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D E C I S I O N
of 14 January 2000

Case Number: T 0014/96 - 3.3.2

Application Number: 87310834.4

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IPC: A61K 9/08

Language of the proceedings: EN

Title of invention:
Topical drug release system

Applicant/Patentee:
BEECHAM GROUP PLC

Opponent:
Henkel Kommanditgesellschaft auf Aktien Goldwell AG

Headword:
Single phase drug composition/BEECHAM

Relevant legal provisions:
EPC Art. 123(2), (3), 102(3), 54, 56

Keyword:
"Deletion and renumbering of claims as substantive amendment -
(no)"
"Novelty (yes) - property in citation not demonstrated by
respondent-opponent"
"Inventive step (no) - predictable advantage"

Decisions cited:
-

Catchword:

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Boards of Appeal

Chambres de recours

Case Number: T 0014/96 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 14 January 2000

Appellant/other party: Henkel
(Opponent) Kommanditgesellschaft auf Aktien
TFP/Patentabteilung
D-40191 Düsseldorf (DE)

Representative: Goldwell AG
Appellant/other party Zerninstr. 10-18
(Opponent) D-64297 Darmstadt (DE)

Respondent: BEECHAM GROUP PLC
(Proprietor of the patent) Beecham House
Great West Road
Brentford
Middlesex TW8 9BD (GB)

Representative: White, Susan Mary
SmithKline Beecham plc
Corporate Intellectual Property
Two New Horizons Court
Brentford, Middlesex TW8 9EP (GB)

Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 7 December 1995
rejecting the opposition filed against European
patent No. 0 271 332 pursuant to
Article 102(2) EPC.

Composition of the Board:

Chairman: P. A. M. Lançon

Members: J. Riolo
C. Rennie-Smith

Summary of Facts and Submissions

- I. European Patent No. 0 271 332 based on application No. 87 310 834.4 was granted on the basis of 12 claims.

The independent claims as granted read as follows:

- "1. A single phase drug composition suitable for forming a supersaturated composition *in situ* when applied to a water-wetted area of a human or animal body, comprising a drug dissolved in a carrier system which contains from 0.01 to 1.0% by weight of an antinucleating agent, based on the total weight of the composition, the carrier system comprising from 0 to 50% by weight of water and from 50 to 100% by weight of a solubiliser, based on the total weight of the carrier system.
7. Use of a single phase drug composition as claimed in any one of claims 1 to 6 for the manufacture of a medicament for topical treatment of a human or animal body by forming a supersaturated drug composition *in situ* on application of the composition to a water-wetted area of the body, characterised in that the composition has dissolved therein sufficient drug such that, on mixing with water on the body, the resultant drug concentration is greater than the saturated drug solubility in the initially formed resultant mixture.
8. A method of cosmetic treatment of a human or animal body comprising applying a composition as

defined in any one of claims 1 to 6 wherein the drug is a cosmetic substance to a water-wetted area of the body, characterized in that the composition comprises a solubiliser and sufficient dissolved drug such that on mixing with the water on the body, the resultant drug concentration is greater than the saturated drug solubility in the initially formed resultant mixture."

II. Notices of opposition were filed against the granted patent by two parties (hereinafter referred to as the appellant and the opponent 02).

The patent was opposed under Article 100(a) EPC for lack of novelty and lack of inventive step.

The following document was inter alia cited during the proceedings.

(1) EP-A-0 151 953

III. The decision of the Opposition Division of 8 November 1995 posted on 7 December 1995 rejected the oppositions under Article 102(2) EPC.

The Opposition Division took the view that the patent in suit met the requirements of Articles 52(1), 54 and 56 EPC.

As regards novelty, the Opposition Division was of the opinion that the alleged novelty destroying document (1) did not disclose a single phase drug composition comprising an **antinucleating agent** since the opponents failed to prove that Carbopol 940® in the

form as used in (1) had an antinucleating effect.

Accordingly the main claim was acknowledged by the Opposition Division as complying with Article 54 EPC.

The Opposition Division also concluded that document (1), representing the closest state of the art and disclosing a two-phase system, contained no information on how to produce a stable single phase drug composition which would provide a supersaturated composition *in situ*.

In particular this document did not suggest that the skilled person could ignore one of the two phases of the compositions disclosed therein nor that the addition of an antinucleating agent would stabilise the single phase composition.

- IV. The appellant (opponent 01) lodged an appeal against the said decision.

- V. Oral proceedings were held before the Board on 14 January 2000. During these proceedings, the respondent (proprietor) filed an amended set of claims and requested that the patent be maintained on the basis of this set of claims.

The newly filed set of claims corresponded to the set of claims as granted with the product claims 1 to 6 deleted and the remaining claims renumbered accordingly.

- VI. The submissions of the appellant and of the opponent 02, both in the written procedure and at the

oral proceedings, can be summarized as follows:

For the question of novelty under Article 54 EPC the appellant took the view that the disclosure in (1) of the compositions of gels B and gel E comprising 1% w/w Carbopol 940® corresponded in all parameters to the compositions comprising 0.01 to 1% w/w of an antinucleating agent involved in the use and method claims. This argument relied on the contention that, because Carbopol 940® was a polyacrylic acid and polyacrylic acids were disclosed as suitable antinucleating agents in the patent in suit, it must follow that (1) anticipated compositions containing an antinucleating agent.

Furthermore, as the compositions of gels B and E were also suitable for forming a supersaturated composition *in situ* when applied to a water-wetted area of human or animal body, the appellant considered that claim 1 of the set of claims filed during oral proceedings lacked novelty.

As regards inventive step the appellant contended that the composition according to gel E, a single phase drug composition, disclosed in (1) was the most relevant prior art item. As it clearly appeared from the test carried out in table 2 that this single phase drug composition was less efficient than the two-phase drug compositions described in (1), the claimed single phase drug composition could not be regarded as inventive.

The opponent O2 shared the view of the appellant in all respects. He moreover pointed out that PVK K-30 used as antinucleating agent in the patent in suit was a

gelling agent as well, which confirmed the view that both properties could be possessed by the same product.

He also emphasized that document (1) recited on page 4, paragraph 3, that supersaturation of a drug solution could also be achieved *in situ* as required by claim 1 of the set of claims filed during the oral proceedings.

VII. The respondent's arguments submitted both in the written procedure and at the oral proceedings can be summarized as follows:

In the respondent's view the subject-matter of claim 1 of the set of claims filed during the oral proceedings was readily novel because (1) was absolutely silent about any single phase drug compositions to be applied on a water-wetted area of the body. It emphasized that neither gel E nor any of the other gels disclosed in (1) were obviously intended to be applied to a water-wetted area of the body in order to achieve a supersaturated drug composition *in situ*.

Moreover, as Carbopol 940® used in (1) was mentioned as a thickening agent and also acting as such in the various examples, (1) was clearly not disclosing any antinucleating agents at all. It further maintained that the skilled person reading the patent in suit would have been aware that there was a clear distinction, based on molecular weight, between high molecular weight polymers such as carbopol 940® which had utility as thickening agents and low molecular weight polymers which were useful as antinucleating agents.

As regards inventive step, the respondent was of the opinion that the problem to be solved could be seen in the simplification of the prior art packing, which resulted in reduced packaging costs.

In its opinion, the solution to this problem involved an inventive step because it would not have been obvious for a person skilled in the art to consider adapting a drug-containing phase of a drug/carrier system of the type disclosed in (1) to render it stable by addition of an antinucleating agent and because it would also not have been obvious to consider taking a drug-containing phase thus adapted and applying it directly to a water-wetted body with the intention of producing *in situ* a concentration of the drug above its saturated solubility in the solvent mixture so created.

As regards gel E of document (1), the respondent argued that it was irrelevant since it was merely provided in (1) as a yardstick against which to measure the level of supersaturation which could be achieved by mixing together two phases which were primed for supersaturation.

It finally stressed that neither gel E nor any of the other gels disclosed in (1) were intended to be applied to a water-wetted area of the body in order to achieve a supersaturated drug composition *in situ*.

VIII. The appellant requested that the decision under appeal be set aside and that the European patent n° 271 332 be revoked.

The respondent requested that the appeal be dismissed

and that the patent be maintained on the basis of the amended set of claims filed during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.
2. *Article 123(2) and (3) EPC*

The amended set of claims filed during the oral proceedings corresponds to the set of claims as granted but with the product claims 1 to 6 deleted and the remaining use and method claims renumbered accordingly.

No objection under Article 123(2) and (3) EPC was raised by the parties with respect to this set of claims and the Board sees no reason to differ.

3. *Article 102(3) EPC*

The Board cannot share the appellant's point of view that Article 102(3), which confers the power to consider the whole EPC with respect to amendments in the course of opposition and appeal proceedings, should also apply in the present case with respect to the set of claims filed during the oral proceedings.

In fact, according to the case law of the Boards of Appeal such a power can only be exercised if **substantive** amendments have been made.

In the present case the amendments in the set of claims filed during the oral proceedings, compared with the set of claims as granted, comprise merely renumbering of the claims and deletion of the product claims. While the characteristics of the deleted product claims, previously incorporated in the use claims by formal reference to the product claims have now been of course incorporated in the use claims, there have clearly been no substantive amendments in any of the claims now under consideration.

4. *Novelty*

The independent use and method claims 1 and 9 of the set of claims filed during the oral proceedings both involve the presence of an antinucleating agent.

The Board agrees with the appellant that the patent in suit recites that polyacrylic acids are suitable antinucleating agents (page 2, lines 49 and 50) and that Carbopol 940® belongs to the class of polyacrylic acids.

The Board can however not share the appellant's conclusion that Carbopol 940® in the form as used in document (1) is therefore inevitably an antinucleating agent.

Chemically speaking, it is, as a rule, clear to the skilled person that, when a given property is related to an infinite class of compounds, all the members of the class do not possess and express that property equally and that there are furthermore many intrinsic and extrinsic parameters influencing that property such

as the molecular weight and the chemical nature of the other products present.

This general principle is highlighted in the patent in suit which mentions three classes of compounds as examples of suitable antinucleating agents, recites that the choice of a suitable antinucleating agent will in fact depend on various factors, and then suggests a simple experiment in order to determine whether or not a selected compound does indeed possess the desired antinucleating property (page 2, lines 51 to 57).

The Board notes, on the one hand, that document (1) is silent about any antinucleating property in general and that it moreover discloses Carbopol 940® as being merely a thickening and gelling agent (page 4, paragraph 2) and, on the other hand, that the appellant has not provided any evidence (such as the simple test proposed in the patent in suit) in order to demonstrate that Carbopol 940® does display an antinucleating property in its form as used in the compositions disclosed in (1).

In these circumstances, the Board acknowledges the novelty of the subject-matter of the set of use and method claims filed during the oral proceedings readily on the basis of the presence of an antinucleating agent.

5. *Inventive step*

- 5.1 The patent provides for the use of a single phase composition for the manufacture of a medicament for topical treatment of a human or animal body by forming a supersaturated drug composition *in situ* on

application of the composition to a water-wetted area of the body.

Document (1), relates to a pharmaceutical composition for topical application to the human and animal body comprising a first liquid phase containing a drug and a second liquid phase which form a supersaturated drug composition on admixture of the phases.

The Board agrees with the parties that document (1) represents the closest prior art.

- 5.2 Examples 1, 2 and 3 of this document describe gel systems comprising a first single phase composition containing a drug (gels B) and a second single phase composition (gels A) containing mainly water (97% or 98,5%). It is moreover clearly foreseen in document (1) that the second phase may be only water (page 3, lines 5 to 16).

These two single phase compositions are intended to be mixed together in order to generate a mixture supersaturated with the drug, ie the resulting single phase compositions of gels C.

According to the description (page 4, paragraphs 3 and 4), the compositions (ie the first and second phases such as the compositions A and B) may be packaged into a twin compartment pack and applied to the treatment area either simultaneously in order to create the supersaturated drug *in situ* or after previously mixing the two compositions, ie readily as a supersaturated drug system.

Having regard to the patent in suit (page 2, lines 46 to 48; page 2, lines 20 to 22), it was found advantageous to incorporate an antinucleating agent in the drug composition to preserve the stability of the supersaturated state. The drug containing composition is moreover applied directly to a water-wetted area of the body.

Accordingly, the problem to be solved as against document (1) can be seen as the provision of a drug composition having a preserved stability to be used in the manufacture of a medicament and of an alternative method of administration of the drug composition.

5.3 This problem is solved by the subject-matter of claim 1 and, in the light of working examples 1 and 2 and figure 1 of the patent in suit, the Board is satisfied that the problem has been plausibly solved.

5.4 Thus, the question to be answered is whether the proposed solution, ie the addition of an antinucleating agent to the prior art drug-containing compositions and the direct application of the prior art drug-containing compositions to previously water-wetted area of the body, was obvious to the skilled person in the light of the prior art.

As regards the first aspect, the Board notes that document (1) is silent about the addition of any antinucleating agent. In fact this document merely foresees the optional addition of a thickening and gelling agent (page 4, paragraph 2).

It is however a well-known phenomenon that, for thermodynamical reasons, a supersaturated solution tends to precipitate in order to revert to its saturated state as this latter is more stable.

Therefore, the Board is satisfied that the skilled person faced with the problem of preserving the stability of a supersaturated drug composition would always try to avoid such precipitation. The addition of a product precisely to inhibit crystal growth, ie an antinucleating agent, as a solution to this problem represents the obvious step to take.

Concerning the mode of administration of the single phase drug composition, ie by application to a water-wetted area of the body in order to form a supersaturated drug composition *in situ*, the Board notes that the teaching of document (1) (page 4, paragraph 3) implicitly encompasses three different ways of application to form a supersaturated drug composition *in situ*.

In fact, it recites that "the patient would **normally** apply the two phases simultaneously to the treatment area, and then mix the phases together *in situ* to create the supersaturated system". It therefore obviously also contemplates applying either the single phase containing mainly water first (such as A) and then the single phase containing the drug (such as B) or *vice versa*.

Moreover, as was acknowledged by the respondent during the oral proceedings, document (1) teaches that the phase without drug may be only water (page 3, lines 5

to 16).

Accordingly, in the absence of any evidence to the contrary the method of administration of the drug according to claim 1 of the set of claims filed during the oral proceedings represents an arbitrary choice among three possibilities already disclosed in the prior art.

5.5 The main arguments raised by the respondent were that the subject-matter of claim 1 filed during the oral proceedings was inventive over document (1) firstly because this document did not disclose a single phase drug composition which was intended to be applied to a water-wetted area of the body to form a supersaturated composition *in situ* and, secondly, because the recognition of the ability of a single phase drug composition according to the patent in suit to form a supersaturated composition *in situ* enables the use of a single compartment pack instead of the twin compartment pack of the prior art, which results in reduced packaging costs.

5.6 The Board cannot share the opinion of the respondent.

It is indeed true that document (1) does not recite *expressis verbis* that a single phase drug composition (such as B) should be applied a water-wetted area of the body to form a supersaturated composition *in situ*. However, this teaching follows implicitly from the disclosure on page 4, paragraph 3 as pointed out above (see paragraph 6 under point 5.4). Accordingly, the mode of administration of the drug according to the patent in suit is encompassed in the teaching of the

prior art document (1).

Moreover, as this mode of administration does not provide for any medical effect different from the mode of administration of document (1), as the respondent accepted during the oral proceedings, it just amounts to an arbitrary choice among a very limited number of alternatives.

It is furthermore pointed out that the subject-matter of claim 1 of the set of claims filed during the oral proceedings is a use claim ie a claim to an activity. Therefore the respondent's arguments (see under point 5.5) which apply to the improvement of the packaging (use of a single compartment pack), ie a physical entity, are not relevant for the subject-matter of claim 1 as drafted as this claim does not imply the use of any particular kind of pack.

The Board does nevertheless not share the respondent's point of view that an inventive step could be recognised on the basis of the use of a single compartment pack instead of the twin compartment pack of the prior art.

As a matter of fact, the Board is convinced that not only the skilled person, but also any patient using a prior art twin pack having the drug composition on one side and water on the other, would immediately realize that he could dispense with using water from the twin pack and instead use water from, for instance, a water tap.

The simplification of the prior art packaging when

water is used as the second phase therefore represents an obvious step that the skilled person could not miss.

As no further argument was put forward, the Board's conclusion in paragraph 4 of point 5.4 above is unaffected by the manner of administration.

In view of the foregoing the Board judges that the subject-matter of claim 1 of the set of claims filed during the oral proceedings does not involve an inventive step as required by Article 56 EPC.

Since claim 1 of the only set of claims under consideration is not allowable, there is no need for the Board to consider the remaining claims.

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. Dainese

P. Lançon