further. It is possible that this may involve incorporating the subject-matter of these newly introduced dependant claims into the corresponding main claims. The Board thus does not find it appropriate to insist on the deletion of said claims before remittal of the case for further prosecution to the Opposition Division.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the first instance for further prosecution.

The Registrar:

The Chairman:

P. Martorana

P. A. M. Lançon