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**Datasheet for the decision
of 24 September 2015**

Case Number: T 0489/10 - 3.3.02

Application Number: 02804895.7

Publication Number: 1455854

IPC: A61L27/38, A61L27/24,
A61L27/60, A61F2/10, C12N5/06

Language of the proceedings: EN

Title of invention:
SKIN/HAIR EQUIVALENT WITH RECONSTRUCTED PAPILLAE

Patent Proprietor:
Henkel AG & Co. KGaA

Opponent:
The Procter & Gamble Company

Headword:
Skin-hair equivalent/HENKEL

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step of product-by-process - (no)

Decisions cited:

Catchword:



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Case Number: T 0489/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 24 September 2015

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
17 December 2009 concerning maintenance of the
European Patent No. 1455854 in amended form.**

Composition of the Board:

Chairman U. Oswald
Members: K. Giebeler
L. Bühler

Summary of Facts and Submissions

- I. European patent No. 1 455 854, based on European patent application No. 02804895.7, published as WO 03/051419 and entitled "Skin/hair equivalent with reconstructed papillae", was granted with 38 claims.
- II. Notice of opposition was filed against the granted patent. The opponent based its opposition on the grounds of lack of novelty and inventive step and exclusion from patentability (Article 100(a) EPC) and insufficiency of disclosure (Article 100(b) EPC); Article 100(c) EPC was also mentioned in the notice of opposition, but this ground was not substantiated.
- III. In its interlocutory decision, the opposition division held that the claims of auxiliary request 1a before it met the requirements of the EPC.

Claims 1 and 31 of said request read as follows:

"1. A process for the production of a skin/hair equivalent, more particularly a skin/hair model with reconstructed papillae (pseudopapillae; PP) in a reconstructed dermis (pseudodermis; PD), the process comprising the following steps:
(a) providing a reconstructed dermis (pseudodermis; PD) or a pseudodermis preparation;
(b) providing reconstructed papillae (pseudopapillae; PP) comprising cultivated dermal papilla cells (hair papilla cells), on a suitable carrier and/or in a suitable matrix, more particularly gel matrix, or providing corresponding precursors of such reconstructed papillae (pseudopapillae; PP) comprising cultivated dermal papilla cells, in a suitable matrix-forming, more particularly gel-forming, medium MFMpp

which is capable of forming a matrix, more particularly a gel matrix, *in situ*, more particularly in the reconstructed dermis (pseudodermis; PD);

(c) introducing or inserting the reconstructed papillae (PP) or their precursors provided in step (b) into the pseudodermis (PD) or the pseudodermis preparation provided in step (a);

(d) optionally applying a reconstructed epidermis (pseudoepidermis; PE) or a reconstructed periderm (pseudoperiderm; PI) to the pseudodermis (PD)."

"31. A hair/skin equivalent, more particularly a hair model with reconstructed papillae (PP) in a pseudodermis (PD), obtainable by the process claimed in claims 1 to 30."

- IV. The opponent (hereafter: appellant) lodged an appeal against the opposition division's decision.
- V. The patent proprietor (hereafter: respondent) did not respond to the appeal within the prescribed time limit.
- VI. On 20 January 2015, the board summoned the parties to oral proceedings.
- VII. The respondent filed submissions with letter of 18 May 2015, including new evidence and auxiliary requests 1 and 2.

Claim 1 of **auxiliary request 1** reads as follows:

"1. A process for the production of a skin/hair equivalent, more particularly a skin/hair model with reconstructed papillae (pseudopapillae; PP) in a reconstructed dermis (pseudodermis; PD), the process comprising the following steps:

- (a) providing a reconstructed dermis (pseudodermis; PD) or a pseudodermis preparation;
- (b) providing reconstructed papillae (pseudopapillae; PP) comprising cultivated dermal papilla cells (hair papilla cells), on a suitable carrier and/or in a suitable gel matrix, or providing corresponding precursors of such reconstructed papillae (pseudo-papillae; PP) comprising cultivated dermal papilla cells, in a suitable gel-forming medium MFMpp which is capable of forming a gel matrix *in situ* in the reconstructed dermis (pseudodermis; PD);
- (c) introducing or inserting the reconstructed papillae (PP) or their precursors provided in step (b) into the pseudodermis (PD) or the pseudodermis preparation provided in step (a);
- (d) optionally applying a reconstructed epidermis (pseudoepidermis; PE) or a reconstructed periderm (pseudoperiderm; PI) to the pseudodermis (PD)."

Claim 1 of **auxiliary request 2** reads as follows:

"1. A process for the production of a skin/hair equivalent, more particularly a skin/hair model with reconstructed papillae (pseudopapillae; PP) in a reconstructed dermis (pseudodermis; PD), the process comprising the following steps:

- (a) providing a reconstructed dermis (pseudodermis; PD) or a pseudodermis preparation;
- (b) providing reconstructed papillae (pseudopapillae; PP) comprising cultivated dermal papilla cells (hair papilla cells), on a suitable carrier and/or in a suitable gel matrix, or providing corresponding precursors of such reconstructed papillae (pseudo-papillae; PP) comprising cultivated dermal papilla cells, in a suitable gel-forming medium MFMpp which is

capable of forming a gel matrix *in situ* in the reconstructed dermis (pseudodermis; PD);
(c) introducing or inserting the reconstructed papillae (PP) or their precursors provided in step (b) into the pseudodermis (PD) or the pseudodermis preparation provided in step (a);
(d) applying a reconstructed epidermis (pseudoe-pidermis; PE) or a reconstructed periderm (pseudoperi-derm; PI) to the pseudodermis (PD)."

Claims 31 of auxiliary requests 1 and 2 have the same wording as claim 31 held allowable by the opposition division.

- VIII. The appellant replied to the respondent's submissions with letter of 20 August 2015.
- IX. Oral proceeding before the board were held on 24 September 2015.
- X. The following document is mentioned in this decision:
A: WO 00/29553.
- XI. The appellant's arguments, insofar as they are relevant for the present decision, can be summarised as follows:

The evidence and requests submitted by the respondent with letter of 18 May 2015 should not be admitted into the proceedings because there was no justification for not having filed them earlier, i.e. before the opposition division or at least within the time limit set by the board for responding to the grounds of appeal.

The claimed subject-matter lacked inventive step under Article 56 EPC over the closest prior art represented

by Example 12 of document A. The technical problem was merely the provision of an alternative product, since no improvement was achieved over the whole scope of the claims. The claimed solution was obvious from page 22, lines 11-15 of document A.

XII. The respondent's arguments, insofar as they are relevant for the present decision, can be summarised as follows:

The table submitted with letter of 18 May 2015 should be admitted into the proceedings because it merely showed that the claimed models expressed papillae-specific markers, and this had already been stated on page 13 of the respondent's reply of 10 November 2006 to the notice of opposition.

The appellant's argument, during the discussion of sufficiency of disclosure at the oral proceedings, that aggregates of dermal papilla cells comprised a matrix produced by the papilla cells themselves should not be admitted into the proceedings because it had been presented too late.

The claimed subject-matter involved an inventive step under Article 56 EPC over the closest prior art represented by Example 12 of document A. The technical problem to be solved was the provision of standardised, and thus improved, skin/hair equivalents, which were suitable for testing active substances and in which the essential cells of hair follicles were present in physiological form and showed the same interactions as *in vivo*. But even if the technical problem was merely the provision of alternative skin/hair equivalents, the skilled person would not have combined the teaching of Example 12 with that of page 22, lines 10-15 of

document A, because he/she knew that the aggregates of Example 12 were difficult to handle and too sensitive to be injected into a pseudodermis. Moreover, page 22, lines 10-15 concerned injecting cells into a cell-matrix with the aim that they formed specialised structures performing their specialised function after their injection, whereas in Example 12 the aggregates already had such specialised function. Furthermore, document A did not suggest that dermal papillae cells should be in a suitable matrix or matrix-forming medium when being introduced into the pseudodermis, as required by the process of claim 1.

Auxiliary requests 1 and 2 submitted with letter of 18 May 2015 should be admitted into the proceedings despite the fact that they had been filed late, because filing them five months before the oral proceedings had given the appellant enough time to consider them.

XIII. The final requests of the parties were:

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

The respondent requested that the appeal be dismissed and that the patent be maintained on the basis of the claims upheld by the opposition division (main request) or, alternatively, that the patent be maintained on the basis of the claims of either auxiliary request 1 or 2 filed with letter dated 18 May 2015.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of experimental evidence*

2.1 The respondent did not file any reply to the grounds of appeal within the time limit set by the board, nor did it request an extension of said time limit. About five months before the oral proceedings, the respondent filed observations containing new requests as well as experimental evidence, notably a table and a photograph, in support of its arguments concerning sufficiency of disclosure (Article 83 EPC). These observations, requests and evidence were filed more than four and a half years after expiry of the time limit to respond to the appeal, without any justification whatsoever as to why they had not been filed any earlier. Moreover, they were filed only after oral proceedings had been arranged.

2.2 As concerns the experimental evidence, the board cannot accept the respondent's argument that the submitted table merely showed what had already been asserted during the first instance proceedings, on page 13 of the response to the notice of opposition. This is because the marker proteins appearing in said table are not identical to those mentioned in the response to the notice of opposition.

2.3 In these circumstances, the board made use of its discretionary power under Article 13 RPBA and decided not to admit the late-filed experimental evidence into the proceedings.

3. *Admissibility of the appellant's argument*

3.1 During the discussion of sufficiency of disclosure (Article 83 EPC) at the oral proceedings, the appellant referred to document A and submitted that aggregates of

dermal papilla cells comprised a matrix produced by the papilla cells themselves.

- 3.2 The respondent submitted that this argument had not been raised before and objected to admitting it into the proceedings.
- 3.3 Document A was already cited in the appellant's notice of opposition against the novelty and inventive step of the subject-matter claimed, and was extensively discussed throughout the opposition and appeal proceedings. The appellant's argument based on this document can thus not be considered surprising. Therefore, the board decided to admit it into the proceedings (Article 13 RPBA).
4. In view of the following reasoning on the question of an inventive step (Article 56 EPC), the issues of sufficiency of disclosure (Article 83 EPC) and novelty (Article 54 EPC) can be left undecided in the present circumstances.
5. *Inventive step (Article 56 EPC) - Claim 31*
- 5.1 Claim 31 is directed to a hair/skin equivalent obtainable by the process claimed in claims 1 to 30, and is thus formulated as a "product-by-process" claim. According to the established case law of the boards of appeal, "product-by-process" claims have to be interpreted in an absolute sense, i.e. independently of the process; they have to be examined like any other product claim, namely as to whether or not the claimed product fulfills the requirements for patentability.

Process claim 1, to which claim 31 refers, specifies both mandatory and optional, non-limiting features.

Disregarding the optional features, claim 1 is directed to a process for the production of a skin/hair equivalent comprising the following steps:

(a) providing a reconstructed dermis (pseudodermis; PD) or a pseudodermis preparation;

(b) providing reconstructed papillae (pseudopapillae; PP) comprising cultivated papilla cells on a suitable carrier and/or in a suitable matrix, or providing corresponding precursors of such reconstructed papillae (pseudopapillae; PP) comprising cultivated papilla cells, in a suitable matrix-forming medium MFMpp which is capable of forming a matrix *in situ*;

(c) introducing or inserting the reconstructed papillae (PP) or their precursors provided in step (b) into the pseudodermis (PD) or the pseudodermis preparation provided in step (a).

The board considers that the terms "skin/hair equivalent" used in claim 1 and "hair/skin equivalent" used in claim 31 are synonymous in the context of the patent in suit.

- 5.2 Due to the different alternatives in claim 1, claim 31 encompasses various kinds of products. One kind of product encompassed by claim 31 results from introducing or inserting precursors of reconstructed papillae, comprising cultivated dermal papilla cells in a suitable matrix-forming medium which is capable of forming a matrix *in situ*, into a pseudodermis or a pseudodermis preparation. Claim 1 does not require that, in the claimed process, reconstructed papillae are actually formed from said precursors; this is merely an optional feature (see also dependent claims 18 and 19). The presence of reconstructed papillae is also not implied by the mere reference to the expression "skin/hair equivalent", particularly since

both in claim 1 and paragraph [0001] of the patent in suit their presence is merely an optional feature ("more particularly a skin/hair model with reconstructed papillae (pseudopapillae; PP) in a reconstructed dermis (pseudodermis; PD)"). Claim 31 thus encompasses products which do not comprise reconstructed papillae. The following discussion of inventive step (Article 56 EPC) deals only with such products.

- 5.3 The closest prior art is represented by Example 12 of document A. Document A relates to bioengineered tissue constructs of cultured cells and endogenously produced extracellular matrix components (page 1, lines 20-21). Example 12 (pages 40-42) describes the *in vitro* formation of a bilayer skin construct containing dermal papilla cells. First, a cell matrix (i.e. a pseudo-dermis) was made using fibroblasts producing a matrix. It is stated that dermal papilla cells were cultured and re-formed dermal papilla-like structures or aggregates, each having a diameter of between approximately 90 and 210 microns; the aggregates were then removed from the culture plate by vigorous pipetting of medium against them, and then seeded onto the collagenous matrix at a density of 200 aggregates per cm². It is further described that the cell-matrix cultures containing dermal papilla cells thereon were seeded with keratinocytes and cultured to form a continuous epidermal layer over the cell-matrix and the dermal papillae; the dermal papilla maintained a packed structure that induced small undulations of the overlaid epithelium. The tissue construct resulting from the process of Example 12 thus has cultivated dermal papillae cells located **on** the pseudodermis.

- 5.4 In view of this closest prior art, the technical problem to be solved is seen as the provision of an alternative skin/hair equivalent.
- 5.5 The solution to the problem posed, as proposed by claim 31, is a skin/hair equivalent obtainable by introducing or inserting cultivated dermal papilla cells in a suitable matrix-forming medium which is capable of forming a matrix *in situ*, **into** a pseudodermis or a pseudodermis preparation; this implies that the product has dermal papilla cells **within** the pseudodermis or pseudodermis preparation.
- 5.6 Having regard to the description and the examples of the patent in suit, the board is satisfied that the problem has indeed been solved.
- 5.7 It has to be decided whether or not the skin/hair equivalent according to claim 31 is obvious from the cited prior art.
- 5.8 Document A states on page 22, lines 10-15, that for delivery of a second cell type to the cell-matrix construct, "the cells may locally seeded as a spot or as an arrangement of any number of spots of cells **on or within** a forming or completely formed cell-tissue matrix for localized development of these structures. To seed the cells **within** the cell-matrix construct, the cells may be injected between the top and bottom surfaces, **within** the cell-matrix, for the cells to grow, form specialized structures and perform their specialized function" (emphasis added by the board).

In view of this disclosure, the board is convinced that, in the context of the cell constructs of document A, the skilled person would have considered

injecting cells **into** a pseudodermis as an alternative to seeding the cells **onto** a pseudodermis as described in Example 12 of the same document. Therefore, the board considers that a skilled person faced with the problem posed would have applied the teaching of page 22, lines 10-15 of document A to dermal papilla cells and would thus have injected these cells into the pseudodermis. Consequently, the skilled person would have arrived in an obvious manner at subject-matter falling under claim 31.

5.9 As regards the respondent's arguments, the following has to be noted:

5.9.1 The respondent's definition of the technical problem as being the provision of a standardised, improved product cannot be accepted, because the process of claim 1 does not require any standardisation step to be performed, for example by using defined concentrations of dermal papilla cells. Consequently, the product of claim 31 does not have to be standardised in any way or contain a defined number of papilla cells. It follows that the technical problem has to be formulated in a less ambitious way, i.e. as the mere provision of an alternative product.

5.9.2 The respondent submitted that in contrast to claim 1, document A did not suggest providing the cultivated dermal papilla cells in a suitable matrix-forming medium before introducing or inserting them into the pseudodermis.

However, with respect to the products according to claim 31, the board is not convinced that providing the dermal papilla cells in a matrix-forming medium as defined in claim 1 before introducing/inserting them

into the pseudodermis would necessarily result in a different product when compared to introducing/ inserting the dermal papilla cells into a pseudodermis without such matrix-forming medium. This is because the components which form the extracellular matrix of the pseudodermis in document A, e.g. collagen, may also be used in the matrix-forming medium of the process of claim 1. Consequently, the resulting products will inevitably comprise the dermal papilla cells embedded in the matrix, regardless of whether or not the dermal papilla cells are provided in a matrix-forming medium before being introduced or inserted into the pseudodermis.

- 5.9.3 The respondent further submitted that the skilled person would have been aware that the aggregates described in Example 12 of document A were very sensitive, and he/she would therefore have avoided injecting them into the pseudodermis.

The board cannot follow this line of argument, because nothing in document A or any other cited document suggests that the aggregates in question would be unsuitable for being injected into a pseudodermis. Moreover, Example 12 of document A teaches that "when a culture of dermal papilla cells reach confluence they form aggregates" (see page 41, line 9), and a skilled person wishing to avoid the use of aggregates thus knew that dermal papilla cells which had not reached confluence could be used instead.

- 5.9.4 The respondent further submitted that the passage on page 22, lines 10-15 of document A described that injecting cells within the cell-matrix had the purpose that the cells formed specialised structures performing their specialised function after injection, whereas

Example 12 concerned aggregates which were already specialised structures with a specialised function; therefore, the skilled person would not have combined these teachings.

The board cannot agree and takes the position that the skilled person faced with the problem posed would have understood from the disclosure on page 22, lines 10-15 of document A that placing cells such as dermal papilla cells within a cell-tissue matrix represented an alternative to placing them onto the cell-tissue matrix, regardless of whether or not the cells were to be considered as specialised structures.

5.10 In view of the above, the board comes to the conclusion that the subject-matter of claim 31 does not involve an inventive step and that the main request is not allowable under Article 56 EPC.

6. *Admissibility of auxiliary requests 1 and 2*

6.1 Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that in step (b) the matrix is defined as a gel matrix and the matrix-forming medium is defined as a gel-forming medium which is capable of forming a gel matrix *in situ* in the reconstructed dermis (pseudodermis). Claim 1 of auxiliary request 2 contains the same amendments, but additionally has step (d), applying a pseudoepidermis or a pseudo-periderm to the pseudodermis, as a mandatory step.

6.2 As already mentioned in point 2.1 above in the context of late-filed evidence, the respondent did not file any reply to the grounds of appeal within the set time limit, or request an extension of the time limit.

The auxiliary requests were filed only after oral proceedings had been arranged and cannot be seen as a reaction to unforeseeable developments. Moreover, the respondent did not present any justification whatsoever as to why the auxiliary requests had not been filed any earlier.

6.3 Additionally, the board observes that in the cell constructs of Example 12 of document A the endogenously formed collagenous matrix represents a gel matrix, and the continuous epidermal layer formed over the cell matrix and the dermal papillae (see page 41, lines 19-21) represents a pseudoepidermis. The presence of a gel matrix and of a pseudoepidermis in the skin/hair equivalent, as referred to in claims 1 of auxiliary requests 1 and/or 2, is thus also disclosed in Example 12 of document A. The subject-matter of claims 31 of auxiliary requests 1 and 2 would therefore lack inventive step under Article 56 EPC for the same reasons as those given in points 5.1 to 5.8 above for claim 31 of the main request.

6.4 In these circumstances, the board decided to make use of its discretionary power not to admit auxiliary requests 1 and 2 into the proceedings (Article 13 RPBA).

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:



N. Maslin

U. Oswald

Decision electronically authenticated